

TECHNICAL REPORT

Terminology and labeling of cellular products: 1. Standards

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International Cellular Therapy Coding and Labelling Advisory Group

The International Cellular Therapy Coding and Labeling Advisory Group was established to address the growing need for standardization of terminology and labeling for cellular therapy products as a result of increasing international transfer of these products. This paper presents new standards for terminology and labeling. These standards have been developed through a consultative process and are supported by key professional and accreditation bodies. By using these standards, together with the unique donation identification numbers and international product reference tables provided by the International Society of Blood Transfusion (ISBT) 128 Standard, consistency and traceability can be assured at the global level. A companion paper provides guidance on the implementation of the ISBT 128 system.

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These standards have been developed through the cooperative endeavor of the following organizations: AABB, 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), ISCT Europe, Joint Accreditation Committee of ISCT and EBMT (JACIE), National Marrow Donor Program (NMDP) and the World Marrow Donor Association (WMDA).

The use of standard terminology will help to ensure a common understanding of product definitions. The labeling standard, supported by the *ISBT 128* information system, will ensure unique global identification of cellular therapy products, an international reference table for product descriptions, and label design that is consistent worldwide. The organizations supporting these standards believe that

their adoption will significantly improve the quality, safety and traceability of cellular therapy products.

In developing the terminology standard the Advisory Group recognized that the frequent movement of cellular therapy products between countries (and continents) required a consistent use of terminology between *ISBT 128* and published standards (for example, Circular of Information, AABB, FACT, JACIE, Netcord).^{1–5} The Advisory Group has attempted to achieve these aims by removing complexity and redundancy from the coding system wherever possible, and, by wide consultation, agreeing to terminology acceptable to all for inclusion in future publication of their standards and guidance.

Terminology standard

The terminology standard provides a dictionary of terms with associated definitions, which has been constructed by international consensus to ensure global consistency in use and understanding. This provides the basis for assigning product descriptions within the *ISBT 128* product database, thus providing a comprehensive and highly flexible system for describing products and assigning product codes. New products are defined by combining pieces of information from the dictionary in a way that unambiguously describes the product.

The tables presented in this standard can be extended as new products become developed. Proposed additions will be reviewed by the Advisory Group to ensure an appropriate level of definition and coding detail is maintained.

This standard replaces some of the previously defined terminology used within *ISBT 128*⁶ and a summary of these changes, together with the rationale behind them, is described in the consultation documentation.

Structure of the terminology

The *ISBT 128* product description database uses the concepts of ‘Class’, ‘Modifier’ and ‘Attribute’ to describe products.

Classes are broad descriptions of products. Examples are HPC, Cord Blood; HPC, Marrow and HPC, Apheresis.

Modifiers are applied to Classes in order to provide the next step in the categorization of the product. Examples are Cryopreserved, Thawed Washed and Mobilized.

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Attributes provide the means to uniquely define the product. There is a mandatory attribute group called Core Conditions, which must be explicitly selected.

Core Conditions convey three types of information:

- anticoagulant and/or additive
- nominal collection volume and
- storage temperature.

There are also a range of optional attribute groups that have a default value if not explicitly assigned. These remaining attribute groups are the general categories used to describe detailed characteristics of products. Within each attribute group, there are a number of possible values, referred to as variables, of which only one can be selected. For example, 'intended use' is a group; 'for transfusion' is a variable within that group. Where a product does not have a variable assigned for a particular group, the default variable for that group will apply.

The terminology standard is designed to allow distinction between products where it is required on safety or inventory management grounds. In some cases, there will be additional information, which may be of value to the administering clinician, but it does not need to be encoded. Such information can be included in eye-readable text on the label and/or in the accompanying documentation.

The full data structure for the product code is eight characters long, with the first five characters describing the product as discussed above. The type of donation or collection/intended use is specified in the sixth data character of the product code data structure. Data characters seven and eight are reserved for encoding information about divisions of products. Up to 26 divisions can be encoded with each of these characters. Further details are available in the *ISBT 128 Standard Technical Specification*.¹

Terminology tables

Class table

HPC, apheresis	Peripheral blood collected by apheresis as a source of hematopoietic progenitor cells. Mobilized unless otherwise stated in modifier
HPC, cord blood	Umbilical cord blood and/or placental blood collected as a source of hematopoietic progenitor cells
HPC, marrow	Bone marrow collected as a source of hematopoietic progenitor cells
HPC, whole blood	Whole blood collected as a source of hematopoietic progenitor cells. Mobilized unless otherwise stated in modifier
Concurrent plasma, apheresis	Plasma collected from the donor as part of an apheresis cell collection procedure for use by the laboratory in further processing of that donor's product
TC, apheresis	Source of nucleated cells obtained by an apheresis procedure intended for

Continued

Class table

	therapeutic use other than HPCs. Non-mobilized unless otherwise stated in the modifier
TC, marrow	Bone marrow collected as a source of nucleated cells intended for therapeutic use other than HPCs
TC, whole blood	Whole blood collected as a source of nucleated cells intended for therapeutic use other than HPCs
TC, cord blood	Umbilical cord blood and/or placental blood collected as a source of nucleated cells intended for therapeutic use other than HPCs
TC-T cells	A therapeutic cell product from any source containing a quantified T-cell population
TC-CTL	A therapeutic cell product containing cytotoxic lymphocytes for therapeutic use
TC-T Reg cells	A therapeutic cell product containing T regulatory lymphocytes for therapeutic use
TC-DC	A therapeutic cell product containing dendritic cells for therapeutic use
TC-NK cells	A therapeutic cell product containing natural killer cells for therapeutic use
TC-tumor derived	A product containing malignant cells or elements derived from them
TC-MSC	A therapeutic cell product containing mesenchymal stromal cells for therapeutic use
TC-APC	A therapeutic cell product containing antigen presenting cells other than dendritic cells for therapeutic use
TC-INV	This class is reserved for use only in blinded studies of therapeutic cells accompanied by appropriate identifying study information

Modifier table

Mobilized	Applies to cells that have been obtained from a donor treated with an agent to increase the concentration of the target cell population(s) (to be used only for TC, apheresis or bone marrow)
Non-mobilized	Applies to cells that have been obtained from a donor not treated with an agent to increase the concentration of the target cell population(s) (to be used only for HPC, apheresis or HPC, whole blood)
Cryopreserved	Applies to cells in the frozen state after the addition of cryoprotectant(s)
Pooled, single donor	Applies to the combination of multiple collections of the same product type from the same donor
Thawed washed	Applies to cryopreserved cells that have been thawed and subsequently washed to remove cryoprotectant or other solution(s).

Modifier table

Washed	Applies to cells from a non-cryopreserved product that have been washed to reduce the amount of plasma, anticoagulant and/or other solution(s)
Thawed	Applies to cryopreserved cells that have been thawed without washing prior to final issue for administration

Attribute-core conditions tables

Anticoagulant type Anticoagulant description

Citrate	Any anticoagulant containing citrate used as the sole method of anticoagulation
Heparin	Heparin used at any concentration as the sole method of anticoagulation
Citrate and heparin	Combined use of citrate and heparin at any concentration in the anticoagulant medium
NS	Anticoagulant not specified in coding
None	No anticoagulant

Volume

XX	Volume not specified in coding
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Storage temperature Definition

Refrg	Refrigerated (between 1 and 10° C; narrower range may be nationally specified)
RT	Ambient room temperature (range may be nationally specified)
≤ -18° C	Less than or equal to -18° C
≤ -80° C	Less than or equal to -80° C
≤ -120° C	Less than or equal to -120° C
≤ -150° C	Less than or equal to -150° C
N ₂ liquid	Completely immersed in the liquid phase of nitrogen

Attribute groups table

Group name	Description
Intended use	Describes the expected use of the product
Preparation—cryoprotectant	Active cryoprotectant in the product
Manipulation	Describes processing applied to the collection
Preparation—blood component from third party donor	Describes blood products from other donors used during processing, such as albumin, fresh frozen plasma, AB serum, red blood cells
Preparation—other additives	Describes additives introduced other than as part of the

Attribute groups table

Group name	Description
	anticoagulant solution at the time of collection
Genetically modified	Cells that have been modified by the insertion of exogenous genetic material

Attribute variable tables

Intended use group

Default: for administration	For patient use: the product is intended for administration to patients
Not for administration	Not for patient use; a product that is not intended for use in patient treatment or further processing
For further processing	Not intended for direct administration

Preparation: cryoprotectant group

Default: no cryoprotectant	No cryoprotectant has been added
6% HES + 5% DMSO	The cells were frozen using 6% HES and 5% DMSO by volume as cryoprotective agents
10% DMSO	The cells were frozen using 10% DMSO by volume as a cryoprotective agent
5% DMSO	The cells were frozen using 5% DMSO by volume as the cryoprotective agent
DMSO reduced	The cells were frozen using DMSO as a cryoprotective agent that has subsequently been partially removed using a wash procedure after thawing

Manipulation group

Default: no manipulation	No further processing has occurred following collection
Diluted	A product to which an additional diluent (e.g. Concurrent Plasma) has been added after collection to reduce cell concentration for transit, storage, processing or cryopreservation
Plasma reduced	Cells remaining after a portion of the plasma has been depleted by sedimentation or centrifugation
RBC reduced	Cells remaining after reduction of mature erythrocytes
Buffy coat enriched	Cells remaining after reduction of mature erythrocytes and plasma
Mononuclear cells enriched	Cells remaining after reduction or depletion of mature erythrocytes, granulocytes and plasma

Manipulation group

<i>Default: no manipulation</i>	<i>No further processing has occurred following collection</i>
T-cell reduced	Cells remaining after T cells have been reduced
B-cell reduced	Cells remaining after B cells have been reduced
T/B-cell reduced	Cells remaining after T and B cells have been reduced
CD8 reduced	Cells remaining after the CD8 cell population has been reduced
CD34 enriched	Product in which the CD34 cell population has been enriched
CD133 enriched	A product in which the CD133 cell population has been enriched
Tumor cells reduced	An identified tumor cell population has been reduced
PUV treated	Cells treated with psoralen/ultraviolet light
Cultured	Cells that have been maintained <i>ex vivo</i> to activate, expand or promote development of a specified cell population in the presence of specified additive(s)

Preparation: blood component from third party donor group

<i>N/S</i>	<i>Default. not specified</i>
Third party component: no	No third party blood component added
Third party component: yes	Third party blood component added. See accompanying paperwork

Preparation: other additives group

<i>N/S</i>	<i>Default. not specified</i>
Other additives: no	No additives other than as part of the anticoagulant solution at the time of collection
Other additives: yes	Other additives. See accompanying paperwork

Genetically modified group

<i>N/S</i>	<i>Default. not specified</i>
Genetically modified: no	Not genetically modified
Genetically modified: yes	Genetically modified by the insertion of exogenous genetic material. See accompanying paperwork

Labeling standard

This standard provides information on the design of labels for use on cellular therapy products. The *ISBT 128*

data structures referred to in this document are fully described in the *ISBT 128 Standard Technical Specification*¹ together with other essential information on the *ISBT 128* standard.

The proper names for cellular therapy products are identified above and in the *ISBT 128 Standard Product Coding: Bounded Lists and Definitions*.⁶

The labeling guidance provided satisfies the labeling requirements of AABB, FACT and JACIE accreditation bodies.

Electronic delivery mechanisms

The *ISBT 128* standard defines data structures for the structured delivery of electronic information. In order to transfer this information on a label, a 'delivery mechanism' is required. The most common such mechanism is the linear barcode. There are many types of linear barcodes, each using a discreet symbology. Where *ISBT 128* information is being encoded into a linear barcode, Code 128 symbology must be used.

One of the limitations of linear barcodes is that they require a relatively large amount of label space to encode even a small amount of information. This is acceptable in situations where there is adequate label space but this is not true for some very small containers used in cellular therapy.

To address this problem, two-dimensional (2D) barcodes can be used. These allow a far greater amount of information to be stored in a small space. Once again, there are many types of 2D codes each using a different symbology. Where *ISBT 128* information is being encoded into a 2D barcode, Data Matrix symbology is recommended.⁷ Several pieces of *ISBT 128* information can be combined into one 2D code using the compound message structure within *ISBT 128*.

When selecting printers and barcode scanners for use with cellular therapy products, care should be taken to choose those that can support both of these symbologies.

In this document, examples of both linear (Code 128) and 2D (Data Matrix) codes are used.

This standard recognizes that at a national level some agencies may have further labeling requirements. It is recommended that national bodies should publish guidelines for cellular therapy product labeling in their own country, which adhere to the *ISBT 128 Standard Technical Specification*, the *ISBT 128 Standard Product Coding: Bounded Lists and Definitions*, and this labeling document. These national guidelines should identify any additional labeling, or restrictions on labeling, required by local regulations.

Label design—general principles

Two label types are specified in *ISBT 128*: the label applied by the manufacturer of the container, referred to as the base label, and the label placed on a product container by the collection or processing facility, referred to as the final label.

Because of the large variety of containers used in the preparation and storage of cellular therapy products,

a number of designs are presented for the final label layout.

The following general principles apply to label design:

Primary considerations in label design will include improving the *safety* of the product and the *efficiency* of processing/administering. When these two conflict, safety must take precedence over efficiency.

Critical information on the container must dominate the label via position and prominence and must take precedence over information that is of little importance to the end-user (clinician, nurse, laboratory staff and other hospital personnel).

Printing text

There are three types of text used in *ISBT 128* labeling:

- Eye-readable text* The eye-readable representation of the data characters in a bar code (usually printed left justified immediately below the bar code, unless otherwise specified)
- Bar code text* The interpretation of the eye-readable text (the data content of the bar code)
- Additional label text* All other information on the label that is not associated with a bar code

Particular font sizes and types are not specified but designers must ensure clarity of all text and use larger fonts to emphasize critical information. For Latin alphabets, it is recommended that proportionally spaced sans serif fonts be used.

Dates shall be printed in the order day, month and year. The day shall be numerical and the month alphabetical, using a standard three-letter abbreviation (JAN, FEB, MAR, APR, MAY, JUN, JUL, AUG, SEP, OCT, NOV and DEC). The year shall be a four-digit numerical representation (for example 14 MAR 2006).

Times shall be printed based on a 24-h clock, with a colon placed between the hours and minutes. The date and time shall be based on the local time zone at the place of labeling. For example: 14 MAR 2006 14:00.

Where product is to be shipped across time zones, it is recommended that the expiry date and time also be shown in GMT (Greenwich Mean Time) as the international reference time. This date and time should be bracketed, be printed in italics beneath the local date and time, and should have the suffix GMT. For example 14 MAR 2006 14:00 (14 MAR 2006 19:00 GMT).

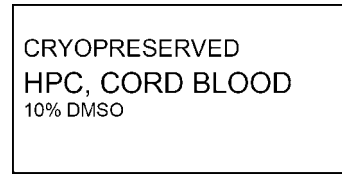
It should be noted that there may be occasions where both date and time are different in GMT. For example 14 MAR 2006 23:00 (15 MAR 2006 04:00 GMT).

Product description bar code text will be left justified. Other bar code text may be centered or left justified.

The product proper name (Class) may be printed as large as space allows.

It is recommended that product description bar code text should be printed with the Modifier(s) and Attribute(s) proportionally smaller than the Class proper name (the

example uses bar code text that might appear on a cellular therapy product):



RhD status for the blood groups (ABO and RhD) bar code text may be printed black on white if RhD positive and white on black if RhD negative, but this is not required.

ABO status may be printed black on white if RhD positive, outline black on white if RhD negative, but this is not required.

For Special Testing bar code text, see the Examples of Use in the *ISBT 128 Standard Technical Specification*.

The base label

Where the container is of sufficient size, it shall carry a 100 mm ± 2 mm by 106 mm ± 2 mm (4" × 4.25") base label.

The base label should carry the two manufacturer's information bar codes: the Manufacturer's Identity and Catalog Number (017) bar code in the lower left quadrant and the Manufacturer's Lot Number (018) bar code in the lower right quadrant. The recommended position for these bar codes on 100 mm ± 2 mm by 106 mm ± 2 mm (4" × 4.25") label should allow for a concatenated read of the two bar codes. The positioning is indicated in Table 1 and is illustrated in Figure 1.

Eye-readable text for these two bar codes shall be printed in the 6 mm (0.25") segment of the base label that will remain visible after the application of the final label. Type height of this text shall not be greater than 3.0 mm (0.10"); it shall be printed left justified immediately below the bar code and be centered vertically within the segment.

Some containers may require a smaller base label. In designing such labels, the principles outlined in this section should be applied to the extent possible. They should carry as a minimum the manufacturer's identity, catalog number and lot number in eye-readable and electronically readable

Table 1 Positioning linear bar codes on a 100 mm by 106 mm (4" × 4.25") base label

<i>Bar code</i>	<i>Vertical alignment</i>	<i>Horizontal alignment</i>
Container manufacturer and catalog number (017)	3 mm (0.10") from the bottom of the left quadrant (or 9 mm (0.35") from the bottom of the label)	Bar code right edge should be at 4 mm (0.15") from the right Edge of the left quadrant
Container lot number (018)	3 mm (0.10") from the bottom of the right quadrant (or 9 mm (0.35") from the bottom of the label)	Bar code left edge should be at 4 mm (0.15") from the left edge of the right quadrant



Figure 1 Placement of bar codes on a 100 mm by 106 mm (4'' × 4.25'') base label.

formats. This information may be encoded in a 2D barcode using the appropriate *ISBT 128* Compound Message.⁸

For practical purposes, some cryopreservation bags and other types of containers do not use base labels.

The final label

Final label layout will depend upon the container size and amount of available label space. The default layout is based upon a 100 (±2) mm by 100 (±2) mm (4'' × 4'') label dimension. Smaller (partial) labels have correspondingly less information displayed. Additional necessary information not shown on the label should be included in the accompanying labeling and documentation.

On all labels, the essential minimum requirements of unique donation identification number, product description and, where appropriate, recipient identifier must be present in text. The donation identification number must also be in electronically readable format(s).

This standard supports the use of eye-readable expiry dates. This information is optional within the *ISBT 128* standard but may be required by national authorities.

The standard also supports the use of collection date and time, and if required this may be bar coded using the Collection Date and Time data structure. Where there is a prolonged collection process, this time should be the time that the procedure ended. If necessary, the procedure start time may be included in text only on the label.

The final label may be applied as a single label or may be built up with smaller labels applied at different stages during the process.

All labels are shown using Code 128 linear bar codes to encode the most critical information. As an alternative, 2D bar codes can be used, and are also illustrated. These allow

Table 2 Final label quadrants and bar codes

Quadrant	Data structure (reference number)
Upper left	Donation identification number (required) (001)
Lower left	Product code (required) (003)
Upper right	ABO/RhD blood group (required) (002)

Table 3 Required positioning bar codes on a 100 mm by 100 mm (4'' by 4'') final label

Bar code	Vertical alignment	Horizontal alignment
Donation identification number (001)	3 mm (0.10'') from the top of the upper left quadrant	Bar code right edge should be at 4 mm (0.15'') from the right edge of the upper left quadrant
Product code (003)	3 mm (0.10'') from the top of the lower left quadrant	Bar code right edge should be at 4 mm (0.15'') from the right edge of the lower Left quadrant
ABO/RhD blood groups (002)	3 mm (0.10'') from the top of the upper right quadrant	Bar code left edge should be at 4 mm (0.15'') from the left edge of the upper right quadrant
Expiration date (and time) (005)	3 mm (0.10'') from the top of the lower right quadrant	Bar code left edge should be at 4 mm (0.15'') from the left edge of the lower right quadrant

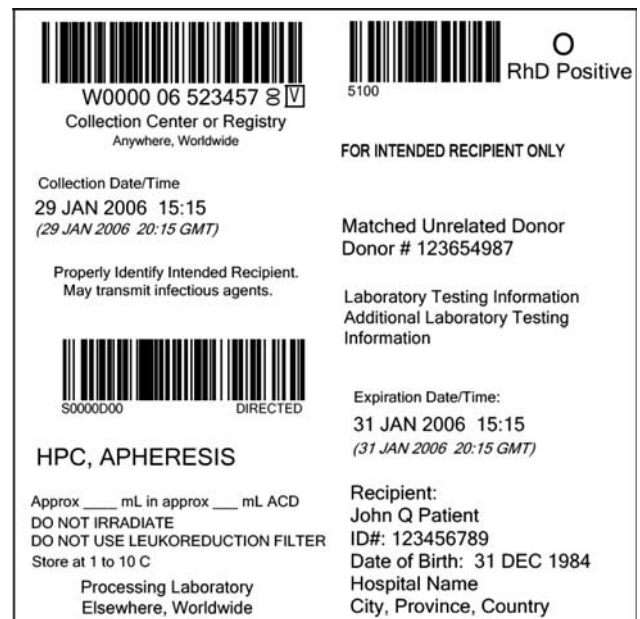


Figure 2 Final label (directed).

much more information to be encoded in a smaller area and hence free up space for additional text. Where 2D bar codes are used, they must hold information in *ISBT 128* data structures in a compound message format and care should be taken to ensure that compatible reading systems are available.



Figure 3 Final label (autologous, biohazardous).

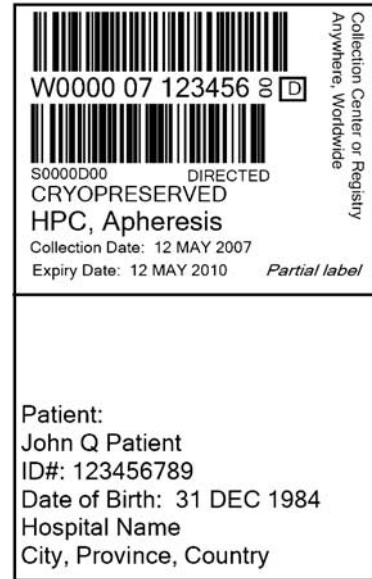


Figure 5 48 mm x 76 mm (2" x 3") Final label (directed).



Figure 4 Final label (autologous, not biohazardous).

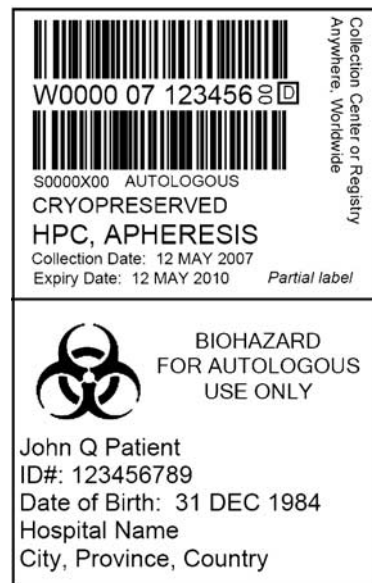


Figure 6 48 mm x 76 mm (2" x 3") Final label (autologous).

The 100 (± 2) mm by 100 (± 2) mm (4" x 4") final label design is based upon the concept of four equal 50 (± 1) mm by 50 (± 1) mm (2" x 2") quadrants. The bar codes are to be placed in these quadrants as shown in Table 2.

Bar codes for Data Structures 001, 002 and 003 must be positioned as described in Table 3. These recommendations place the bar codes in an ideal position for concatenation. Bar coding of the expiry date/time (data structure 005) is not essential, but may be included and positioned as described in Table 3. Similarly, bar coding of the collection

date/time (data structure 007) is not essential but may be included and should appear in the upper left quadrant.

An eye-readable representation of the data characters in the bar code must appear beneath each linear bar code symbol on the container.

Figures 2–4 show final labels printed according to Tables 2 and 3.

Label design for partial labels

The size of partial labels will depend upon the container dimensions. Four examples are given. The examples assume that the label may be folded over the bag providing label space on both sides of the container (Figures 5–8).

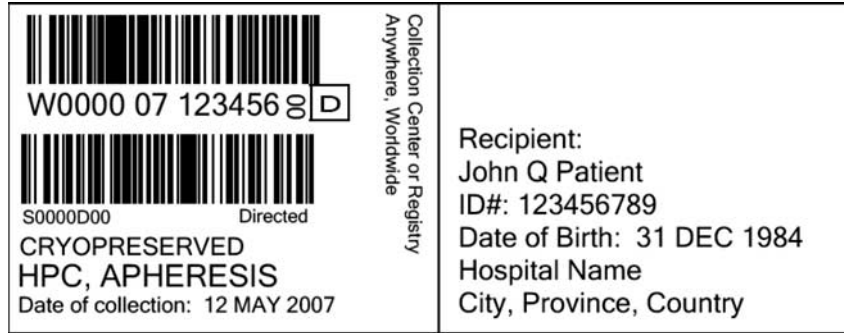


Figure 7 96 mm × 38 mm (3.8" × 1.5") Final label (directed).

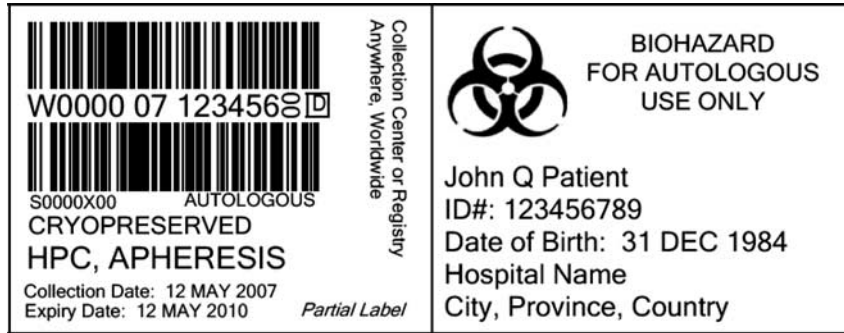


Figure 8 96 mm × 38 mm (3.8" × 1.5") Final label (autologous, biohazardous).



Figure 9 Cryopreservation label.

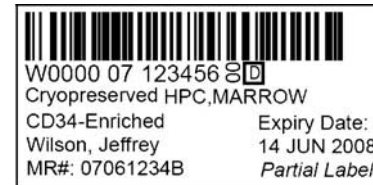


Figure 11 Vial label using Code 128.

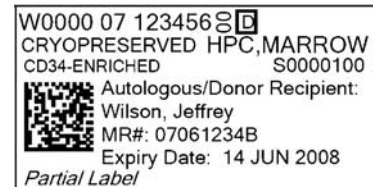


Figure 12 Vial label using data matrix.

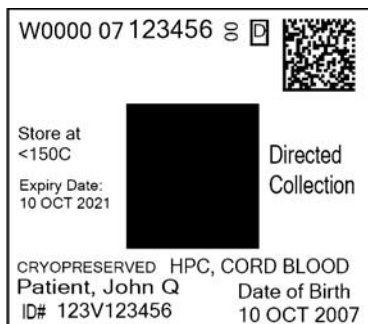


Figure 10 Proposed layout for cryopreservation label using data matrix.

The design presented is based upon typical space availability and may need some modification for specific storage systems. Label dimensions are for guidance only, as these will depend on the container design.

Label design for cryopreservation labels

Using linear bar coding, only the unique donation identification number can be printed in both electronically and human-readable formats. The product description and patient identifier appear in human-readable text format only (Figure 9).

If the design includes use of linear bar codes with an X dimension of <0.25 mm ($0.01''$), care should be taken to ensure that all scanners that will be used to read the label are able to do so.

An alternative approach would be to use a 2D barcode, in which case all three essential pieces of information could be encoded. Although not currently implemented, the diagram shows the possible layout of such a label (Figure 10).

Label design for vials

Vials of typically 1.5 or 2 ml capacity should be labeled in a manner that allows both human and machine reading as shown. Use of 2D barcodes again increases the amount of information that can be encoded and may allow additional space for human-readable information (Figures 11 and 12).

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