From the EU Legislation to the Application of the Single European Code: Support to the Implementation

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Summary

The Italian National Transplant Centre (CNT) is coordinating with the Italian National Blood Centre (CNS) the Joint Action 'VISTART' (EU Grant Agreement n. 676969), which has received funding from the European Union's Health Programme (2014–2020). CNT is also the leader of the Joint Action's Work Package 10 aimed at providing technical support and guidance to European tissue- and cell-competent authorities and to tissue establishments across the European Union in the implementation of the Single European Code (SEC). A consortium of three organizations, built by CNT, the International Council for Commonality in Blood Banking Automation (ICCBBA) and Artman Technologies under the European Commission funded service contract 'Eurocet128' (www.eurocet128.eu), already built the European Tissue Establishment and Tissue and Cell Product Compendia between 2011 and 2014 in order to provide European Member States with a tool which would grant traceability of tissues and cells at human transplant purpose across the European Union. The two compendia are available on an online platform hosted and managed by the European Commission.

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Introduction

The structure of the Single European Code (SEC) and the obligations of Member States' Competent Authorities (MS CAs) have been first set out by the EU Directive 2004/23 which was later expanded through EU Directives 2006/17 and 2006/86 and finally developed into EU Directive 2015/565 which was amended as regards certain technical requirements for the coding of human tissues and cells (T&C). According to EU Directive 2015/565, MS were required to transpose their provisions into their national legislation, by October 29, 2016 and to apply the requirements on the SEC starting from April 29, 2017.

According to the EU Directives which regulate the European coding system, a SEC shall be applied to all T&C distributed for human application. As far as other situations where T&C are released for circulation are concerned, the donation identification sequence shall be applied at least in the accompanying documentation. From this rule, the following cases are excluded: reproductive cells from partner donation; T&C distributed directly for immediate transplantation to the recipient; T&C imported into the European Union in case of emergency authorized directly by the CA/CAs. Also, there might be cases in which a MS exempts from the application of the SEC, such as the following ones: other T&C when T&C remain within the same centre and T&C that are imported into the European Union, when these T&C remain within the same centre from importation to application, provided that the centre comprises a tissue establishment (TE) authorised, designated, accredited or licensed to carry out importing activities [1].

Methods and Means

The SEC consists of a donation identification sequence and a product identification sequence, for a total of 40 alphanumeric

DONATION IDENTIFICATION SEQUENCE		
EU TISSUE ESTABLISHMENT CODE		UNIQUE DONATION NUMBER
ISO country code	Tissue establishment number	
2 alphabetic characters	6 alpha-numeric characters	13 alpha-numeric characters

Fig. 1. Donation identification sequence.

PRODUCT IDENTIFICATION SEQUENCE			
PRODUCT CODE		SPLIT NUMBER	EXPIRY DATE (YYYYMMDD)
Product Coding System identifier	Product number		
1 alphabetic character	7 alpha-numeric characters	3 alpha-numeric characters	8 numeric characters

Fig. 2. Product identification sequence.

characters: 21 for the donation identification sequence and 19 for the product identification sequence [2].

The donation identification sequence (SEC-DI) shall be assigned 'solely by one TE and it identifies the TE which first received the tissues or cells from a procurement organisation (or third country supplier in the case of import from a third country) or which itself carried out the procurement'. The SEC-DI must be applied 'to all tissues and cells prior to distribution for human application or to transfer to another operator (i.e. TE or advanced therapy medical products (ATMP) manufacturer) for further processing (with or without return)' [3]. It comprises an EU TE code as assigned in the EU TE Compendium and a unique donation number allocated by the TE. The code which identifies the TE where the label with the SEC has been applied, is made up by an ISO country code and a TE number which has been assigned in accordance with EU CAs, while the unique donation number is made up by 13 alphanumeric characters (fig. 1):

As far as the EU Product identification sequence is concerned, it includes a product code which carries a product coding system identifier made by 1 alphabetic character and a product number made by 7 alphanumeric characters, followed by a split number and the expiry date of the product [2].

The product coding system identifier could be one of only three alphabetic characters (E, A, B) which represents one of the permitted product coding systems: E for EUTC T&C compendium, A for ISBT T&C compendium, and B for Eurocode T&C compendium. The split number may be numeric or alphabetic as long as they are unique to each product from a donor that carries the same product code in the SEC. If the split number has less than three characters, it should be padded with leading zeros. If the split number is being applied to a product which has not been split, the number will be made of three zeros [3]. The expiry date is made up by 4 numbers for the year, 2 for the month and 2 for the day and is therefore in the format 'YYYYMMDD' (fig. 2).

Through the online platform which is hosted and maintained by the European Commission on its website, both compendia are available for consultation: the EU TE Compendium which is the

register of all TEs which are authorised, licensed, designated or accredited by the MS CA/CAs and which contains their information as set out in Annex VIII of EU directive 2006/86 and the EU T&C Product Compendium, namely the register of all types of T&C circulating in the European Union and their respective product codes under the three permitted coding systems (EUTC, ISBT128 and Eurocode) [4].

'Importing TEs which only import or only import and distribute T&C are also included in the Compendium, while centres that carry out only donation and/or testing and/or procurement (i.e., procurement organisations) as well as centres that only carry out clinical application (i.e., organisations responsible for human application) are not included in the Compendium' [3].

Traceability of T&C within the EU will therefore be granted through the application of the SEC and each of the parties involved (MS, EU CAs and TEs across Europe) will have obligations to fulfil in order to successfully implement the Directives.

MS, for instance, shall ensure the traceability of T&C specifically through the documentation and the use of the SEC from procurement to human application or disposal and vice versa. T&C used for ATMP shall be traceable under EU directive 2006/86 at least until transferred to the ATMP manufacturer. It is also MS' responsibility to ensure that TEs and organisations responsible for human application retain the data set out in Annex VI of EU directive 2006/86 for at least 30 years, using an appropriate and readable storage medium. Moreover, in case of T&C retrieved from a deceased donor by procurement teams operating for two or more TEs, MS shall ensure an appropriate traceability system across the procurements.

As far as CAs are concerned, it will be their duty to ensure the allocation of a unique TE number to all TEs authorised, accredited, designated or licensed in its MS, to decide which system or systems shall be used for the allocation of unique donation numbers in their MS (local, national, international), to monitor and enforce the full implementation of the SEC in their MS and to ensure the validation of the data on the TEs contained in the EU TE Compendium for their MS and update the Compendium without undue delay (no later than 10 working days) in particular in the following situations: when a new TE is authorised, designated, accredited or licensed; when TE information changes or is not correctly recorded in the EU TE Compendium; when the accreditation, designation, authorisation or licence details of a TE, as listed in Annex VIII of EU Directive 2006/86, change.

When it comes to the allocation of unique donation numbers, CAs shall remember that if a TE has different physical locations but has one system for allocating unique donation numbers, it may be deemed to be one, while if a TE uses two or more systems to allocate unique donation numbers, such an entity shall be allocated separate TE numbers corresponding to the number of allocation systems used. The unique donation number may be allocated locally at the TE (for those who apply rules locally), at the national level (in MS which establish centralised allocation of the unique donation number) or by using an international codification system (i.e. ISBT128 or Eurocode) that are compatible with the SEC [3].

TEs across the EU will also share duties and responsibilities. It is their task to allocate a SEC to all T&C requiring application of this code at the latest before their distribution for human application and to allocate a donation identification sequence after procuring the T&C or when receiving them from a procurement organisation or when importing T&C from a third-country supplier. As previously mentioned, the TE code will be assigned through the EU TE Compendium, while the unique donation number will be allocated by the TE, unless such number is allocated centrally at national level or is a globally unique number as used by the ISBT128 coding system. Where allowed, in case of pooling of T&C, a new donation identification number shall be allocated to the final product; traceability with the individual donations shall be ensured by the TE in which pooling is carried out. The donation identification sequence cannot be altered, once it is allocated to T&C released for circulation, unless it is necessary to correct an encoding error; an operation which requires to be properly documented.

Furthermore, TEs shall use one of the permitted product coding systems and the corresponding T&C product numbers included in the EU T&C Product Compendium at the latest before their distribution for human application and make sure they use an appropri-

ate split number and expiry date before their distribution for human application. TEs are also responsible for the application of the SEC on the label of the product concerned in an indelible and permanent manner and on the relevant accompanying documentation. Should the label size preclude the application of the SEC, it must be shown on the product's accompanying documentation and be secured in order to remain clearly and unambiguously associated with its product [3]. Finally, TEs shall notify the CA/CAs when the information contained in the EU TE Compendium requires an update or correction, when the EU T&C Product Compendium requires an update and when the TE observes a situation of significant non-compliance with the requirements relating to the SEC concerning T&C received from other EU TEs.

In order to help EU MS in the implementation of SEC Directives, the EC under the European Union's Health Programme (2014–2020) co-founded the Joint Action VISTART (EU Grant Agreement n. 676969) started on October 2015 for 3 years, where Work Package 10 (WP10) developed a questionnaire to EU T&C CAs in order to collect information on where MS were at that point, with Coding Directive transposition and then implementation. Moreover, Lithuania was provided by a support on-site visit by a WP10 staff expert. In collaboration with VISTART WP10 members, the ICCBA and supervised by the European Commission, an e-learning course was developed and hosted on the CNT e-learning platform. It started on September 5, 2016 and finished on October 17, 2016. Moreover the WP10 team has joined three major congresses where workshops, oral presentations and exhibition booth on VISTART were held in order to provide professionals with the information they might need to successfully implement the SEC in their countries: the 42nd Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT), Valencia, Spain, April 3 to April 6, 2016; the 32nd Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), Helsinki, Finland, July 3 to July 6, 2016; and the 25th Congress of the European Association of Tissue Banks (EATB), Hanover, Germany, November 23 to November 25, 2016 [5].

Fig. 3. TEs recorded by June 23, 2017.

Fig. 4. Total number of TEs for each MS of the EU.

Results

By June 23, 2017 the total number of TEs recorded on the EU TE Compendium, on the European Commission's online platform (<https://webgate.ec.europa.eu/eucoding>) is 3,305 of which 830 are TEs with haematopoietic progenitor cell (HPC) activities only [6] (fig. 3).

Figure 4 shows the total number of TEs for each MS of the EU, and the number of TEs with HPC activities which perform only just one, more than one or all of the following activities: procurement, testing, preservation, processing, storage, distribution, import and export of hepatocyte, keratinocyte, pancreatic islet cells, T cells, bone marrow, cord blood, peripheral blood stem cells and unspecified progenitor cells, haematopoietic cells [6].

Conclusions

The implementation of the SEC and the creation of the two public compendia for TEs and T&C products represent a significant step forward with respect to traceability of human T&C that are applied to patients in the EU, since the ability to trace T&C to their original centre and, therefore, their human origin, is to be considered as paramount for the safeguard of the health of EU citizens.

References

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Disclaimer

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Disclosure Statement

The authors certify that there is no actual or potential conflict of interest in relation to this article.