Movement of gametes and embryos across borders

Strategic delivery:	☒ Safe, ethical, effective treatment	☐ Consistent outcomes and support	☐ Improving standards through intelligence

Details:	
Meeting	Authority
Agenda item	8
Paper number	HFEA (08/03/2018) 872
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Author	Niamh Marren, Regulatory Policy Manager Nick Jones, Director of Compliance and Information

Output:			
For information or decision?	For information		
Recommendation	To note the arrangements for implementing the two Directives To approve the amendments to General Direction 0006 in relation to the application of the Single European Code Note the arrangements for amending General Direction 0006 in relation to importing that will be brought forward in April 2018.		
Resource implications	Within existing resources		
Implementation date	April 2018		
Communication(s)	Implementation to be communicated through Clinic Focus in March and April 2018. Also, Code of Practice review for October 2018 implementation.		
Organisational risk	☐ Low	☐ Medium	☒ High
Annexes	Annex A: Application for import relationship between UK clinic and third country supplier (for information) Annex B: Process for reviewing import relationship applications (for comment) Annex C: Template certificate (for information) Annex D: Amendments to General Direction 0006 in relation to the introduction of the Single European Code (for approval)		

Annex E: Standard licence conditions - compliance with the requirements – (for comment)

Human Fertilisation & Embryology Authority

1. Introduction

1.1. This paper sets out the requirements for the implementation of the EU Directives on import, and coding. The import Directive deals with the importing of tissue and cells into the European Union (EU) from outside the European Economic Area (EEA) and Gibraltar. The coding directive sets out the procedures to ensure the traceability of tissue and cells following movement within the EU.

1.2. The import requirement refers to the EU Commission Directive 2015/566 implementing Directive 2004/23/EC regarding the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells. The coding Directive 2015/565 sets out standards of quality and safety for donation, procurement, testing, processing, preservation and distribution of all human tissue and cells intended for human application.

1.3. These requirements have been transposed into the HF&E Act 1990 (as amended) by regulations (the Human Fertilisation and Embryology (Amendment) Regulations 2018) passed by Parliament on 27 February 2018. The regulations come into force on 1 April 2018, and guidance on their implementation will be included in the HFEA Code of Practice, Directions and standard licence conditions.

1.4. We have been in dialogue with the sector for some time and it was originally expected that the implementation would take place in October 2018. Implementation in the UK has been brought forward to 1 April 2018 due to a speedier passage of the Regulations through Parliament.

2. Import Directive

2.1. The purpose of the import Directive is to ensure that there are procedures for verifying the standards of quality and safety of gametes and embryos that are imported into the UK from non-EEA and Gibraltar establishments. These establishments are classified as “third country” suppliers.

2.2. In deciding how to implement the Import directive we have reviewed the Human Fertilisation and Embryology (Amendment) Regulations 2018 alongside the EU Directive and taken external legal advice.

2.3. The requirements laid out in the Directive and the Regulations means that the HFEA will need to amend the Code of Practice requirements in ‘guidance note 16: imports and exports’ on factors that the licensed centre will need to reassure themselves of before applying for the requisite certificate, Schedule 3 of General Directions 0006, and the decision tree.

2.4. The scale and origin of imported gametes into the UK can be summarised as follows. In 2017 there were 1099 import events from

outside the EEA, 989 of which were from the USA. However, there are only four centres in the USA that UK clinics currently import from.

2.5. The other non-EEA countries that UK clinics imported from in 2017 include:

- Australia (incl Cocos Island/Christmas Island)
- Canada
- Hong Kong
- New Zealand (incl Chatham Island)
- Panama
- Samoa (Formerly known - Western Samoa)
- Singapore
- South Africa
- Tanzania
- Ukraine

2.6. In 2017 some 65 UK clinics imported gametes from one or more non-EEA country. However, the scale of their import activity varies hugely, from 1 import event to 151. Of the 65 importing clinics that year, only 14 did so on more than 20 occasions.

2.7. For the purposes of the EU Directive any clinic that imports gametes or embryos from a third country supplier is referred to as an Importing Tissue Establishment (ITE). In order to import from a Third County supplier (i.e. any supplier in a country which is outside the EEA), a UK centre needs to apply to the relevant regulatory body (in the case of the UK the HFEA) for a certificate to allow them to make qualifying imports. This can be for a one-off import or for ongoing imports. The application form (attached for information at annex A) that UK clinics will use to apply to the HFEA for a certificate sets out the requirements that clinics will have to meet.

2.8. The process works like this. The responsibility of considering/approving any such application lies with the executive Licensing Officer (the delegation by the Authority is proposed in the updated Standing Orders elsewhere at this meeting). In cases where a Special Direction is required for any import, the decision would continue to rest with Statutory Approvals Committee. Annex B sets out the draft process for review of the certificates issued to clinics.

2.9. The regulations give the HFEA a new power to revoke the clinic's licence on grounds that the premises of any clinic in a third country from which the UK clinic imports are not considered suitable. As a result, changes need to be made to the decision tree for the refusal or revocation of a licence. This is the statutory incentive for UK clinics to

ensure that any third country clinic that they import from does indeed meet the standards of quality and safety that the Directive requires.

2.10. The EU Directive provides a template certificate to be issued to those clinics that import from third country suppliers. This certificate is provided at Annex C to this paper, for information.

2.11. Under the Directive, HFEA licensed clinics are required to establish third party agreements (TPA) with all third country suppliers. They will then have to apply to the HFEA for a certificate which allows them to import from those named establishments provided those establishments meet the requirements of quality and safety.

2.12. The importing HFEA licensed clinic must notify us of the following:

1. if the UK centre ceases to import from a third country supplier.
2. if there are any serious adverse events or serious adverse reactions as notified by the third country supplier.
3. if there are any changes in circumstances of the third country supplier that the person responsible (PR) is aware of.
4. if it changes its importing relationship with the third country supplier for example it starts importing embryos where it previously only imported gametes from the supplier.

2.13. The HFEA must consider the application for any importing certificates and the licensing officer will determine whether to grant the certificate. We then monitor compliance through the process of engaging with clinics to work on TPAs

2.14. To give effect to the directive the HFEA will need to amend the import/export General Direction 0006. Given the challenging time constraints and the complexity of the requirements these are being drafted and will need to be agreed by the Authority (delegated as appropriate) during April 2018, coming into effect as soon as possible thereafter.

3. Coding Directive

3.1. The coding Directive is designed to facilitate traceability by establishing a unique identifier applied to tissues and cells (including reproductive cells) by way of a Single European Code (SEC) providing information on the main characteristics and properties of those tissues and cells. This traceability is for tissues and cells distributed between EU, EEA and Gibraltar (hereafter referred to as EU).

3.2. The SEC is applied to the movement of donor gametes and embryos between licensed clinics (or ‘tissue establishments’ in EU terms) within and outside the UK (partner gametes and embryos are excluded). A clinic importing gametes and embryos from a tissue establishment and

not distributing thereafter (that is importing for use in that clinic only) is exempt from applying the code.

3.3. The SEC is the unique identifier for tissues and cells distributed in the EU. It comprises of 40 alpha-numeric characters; it must be 'eye-readable', that is, if a bar code is used, it must be accompanied by the SEC. Ideally it will be attached to the container of the tissue/cell but where that is not possible due to its size it is attached to the documentation accompanying and linked to the tissue/cell. That is likely to be the case for many reproductive products, for example straws of sperm.

3.4. The SEC is made up of the following (six) features.

Donation identification sequence			Product identification sequence		
ISO Country code	Tissue Establishment code	Unique Donation Number	Product code	Split number	Expiry date
2 alpha characters	6 alpha-numeric characters	13 alpha-numeric characters	1+7 alpha-numeric characters	3 alpha-numeric characters	8 numeric characters Yyyy/mm/dd
GB	**000123** 00 then HFEA licensed centre number	**0000000000456** Clinic's donor registration number – submitted to HFEA now	**E0000059** 1 of 5 for reproductive cells (EUTC system), 00000 then -Embryos (56) -Sperm (59) -Oocytes (57) -Ovarian tissue (58) -Testicular tissue (60)	**001** If sperm, for example, is distributed to more than one TE	**20181231** Date of expiry of consent, for example, 31 December 2018
SEC GB000123000000000456 E000059001201812 31					

3.5. It enables the recipient tissue establishment to trace the primary distributing tissue establishment if there is an issue (now and in the future) relating to the quality or safety of the gametes or embryos, for example a child develops a genetic condition associated with the use of donor sperm.

3.6. The Human Fertilisation and Embryology Act 1990 (amended) requires licensed clinics to ensure full traceability. Our requirements are set out in the HFEA Code of Practice, (General) Direction 0006, and standard licence conditions (SLC 99-104). We also already require clinics to register a unique donor registration code with the HFEA through the data submission system.

3.7. The requirements introduced by the Directive are additional to our extant requirements, but are not substantially different – the format of the code is prescribed and incorporates the current clinic donor code. It will necessitate additional work for clinics, particularly for those distributing gametes and embryos to other clinics, either within the UK or elsewhere. We are not requiring clinics to submit the SEC to the HFEA.

3.8. The necessary changes we need to make to ensure licensed clinics meet the requirements of the Directive are comprised of three main components:

1. Instructions to clinics with detail as to their obligations in meeting the requirements of the Directive, by way of a Chair's letter

2. The Regulations stipulate, amongst other things, that Directions (from the HFEA to licensed clinics) must specify the system to be adopted for the identification of gametes and embryos intended for human application, together with the information that must be provided to the Authority. This stipulation will be met by way of amendments to General Direction 0006 – Annex D
3. Consequential amendments to standard licence conditions, affecting treatment and storage clinics (standard licence condition T100 and T101) - Annex E

3.9. As the UK Competent Authority for reproductive tissues and cells, the HFEA has other obligations (including ensuring compliance by licensed clinics) to ensure that the SEC system works effectively, as follows and in summary:

- Ensure that all UK licensed clinics' details (name, licence number, and contact details) are held (and updated) in the EU tissue establishment compendium (EU web-based database). This is currently up to date, and as new licences are granted and the details of existing clinics change it will need updating in line with our own Register of licensed clinics;
- Inform another country's competent authority where a tissue establishment in that country is not shown on the Compendium or its details are erroneous;
- Monitor the implementation of the SEC by licensed clinics – at inspection, checking that the SEC has been incorporated within the documentation.

4. Recommendation

4.1. The Authority is recommended to:

- Note the arrangements for implementing the two Directives
- Approve the amendments to General Direction 0006 in relation to the application of the Single European Code
- Note the arrangements for amending General Direction 0006 in relation to importing that will be brought forward in April 2018.

Annex A: Application for import relationship between UK clinic and third country supplier

Application to authorise an importing tissue establishment

General information on the Importing Tissue Establishment (ITE)

Name of ITE (centre number)	
EU Tissue Establishment Compendium Code	
ITE Address and postal address (if different)	
Status of the applicant: first accreditation, designation, authorisation or licence as ITE or renewal	First time ☐ Renewal ☐
Name of the applying unit (if different from the above address)	
Address of the applying unit (if different)	
Name of the site of reception of imports (if different from the above)	
Visiting address of the site of reception	
Postal address of the site of reception (if different)	

Contact details for the application

Name of PR	
Address of PR	
Telephone number of PR	
E-mail address of PR	
URL of ITE website	

Details of tissues and cells to be imported

A list of the tissues and cells to be imported, including one-off imports	
One-off imports	☐
Product name(s) of imported tissues and cells	
The trade name (if different to the product name)	
Name of the third country supplier for each type of tissue and cell to be imported	

Location of activities

Which activities are carried out prior to import by the third country supplier per type of tissue or cell	Donation	Procurement	Testing	Processing	Preservation	Storage
	☐	☐	☐	☐	☐	☐
Which activities are carried out prior to import by sub-contractors of the third country supplier per type of tissue or cell	Donation	Procurement	Testing	Processing	Preservation	Storage
	☐	☐	☐	☐	☐	☐
A list of all activities carried out by the ITE subsequent to import per type of tissue or cell						
Names of the third countries in which the activities prior to import take place per type of tissue or cell						

Details of third country suppliers

Name of the third country supplier	
Name of the contact person	
Visiting address	

Postal address (if different)	
Telephone number (including international dialling code)	
Emergency contact number (if different)	
E-mail address	

Documentation to accompany the application

Have you provided the following:	
A copy of the written agreement with the third country supplier	☐
A detailed description of the flow of imported tissues and cells from their procurement to their reception at the ITE	☐
A copy of the third country supplier's export authorisation certificate1. This should include the contact details of the third country's competent authority.2	☐

[1] Or where a specific export authorisation certificate is not issued, certification from the r3elevant third country competent authority or authorities authorising the third country supplier's activities in the tissue and cells sector including exports.

[2] Where this documentation is not available, alternative forms of documentation shall be provided such as reports of audits of the third country supplier.

Annex B Process for reviewing import relationship applications

1. Process 1 – first time application, for an import relationship with a third country supplier, has been received

1.1. The UK clinic who receives the relevant paperwork from the third country supplier to satisfy the quality and safety standards

1.2. The UK clinic finds the HFEA application form on the website (Word format)

1.3. The UK clinic sends the paperwork and application form (outlined in Annex A) to a member of the compliance team

1.4. A Compliance team member reviews the paperwork and the application form and develops an executive summary for the Licensing Officer to review

1.5. The paperwork, application form and executive summary are sent to the licensing officer

1.6. The licensing officer will review the executive summary and application form and make the decision whether to allow or refuse the import using a decision tree

1.7. If the relevant requirements are met:

1. the licensing officer will grant a certificate and issue the certificate in Annex C with the information provided in the paperwork, application form and executive summary;
2. the third country supplier needs to be added to a spreadsheet which holds all the information of each third country supplier.

1.8. If a certificate cannot be granted, – letter of refusal, setting out the requirements which were not met, to be sent to the UK clinic

2. Process 2 – when an Importing Tissue Establishment (ITE) wants to import from a third country supplier who was approved previously

2.1. The UK clinic checks the HFEA website to check if any other UK clinic has a certificate authorising it to import from the particular the third country supplier.

2.2. If no – follow process 1

If yes – follow process 2

2.3. The UK clinic requests the third country supplier's paperwork from the HFEA.

2.4. The compliance team member provides the paperwork to the UK clinic.

2.5. The UK clinic must complete their own checks to ensure that the third country supplier continues to meet the quality and safety standards and that no changes have occurred at the third country supplier since the HFEA previously issued the certificate naming that third country supplier.

2.6. The UK clinic sends the updated paperwork and application form to the Compliance team.

2.7. Compliance reviews the paperwork and application form and develops an executive summary for the licensing officer.

2.8. The executive summary and the application form are sent to the licensing officer.

2.9. The licensing officer makes a decision, using the decision tree, whether to grant the certificate.

2.10. If a certificate is granted,

1. the licensing officer completes the certificate in Annex C with the information provided in the paperwork, application form and executive summary and
2. issues the certificate to the UK clinic.

2.11. If a certificate is not granted,

1. letter of refusal to be sent the ITE setting out the reasons for the refusal;
2. other ITE's need to be notified to cease import and an updated certificate will need to be issued, removing the third country. This will happen if the certificate is not granted because of concerns about the quality and safety standards of that supplier;
3. the third country supplier needs to be removed from the spreadsheet where all approved certificates are captured.

Annex C: Template Certificate

Certificate of authorisation of an importing tissue establishment

Importing Tissue Establishment (ITE) Details

Name of ITE (centre number)	
EU Tissue Establishment Compendium Code	
ITE Address and postal address (if different)	
Site of reception of imports (if different from the above address)	
Name of PR	
Address of PR	
Telephone number of PR (optional)	
E-mail address of PR (optional)	
URL of ITE website	

Scope of activities

Type of Tissues and Cells (list below using categories of tissues and cells listed in the EU Tissue Establishment Compendium adding rows as necessary)	Activities in third countries						
	Donation	Procurement	Testing	Preservation	Processing	Storage	Import Accreditation, Designation, Authorisation or Licence Status
	3CS – Third country supplier SC – Sub-contractor of third country supplier						G – Granted S – Suspended R – Revoked C – Cessation

One-off imports	
Product name(s) of imported tissues and cells	
Any conditions placed on the import or clarifying remarks	
Third country or countries of procurement (per tissue and cell import)	
Third country or countries in which other activities take place (if different)	
Name and country of third country supplier(s) (per tissue and cell import)	
EU Member States in which imported tissues and cells will be distributed (if known)	

Competent Authority (CA) Authorisation

National accreditation, designation, authorisation or licence number		
Legal basis of accreditation, designation, authorisation or licence		
Date of expiry of accreditation, designation, authorisation or licence (if any)		
First accreditation, designation, authorisation or licence as ITE or renewal	**First time** ☐	**Renewal** ☐
Additional remarks		
Name of CA		
Name of CA Officer		
Signature of CA Officer (electronic or otherwise)		
Date of accreditation, designation, authorisation or licence		
CA Stamp		

Annex D – Amendments to General Direction 0006

General Direction 0006 Single European Code (April 1 2018)

2.1. Licensed clinics must apply the Single European Code (SEC) to all tissues and cells before distribution for human application within the EU (including the UK), EEA or Gibraltar.

2.2. The following exemptions to the requirements for a SEC apply:

- Gametes and embryos for 'partner donation'. This is a term used in the Directive defined as the reproductive cells between a man and a woman who declare that they have an intimate physical relationship
- Where gametes and embryos are provided at a clinic and are going to be used in treatment at the same clinic remain within the same centre (that is they are not distributed).
- Where gametes and embryos are imported into the licensed clinic and will be used in treatment in the same clinic remain within the clinic for use in treatment.
- Tissues and cells already in storage on 29 October 2016 (see transitional period, below).

2.3. The SEC shall be in the form specified in Annex VII of the amended Directive 2015/565.

2.4. The SEC is the unique identifier for tissues and cells distributed in the EU. It is made up of the following (six) features:

Donation identification sequence			**Product identification sequence**		
ISO Country code	Tissue Establishment code	Unique Donation Number	Product code	Split number	Expiry date
2 alpha characters	6 alpha-numeric characters	13 alpha-numeric characters	1+7 alpha-numeric characters	3 alpha-numeric characters	8 numeric characters Yyyy/mm/dd
GB	**000123** HFEA Licensed Centre number	**00000000XX456** Clinic's donor registration 'number' – submitted to the HFEA currently in registering the donor, with zeros added	**E0000059** 1 of 5 for reproductive cells (EUTC system) -Embryos (56) -Sperm (59) -Oocytes (57) -Ovarian tissue (58) -Testicular tissue (60)	**001** If sperm, for example, is distributed to more than one TE	**20181231** Date of expiry of consent, for example, 31 December 2018
SEC GB00012300000000XX456 E000005900120181231					

Licensed clinics are permitted to use one of three coding platforms to identify the SEC.

1. The EU coding platform is available at https://webgate.ec.europa.eu/eucoding/reports/te/index.xhtml and incorporates the EU Tissue Establishment Compendium.
2. ICCBBA ISBT128 https://www.iccbba.org
3. Eurocode IBLS http://www.eurocode.org/

2.5. In all cases the 'unique donation number' must be the unique HFEA donor registration number applied by the licensed clinic, and submitted to the HFEA further to the donor registration process, preceded by zero(s) – as necessary such that it is formed of 13 alpha-numeric characters.

2.6. The 'expiry date' shall be the date on which consent to storage and use expires. This date will be sourced from the patient consent form.

2.7. Once the SEC is allocated it must not be altered unless there is an encoding error. If this happens, a new code should be correctly issued and a record should be kept of the error and amended code.

2.8. The SEC must be attached to the container of the tissue/cell or where that is not possible it must be attached to the accompanying documentation and linked to it. It must be 'eye-readable' that is, if a bar code is used, it must be accompanied by the SEC. When printed, the 'donor identification sequence' and product identification sequence must be separated by a space or as two successive lines.
GB0001230000000000456 E000005900120181231

2.9. Transitional period: Tissues and cells in storage on 29 October 2016 are exempt from obligations to attach the SEC where those tissues and cells are distributed, until 29 October 2021, but they must be traceable. After this date the SEC must be attached to accompanying documentation. See (9) above.

2.10. The SEC shall not be submitted to the HFEA as part of a clinic's data treatment data submission obligations set out in General Direction 0005.

2.11. A licensed clinic must inform the HFEA when:

- Information about it held in the EU Tissue Establishment compendium requires updating or correction;
- The EU Tissue and Cell Product compendium requires an update;
- It identifies a significant non-compliance with the requirements relating to the SEC concerning tissues and cells received from other EU tissue establishments.

Annex E Standard licensing conditions - compliance with the requirements

The following standard licence conditions have been **amended**:

T100: The documented procedures referred to in licence condition T99 include the following information:

1. the unique and accurate identification of each patient/donor
2. the unique and accurate identification of each set of gametes and embryos, **including the Single European Code applied to each set of gametes and embryos when required by General Direction 0006**
3. date of procurement
4. place of procurement
5. type of treatment
6. description and origin of any and all products associated with the procurement, processing, use and storage of gametes and embryos, and
7. description of all processing steps applied to the procurement, use and storage of gametes and embryos.

T101: The centre must ensure that all containers (dishes, vials, ampoules, tubes etc) used in the course of procurement, processing, use and storage of gametes and embryos are labelled with the patient's/donor's full name and a further identifier. If at some stages (eg, labelling patient/donor sperm) it is not possible to label the dishes or tubes with the patient/donor name then it must be ensured that the patient/donor code used is uniquely identifying. **Containers holding gametes and embryos or the paperwork attaching to any containers must be labelled with a SEC in those circumstances specified in General Direction 0006.**