Tissue and cell inspection systems in Europe: a EUSTITE survey

MARINA ALVAREZ1, GREGORIO GARRIDO1, DEIRDRE FEHILY2, CATERINA DELVECCHIO3, ALESSANDRO NANNI COSTA2, RAFAEL MATIKSANZ1 (on behalf of EUSTITE Consortium)

1Organización Nacional de Trasplantes, Spain
2Centro Nazionale Trapianti, Italy

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SUMMARY - The EUSTITE project (European Union Standards and Training for the Inspection of Tissue Establishments), funded under the European Commission Public Health Programme, aims to optimise and harmonise the standards and methods applied in the inspection and authorisation of tissue procurement and tissue establishments within the EU. This paper reports on a EUSTITE survey undertaken to collect detailed information on existing inspection systems, and to disclose differences in approach, areas of good practice and gaps that need to be filled by the provision of guidance and training.

INTRODUCTION

The EUSTITE project (European Union Standards and Training for the Inspection of Tissue Establishments) is a 3 year project funded under the European Commission Public Health Programme (see www.eustite.org). The primary objective of the project is to optimise and harmonise the standards and methods applied by Competent Authorities (CA) in the inspection and authorisation of tissue procurement and tissue establishments (TE) within the EU, in compliance with Directive 2004/23/EC1, Articles 5, 6 and 7 and its associated implementing directives2-3. The project is carried out by a consortium of 11 organisations from 10 EU Member States and the World Health Organisation (WHO) and is led by the National Transplant Centre in Italy.

Existing inspection systems, their advantages and disadvantages were explored in a survey conducted by ONT and in an exploratory interactive workshop hosted by the Irish Medicines Board in Ireland. The survey aimed to collect detailed information on existing inspection systems for human tissues and cells in all European Union Member States, and it focuses in more depth on the specific areas of supervision, inspection and authorisation (accreditation/licensing) whilst aiming to identify differences in approach, areas of good practice and gaps that need to be filled by the provision of guidance and training.

METHODOLOGY

Scope

All 27 EU Member States and 3 Non EU Member States were invited to participate in the survey. The invitation letter was sent to the Competent Authority Representatives who attended the Meeting of Competent Authorities for Tissues and Cells in Brussels, 8 February 2007.

Data collection

The questionnaire used for this survey was produced by one partner, ONT, with the collaboration of the full membership of EUSTITE and the endorsement of the European Commission. To avoid the need to repeat information already provided to the European Commission as part of a survey conducted earlier in 2007, the questionnaire included a summary of that information and Competent Authorities were asked to confirm if that information was still accurate or if any aspect of it should be updated.
The questionnaire was divided into three parts:
1. General data
2. Inspection Systems: 21 questions: 10 with closed answers (yes/no), and 11 with open answers.
3. Enclosures
ONT distributed the questionnaires in June 2007 and accepted completed returns until September 2007.
ONT reviewed and collated the data.

RESULTS

The questionnaire was sent to 30 European countries; 26 (87%) of them completed and returned it.

AUSTRIA        LATVIA
BELGIUM         LIECHTENSTEIN
BULGARIA        *LITHUANIA
CYPRUS          LUXEMBOURG
CZECH REPUBLIC  MALTA
DENMARK         NORWAY
*ESTONIA        POLAND
FINLAND         PORTUGAL
FRANCE          ROMANIA
GERMANY         SLOVAKIA
GREECE          SLOVENIA
HUNGARY         SPAIN
*ICELAND        SWEDEN
IRELAND         *THE NETHERLANDS
ITALY           UNITED KINGDOM

*These countries did not complete the survey.

At the time of the survey, inspections were being performed in 17 of the 26 countries that responded.
Although 73% (16 of 22) of countries reported that a centrally held register of TE exists, the comments submitted indicated that in many cases it is not yet complete or not yet publicly accessible.
The inspection scheme interacts or overlaps with the systems for the inspection of other activities in 10 out of 21 (47%) countries. The most common overlaps were with medical products and blood inspections or with inspections of hospitals including laboratories and medical activities.
Many countries (21) reported using methods other than site inspections for regulatory purposes. These methods are used between 2-yearly site inspections or as a method for prioritising the scheduling of site inspections by risk assessment or to approve activity carried out by third parties such as testing laboratories or procurement organisations. Methods included remote document review, self-certification and activity reports. Compliance is verified in these cases by cross-checking the documents with requirements or by checking during subsequent inspection or by acceptance of a signed self-declaration.

Tissue and cell procurement is verified with an inspection visit in 6 out of 15 countries, and with inspection visit and accompanying documentation in 4.

![Figure 1 - How the TE inspections are scheduled.](image1)

The CA sends the TE a notification (inspection programme, inspection schedule, etc..) before the Inspection in 7 out of 16 countries and an introductory letter in 4 out of the 16.
There are 2 to 3 inspectors in the inspection team in 10 out of 18 countries. Only 2 countries include an observer in their inspections teams. In 40% of countries, inspectors are specially trained.

In general CA inspectors perform between 1 and 20 TE inspections each year, the most common number is between 5 and 10.
The average length of a normal TE inspection is 2 days.

![Figure 2 - Methods used during the inspection.](image2)

There is a standard programme or agenda and an inspection written procedure or guideline, which details how the inspection should be performed, for each inspection in 6 out of 16 countries that replied to this question.
Inspection findings are referenced directly to the national regulations transposing the EU Directives in 12 out of 18 countries.
Non-compliances are classified in terms of their severity in 7 out of 17 countries.

The reporting process of the inspection to the Responsible Person of the TE is a written report in 10 out of 16 the countries that replied.

Re-inspections are performed to verify corrective actions for selected types of non-compliances in 11 out of 13 States. In 2 out of 17 countries that replied, the Regional Competent Authority authorises the issue of a TE certificate following a successful inspection. In 6, the National Competent Authority authorises the certificate. Finally, four countries have a formal interaction between the Competent Authority and the JACIE inspection and accreditation scheme for haematopoietic stem cell establishments.

CONCLUSIONS

There was a high response to the survey and very useful information was provided by Member States. It is clear that inspection systems are mostly at an early stage of development and have not yet been implemented in a comprehensive way covering all tissues and cells in most Member States. The background of the inspectors varies considerably ranging from pharmaceutical inspectors to medical doctors and general hospital inspectors. Although the EU Directives require inspections of Tissue Establishments to be conducted every 2 years, many Competent Authorities are applying methods other than site inspection in the initial stages or to help with prioritisation of inspection. The results highlight the need for guidelines and training on the conduct of inspections to ensure a common approach. These instruments are being delivered by the EUSTTTE project.

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REFERENCES

