



Brussels,
SANCO D4/IS/ac ARES(2013)

Report on the Rapid Alert system for human Tissues and Cells (RATC) (2010 – 2012)

Background

Article 8 of Directive 2006/86/EC¹ requires the Competent Authorities for human tissues and cells to "*communicate to each other and to the Commission, such information as is appropriate with regard to serious adverse reactions and events, in order to guarantee that adequate actions are taken.*"

The Rapid Alert system for human Tissues and Cells (RATC) was initiated to provide the Member States Competent Authorities for Tissues and Cells and the European Commission with an effective and secure tool for the exchange of information and urgent measures related to human tissues or cells transferred across borders for patients undergoing transplantation and medical procedures involving such products. This system is used in parallel with existing national vigilance systems which collect and manage alerts on human tissues and cells donated and used within a Member State.

RATC system does not include rapid alerts for human or veterinary medicinal products, blood and blood components, human organs intended for transplantation, or medical devices. However, where precautionary/corrective actions taken in these sectors are relevant also to the tissues and cells intended for human application or vice versa, an exchange of information with the national and European regulatory authorities responsible for these sectors should be ensured.

The development of the RATC system started in December 2009 with the designation of the national representatives/contact points of Competent Authorities and the drafting of the RATC Standard Operating Procedures (SOP). In early 2010 a pilot phase followed with a series of case studies to test the functionality and reliability of the system. The latter step included an evaluation phase in which the procedures and templates were improved according to the users' feedback.

The RATC system, hosted by the Commission CIRCA platform (Communication and Information Resource Centre Administrator), was officially launched after the meeting of the Competent Authorities for Tissues and Cells in July 2010. In January 2012, the RATC system

¹ http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_294/l_29420061025en00320050.pdf

was transferred to the new CIRCABC (Communication and Information Resource Centre for Administrations, Businesses and Citizens) platform.

RATC alerts

It was established earlier by the Member States and the European Commission that any rapid alert encoded in the RATC system should fulfil the following criteria:

- i. requires immediate/urgent consideration or follow up measures in two or more Member States
- ii. Risk: a known or potential risk to patients;
- iii. Severity: issues (quality and safety defects, illegal and fraudulent activities, notifications from other sectors, outbreaks of communicable diseases) of a serious or potentially serious nature;
- iv. Public health implications: may constitute a public health risk to other countries, as defined by the International Health Regulation (2005)².

Four types of rapid alerts were defined:

- 1) Quality and Safety Defects, understood as alerts requiring field corrective actions (e.g. recall, quarantine, discard, etc.) of the concerned human tissues/cells potentially impacting patient safety in other Member States.
- 2) Information Notices, defined as alerts related to field corrective actions performed by the medical device sector, medicinal products sector or other sector(s), which were of significance to the tissues and cells sector.
- 3) Illegal and fraudulent activities, defined as alerts used to notify Member States and the European Commission of the possible presence in the distribution network of tissues or cells resulting from illegal and fraudulent activities in the procurement, testing, processing, packaging, distribution, labelling, import/export or promotion of human tissues or cells.
- 4) Epidemiological Notices, which are alerts related to the development of significant epidemiological situations (e.g. disease outbreaks) which may have cross-border implications in the field of tissues and cells intended for human application.

However, it should be noted the last category was not fully defined in 2010, and many epidemiological rapid alerts were circulated to the national representatives of Competent Authorities for Tissues and Cells via mailing lists. Initially it was considered that such information may well be circulated at national and European level via the Early Warning and Response System (EWRS) and a duplication of work was not needed. Meanwhile, taking into account that only some communicable diseases are relevant for this sector, it was decided to further define this category and prepare, with the expertise of ECDC³, a list of communicable diseases relevant for the entire field of substances of human origin (blood, organs, tissues and cells).

² http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf

³ <http://ecdc.europa.eu/en/publications/Publications/diseases-communicable-by-substances-of-human-origin-SoHo.pdf>

Rapid alerts reported in CIRCA/CIRCABC RATC in 2010-2012

In the interest of openness and transparency to regulatory authorities, professional organisations and other interested parties, the communications via CIRCA/CIRCABC RATC system, including the epidemiological outbreaks, reported by the Competent Authorities are collectively presented below. Several of these preceded the formal implementation of the RATC system and the use of the standardised report template/s.

Between 2006, after the transposition of the Directive 2004/23/EC, and July 2010, there have been 11 rapid alerts related to tissues and cells. These were issued by the following 7 Member States: BG (1), DK (1), EE (1), FR (2), IT (2), NL (3), UK (1), of which 6 to quality and safety defects and 5 referred to outbreaks of communicable diseases (Hepatitis A, Chikungunya, Q fever).

After the launch of the CIRCA RATC in July 2010, and until 31 December 2012, there were 19 rapid alerts uploaded into the system by 9 Member States: DE (2), DK (7), EL (3), ES (1), FI (1), IE (1), IT (1), RO (1), UK(1) and the European Commission (1), which are detailed below:

- 7 Quality and Safety Defects, out of which 3 concerned donation of gametes (e.g. genetic predispositions) and 4 referred to imported tissues from third countries (e.g. a warning issued by FDA, a positive donor from USA, donor/procurement practices for bone products);
- 4 Information Notices related to medical devices (e.g. labelling and contaminated media used in the field of Assisted Reproductive Technologies, freezing bags for storage of stem cells).
- 2 Communications regarding illegal and fraudulent activities (e.g. counterfeit GMP certificate for the processing and storage of cord blood stem cells, false documentation for corneas imported from third countries);
- 6 Epidemiological Notices concerning outbreaks of West Nile virus (3), SARS (1), Malaria (1) and Dengue (1).

The aforementioned rapid alerts led to the following types of preventive/corrective actions:

- Quarantine and/or recall of tissues and cells with quality and/or safety defects;
- Recall or replacement of medical devices (e.g. freezing bags, IVF media) used for storage or processing of tissues/cells intended for human application;
- Raising awareness about potential illegal and fraudulent activities in this sector.
- Risk analysis and appropriate recommendations for donors travelling from/residing in the regions where outbreaks of communicable diseases were reported.

New developments

Taking into account the increase in the exchange of tissues and cells among Member States, and internationally, the European Commission started the development of an improved RATC platform, which is more adapted to the needs of Competent Authorities for Tissues and Cells and the European Commission. Its development was assisted by inter consultations with Member States and the input by a technical Working Group led by the European Commission. In this context, on 1 February 2013 the Commission transferred RATC from CIRCABC to a

new web-based platform, available 24/7, for the primary use of Tissues and Cells Competent Authorities and vigilance contact points in the Member States⁴. The Commission foresees publishing on its website regular reports on the rapid alerts circulated via this new RATC platform.

⁴ http://europa.eu/rapid/press-release_MEX-13-0201_en.htm