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Rapid Alert system for human Tissues and Cells (RATC) and for human Blood and Blood Components (RAB)

Summary of 2017 activities

Introduction

The rapid alert platforms for blood (RAB) and for tissues and cells (RATC) give Member States' competent authorities the possibility to effectively launch alerts to each other and/or to request information in case of an alert or crisis. The systems facilitate the communication of information needed to allow competent authorities in other Member States to rapidly assess risks and take adequate and timely measures.

SANTE hosts these two platforms, maintains the standard operating procedures (SOPs) and manages users from the national competent authorities. It is however these national users themselves who draft and send alerts.

This report provides an overview of the functioning of both systems and alerts submitted in 2017.

Background

Article 8 of Directive 2006/86/EC[1] requires the Member States' 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.*"

Article 9 of Directive 2005/61/EC[2] regarding communication of information between Member States' **blood** competent authorities and to the Commission requires that Member States "*ensure that their competent authorities communicate to each other such information as is appropriate with regard to serious adverse reactions and events in order to guarantee that blood or blood components known or suspected to be defective are withdrawn from use and discarded.*"

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

[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:256:0032:0040:EN:PDF

The rapid alert platform for human tissues and cells (RATC) was initiated five years ago and the rapid alert platform for human blood and blood components (RAB) was initiated four years ago, in order to provide the Member States' competent authorities and the European Commission with an effective and secure tool for the exchange of information for situations in which there is a suspicion of serious health risks associated with tissues, cells, blood and blood components distributed across borders.

The system has been used in parallel with existing national vigilance systems which collect and manage alerts on human tissues, cells, blood and blood components donated and used within a Member State. Additionally, messages can come regarding problems in related sectors (e.g. medical devices, human or veterinary medicinal products, human organs intended for transplantation) which might bring a risk for the quality and safety of blood, tissues or cells.

Due to the strong interest showed by the European Centre for Disease Prevention and Control (ECDC) regarding the rapid alert platform and its epidemiological alerts, and following the agreement of the national competent authorities, access has been granted to ECDC users to such alerts, with the possibility to contribute to the alert process.

RATC alerts

The criteria established by the Member States and the European Commission for encoding rapid alerts in the RATC system remained unchanged in the reporting period (e.g. the need for immediate/urgent consideration or follow-up measures in two or more Member States; known or potential risk to patients; issues of a serious or potentially serious nature; potential public health risk to other countries).

Four types of rapid alert were defined and used as follows:

1) Quality and Safety Defects are 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 are defined as alerts related to corrective actions issued in the medical device sector, medicinal products sector or other sector(s), which were of relevance to the tissues and cells sector.

3) Illegal and fraudulent activities are 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 actual or suspected illegal and fraudulent activities in the procurement, testing, processing, packaging, distribution, labelling, import/export or promotion of human tissues or cells.

4) Epidemiological Notices 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.

Bilateral inquiries are defined as rapid ways of communication between competent authorities of only two Member States related to any type of alert to be used in particular situations:

- the need to substantiate/confirm information related to a potential rapid alert before the official submission in the RATC system;

- any other situation which is deemed appropriate for such an alert.

At a later stage, an inquiry can be either closed or converted into another type of alert.

The RATC Standard Operating Procedures (SOP) and User Manual provide guidance on when and how Member States' competent authorities should inform each other.

Rapid alerts reported in RATC during 2017

In the interest of openness and transparency to regulatory authorities, professional organisations and other interested parties, the communications via RATC system, reported by the Competent Authorities are collectively presented below.

A total of 18 alerts were initiated in 2017: sixteen alerts were encoded in relation to quality and safety defects of tissues and cells (DK 15, ES 1), and two alerts were encoded as Information Notice or Other (UK, FR).

The fifteen alerts from Denmark, related to quality and safety defects, concerned sperm donors identified as posing a risk for transmission of genetic disease. Authorities limited further distribution and use of the donations concerned.

The alert from Spain concerned a washing solution that resulted to be contaminated with Cupriavidus metallidurans in one identified batch which was supplied to one tissue establishment in Spain. The released tissues were distributed to six Autonomous Communities in Spain, Andorra (one centre) and Portugal (one centre).

The concerned tissue establishment took some actions related to the tissues processed with the contaminated washing solution, i.e.:

- informed all the concerned centres about this serious adverse event;

- recalled the distributed tissues which have not been implanted yet;

- discarded, as a precautionary measure, the whole stock of tissues that hadn’t been released.

The information notice encoded by UK was related to a verification and thawing media, for oocytes and embryos, for which CE certification was not renewed. The UK Authority was advised the manufacturer was unable to address some non-conformities raised by its notified body. Several months later the CE certificate for this product was reissued by a notified body, and new stock of this product was distributed carrying the appropriate CE mark.

The alert encoded by France regarded a Real Time HIV1 Amplification test for donors leading to false negative results. This problem was raised by a cornea bank in France and it concerns eleven batches of the amplification test.

All these 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.

- Definition by national Competent Authorities in the Member State of preventive and corrective measures to be taken to address the device defect and voluntary withdrawal of the test kit from the market by the manufacturer.

RAB alerts

The RAB Standard Operating Procedures - SOP established the criteria for encoding rapid alerts in the RAB. These have been defined by the Member States and the European Commission and concerned the need for immediate/urgent consideration or follow-up measures in two or more Member States, the known or potential risk to patients, the issues of a serious or potentially serious nature and potential public health risk to other countries.

Three types of rapid alert were defined and used as follows:

1) Quality and Safety Defects are understood as alerts requiring field corrective actions (e.g. recall, quarantine, discard, etc.) for the blood or blood components that might impact patient safety in other Member States.

2) Information Notices are defined as alerts related to field corrective actions performed in the medical device sector, medicinal products sector or other sector(s), which are of relevance to the blood and blood components sector.

3) Epidemiological Notices are alerts related to important epidemiological developments (e.g. disease outbreaks) which may have cross-border implications in the field of blood donation and transfusion.

A fourth type of alert, a bilateral communication, is also possible. Bilateral inquiries are defined as rapid ways of communicating between competent authorities of only two Member States related to any type of alert to be used in particular situations:

- the need to substantiate/confirm information related to a potential rapid alert before the official submission in the RAB system;
- any other situation which is deemed appropriate for such an alert.

At a later stage, an inquiry can be either closed or converted into another type of alert.

The RAB Standard Operating Procedures and User Manual provide guidance on when and how Member States should communicate with each other.

Rapid alerts reported in RAB during 2017

In the interest of openness and transparency to regulatory authorities, professional organisations and other interested parties, the communications via the RAB system, reported by the competent authorities, are collectively presented below.

During the fourth year of activity of the RAB platform 21 rapid alerts have been encoded in relation to Quality and Safety, Information and Epidemiological Notices. These were issued by the following six Member States: AT(2), DE(1), EL(3), FR(3), IT(3) and RO(9).

Nineteen alerts were encoded as Epidemiological Notices (AT, EL, FR, IT and RO) in the context of Malaria, West Nile Virus and Chikungunya cases.

One alert was encoded as Information Notices (FR) concerning an *in vitro* diagnostic kit for donor screening. A defect reagent was the cause of false positive results and the alert was supported by several complaints from testing laboratories.

One alert was encoded as Quality and Safety (DE) concerning the detection and quantification of Human Immunodeficiency Virus type 1 (HIV-1) RNA in donors. After repeated discrepant negative results with the assay compared to reference methods, a specific batch of the testing kit was identified as defect and recommendation to perform additional tests was issued.

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

- Application of a deferral period for donors coming from affected areas;

- Definition of preventive and corrective measures to be taken to address the device defect and voluntary withdrawal from the market of a specific batch of reagents or testing kits.

In comparison with the three previous years the number of alerts has increased. This regards in particular to the encoding of Epidemiological alerts related to a given outbreak. Not all users are reporting new disease case related to the same outbreak as part of an update of the original alert. This should be further clarified in the user network to produce a clear outbreak history and a more consistent final report in the Epidemiological alerts.

Conclusions

The activities of the Member States in the rapid alert platforms RAB and RATC have focused on issues concerning tissues, cells, blood and blood components that are distributed between Member States in Europe and on exchanges of information and description of urgent measures to be taken. Where it mainly concerned quality and safety defects for tissues and cells, epidemiological notices were the main category of issues in the blood sector.

As a result of the number of alerts encoded, the platforms have proved to be an effective tool to respond to the needs of authorities for communication and information dissemination in relation to health threats.