NOTIFYLIBRARY
The Global Vigilance and Surveillance Database for Medical Products of Human Origin
TRANSPLANTATION, TRANSFUSION AND ASSISTED REPRODUCTION

The Italian National Transplant Centre (CNT), as a WHO Collaborating Centre on Vigilance and Surveillance for Human Cells, Tissues and Organs, provides the secretarial and information technology support for the development and maintenance of the library. The information in the Notify Library is collated and updated by international experts across the globe. CNT coordinates the work of a series of 5 Editorial Working Groups that focus on Infectious Transmissions, Malignancy Transmissions, Clinical Complications, Process-related adverse occurrences and Living Donor Reactions. The experts include government regulators, representatives of Competent Authorities, clinicians working in donation programmes or in transplantation, transfusion and assisted reproduction, scientists specializing in microbiology or virology and professional society representatives.

The project relies on collaboration with the Spanish National Transplant Organisation (ONT) and the Catalan Transplant Organisation (OCATT). At a European level, many national competent authorities are contributing to the library, through collaboration with the VISTART Joint Action (Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation) co-funded by the EU Public Health Programme.

Centro Nazionale Trapianti
Italian National Transplant Centre
WHO Collaborating Centre on Vigilance and Surveillance for Human Cells, Tissues and Organs

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Transplantation, Transfusion and Assisted Reproduction

A tool for health professionals, health authorities and the general public

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SECOND EDITION

VIGILANCE PHILOSOPHY - OBJECTIVE - DB CONTENT
SEARCHING THE LIBRARY
DATABASE TAXONOMY

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Background

Vigilance philosophy

Medical products of human origin encompass all biological materials that are derived wholly or in part from the human body and intended for clinical application. WHO promotes the governance of Medical Products of Human Origin (MPHO) in a manner that acknowledges their exceptional nature. From donation to human application, MPHO have a shared exposure to the risk of potential breaches of ethical standards. They also share risks to safety and quality, for example, transmissible infectious diseases and malignancies. Vigilance is a powerful tool for improving safety and quality. Sharing the lessons learned from adverse outcomes can allow significant process improvements for the greater protection of donors and recipients. These benefits apply where the incident occurred but also anywhere else where an identical or similar incident might occur. Detection, investigation and communication of adverse outcomes bring the transparency and openness that these particular medical treatments demand. To ensure the protection of the donor, the recipient and society will require the establishment of globally consensual principles to govern the use of MPHO, including the non-commercial nature of the human body and its parts as such, and strict traceability associated with vigilance and surveillance. The Notify Library is the first WHO initiative that covers the full MPHO scope.

The NOTIFY PROJECT and its LIBRARY

Following the adoption of resolution WHA 63.22.2010 and the 2011 WHO global consultation "Bologna initiative for Global Vigilance and Surveillance", the NOTIFY project was launched in collaboration with the Italian National Transplant Centre (CNT) and the European Union (EU) funded project SOHO V&S (Vigilance and Surveillance of Substances of Human Origin). Experts from across the six WHO regions gathered information on documented types of adverse outcomes in transplantation, transfusion and assisted reproduction and reviewed the cases in order to identify general definitions and principles supporting detection and investigation. Five editorial groups were established (INFECTIONS, MALIGNANCY, PROCESS, LIVING DONOR and CLINICAL COMPLICATIONS) that refined and standardised the enormous collection of didactic cases available in the scientific literature. This was essential to allow the uploading of the information in a relational publicly accessible database, the Notify Library, on the project's website (www.notifylibrary.org). Since then, annual consultations have been organised and, thanks to the collaboration of all the editorial group members, the database is regularly updated and the website continues to improve. Further tools to support vigilance have been developed over the years, including a comprehensive vigilance document and access to a panel of experts providing support and advice on request via the project website.

Objective of the Notify Library

The Notify Library supports the sharing of documented vigilance information for clinical, educational and organisational purposes with the objective of improving both quality and safety resulting in greater public transparency regarding the donation and use of MPHO. The library aims to be comprehensive, describing all types of adverse occurrences to increase knowledge and assist in the estimation and reduction of risk. The goal of NOTIFY is to promote at a global level the benefits of effective vigilance programs for all types of MPHO.

The tool aims to support three key audiences:

- the general public, particularly prospective donors or recipients
- health professionals working in transfusion, transplantation and assisted reproduction
- health authorities responsible for vigilance systems.

Database content

The Notify Library is a relational database but is not a vigilance reporting program. It is a collection and review of information identified primarily by literature review (published articles in scientific journals and/or books). Case reports from regulatory or professional vigilance programmes (grey literature) are also considered for inclusion. For each adverse occurrence type, at least one reference source is cited and the project's collaborating editorial groups provide a structured analysis. The library can be searched by adverse occurrence type, MPHO type or both, or by using free text or keywords. The experts have reviewed cases dating back to 1939 to identify alerting signals, latency, frequency and methods of confirmation of imputability.

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Adverse occurrence search

Adverse occurrence type

(Expand all) (Clear)

- Harm to a Recipient
- Harm to a Donor
- Harm to a Fetus or Offspring
- Risk of harm

Medical Products of Human Origin type - MPHO

(Expand all) (Clear)

- Organs
- Blood
- Cells
- Tissues
- Reproductive
- Derived medicinal products

Keywords

(searches keywords identified by the Notify editors)

Free text

(searches the text in the database cases and includes alerting signals, imputability and keywords)

Notify Library Record ID

(searches by Notify Library Record ID, for multiple records separated by commas)

Limit results 100 per page

SEARCH | Reset | Print/Save selected items | Save XLS selected items | New search

Record ID	Adverse occurrence	References
1580	**Adverse occurrence description:** Urothelial Carcinoma **Adverse occurrence type:** Harm to a Recipient => Malignancy => Kidney and urinary tract => Urothelial (transitional) cell carcinoma **MPHO type:** Organs => Liver **Time to detection:** 14 months **Alerting signals, symptoms, evidence of occurrence:** Episodes of fever and liver enzyme abnormalities. Consecutive ultrasound and CT scan revealed a 5cm hypodense lesion in the transplanted liver. **Estimated frequency:** Most recent risk assessment for urothelial carcinoma (Council of Europe, 2016). Patients with newly diagnosed invasive urothelial carcinoma are considered to represent an Unacceptable Risk for organ donation. In the case of patients with a history of urothelial carcinoma, it must be remembered that these tumors tend to be multicentric and can recur. Kidney transplantation is considered to be associated with an increased risk but the extent of this has not been classified. Similarly, potential donors with a past history of urothelial carcinoma and a disease free interval of at least 5 years should be assessed based on estimate of the probability of cure. No specific recommendations are available from the literature. **Demonstration of Imputability or Root cause:** Open liver biopsy demonstrated a clear cell tumor of urothelial origin. The same tumor had been found in one of the kidney recipients of the same donor 5 months before. **Imputability grade:** 3 Definite/Certain/Proven **Expert comments for publication:** Very unusual example of urothelial carcinoma transmission to a non-renal recipient as well as one of two renal recipients. No detailed documentation beyond routine histology regarding assignment of urothelial origin to the transmitted tumor, however the same diagnosis was given to both recipients. Liver recipient was treated successfully. Patient underwent retransplantation and chemotherapy and is free of tumor at four year followup. **Keywords:** urothelial carcinoma · transitional cell carcinoma · clear cell · histological examination · metastatic · transplantectomy · chemotherapy · fever · ultrasound · biopsy · liver · CT (computed tomography) · elevated liver enzymes · histology	1 reference

Record ID	Adverse occurrence	References
1797	**Adverse occurrence description:** Hepatitis A virus (HAV) **Adverse occurrence type:** Harm to a Recipient => Infection => Viral => Hepatatis A Virus (HAV) **MPHO type:** Organs => Combined => Multivisceral **Time to detection:** 1 year **Alerting signals, symptoms, evidence of occurrence:** Diagnosis of HAV infection in 2 healthcare workers caring for recipient 9 months after transplant; 7 year old multi-visceral organ recipient (liver, small bowel, and pancreas transplantation) had elevated liver enzymes, increased stool output first attributed to other causes; recipient had HAV in serum for over a year and stool for over 15 months but survived. **Estimated frequency:** Unknown (first reported transmission of HAV through organ transplantation) **Demonstration of Imputability or Root cause:** Genetically identical HAV RNA sequences from donor (serum), healthcare workers (serum) and multi-visceral organ recipient (serum, feces, liver and intestine biopsy specimens). The organ donor, an 8-year-old who died in a motor vehicle collision, traveled to Guatemala, a country to which HAV is endemic, 6 months before death. The heart and both kidneys of the same donor were transplanted into 3 other recipients that tested negative for HAV RNA and negative HAV IgM approximately 10 months after transplant (all previously vaccinated). **Imputability grade:** 3 Definite/Certain/Proven **Expert comments for publication:** Example of delayed recognition of transmission because of lack of precedence of pathogen being transmitted through transplant. The infectious period of the multi-visceral organ recipient is among the longest documented in a person infected with HAV, typically an acute disease. The recipient had history of vaccination but immune suppression probably blunted antibody response (role of different immunosuppression and types of organs transplanted in preventing infection transmission unknown). Vaccination of the donor might have prevented infection in the recipient and subsequent transmission to the healthcare workers. **Keywords:** HAV (hepatitis A virus) · organ transplantation · SOT (solid organ transplantation) · healthcare worker infection · multiorgan donor · multivisceral transplantation	1 reference

Search Library

Adverse occurrence searches can be performed by:

- *Adverse occurrence type*

Search by occurrence details (e.g. ONLY DONOR REACTIONS, ONLY INFECTIONS, ONLY INFECTIONS INVOLVING A PARTICULAR ORGANISM)

- *MPHO* (e.g. ONLY LIVER, ALL ORGANS, ONLY PLASMA, ALL BLOOD, etc.)
- *Keywords, free text*
- *Notify library reference ID* (UNIQUE IDENTIFIER FOR EACH DATABASE RECORD)

The result of an Incident search can be printed or saved in Excel or pdf.

Database Taxonomy

In order to facilitate a structured database search, all cases have been classified according to a predetermined set of rules. To this end, a taxonomy of two main groups was developed, the adverse occurrence types (Harm to a recipient, Harm to a donor, Harm to a fetus or offspring, Risk of harm), and the MPHO types (Organs, Blood, Cells, Tissues, Assisted Reproduction Technologies (ART). This predefined classification is further subdivided and allows searching by a single item or a combination of both groups. Figure 1 provides an extract of the taxonomy for adverse occurrence type and Figure 2 provides an extract of the taxonomy applied for MPHO type.