





### PROJECT NOTIFY

# Sharing vigilance experience and knowledge globally







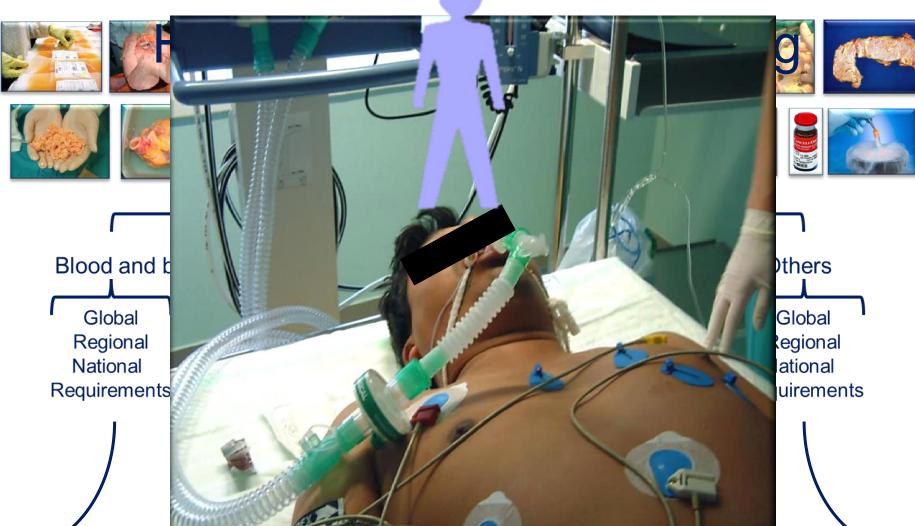
# The NOTIFY Project WHO's Initiative for Medical Products of Human Origin

















### Medical Products of Human Origin (MPHO)

- From human Donor to human Recipient
- The challenge of meeting patient needs with solidarity and reciprocity
  - Equity in donation and in allocation: relying on receiving implies willing to give
  - — →The Self-Sufficiency paradigm
  - Commitment of Society through authorities.
  - Education to donation and prevention
  - Trust through professionalism and transparency
- A common Humanity
- The need for Global governance
- The power of global V&S to improve
  - Regular practice, traceability, risk based quality management,
  - Crisis management
  - The understanding of the importance of MPHO







#### **3 Global Requirements for MPHO**

Standards of practice inherent to the Human Origin

Universal use of ISBT 128 for all MPHO



**Optimized Vigilance** and Surveillance









#### The NOTIFY project

- Mutualizing the global experience of V&S in MPHO services
  - Risk identification
  - Risk assessment
  - Risk based quality management
  - Risk education
- Associating Competent Authorities and Scientific and Professional Societies
- Promoting V&S as a crucial mechanism of quality and transparency in MPHO services
- Deserving trust



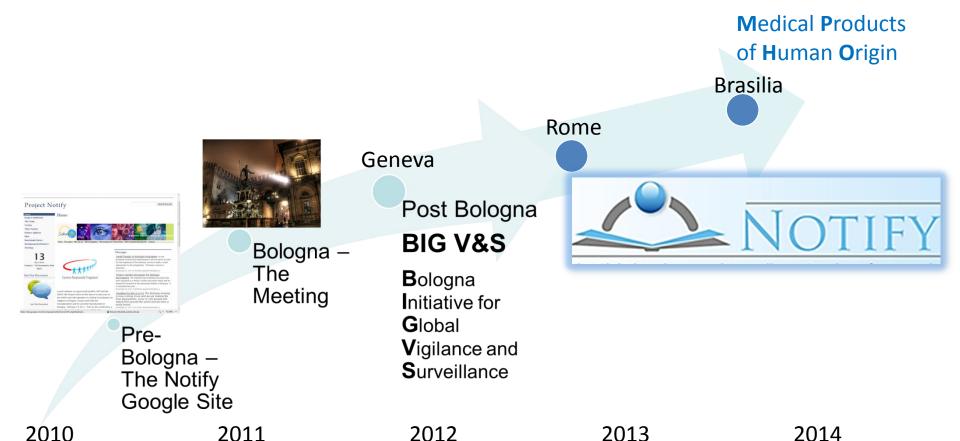
#### Centro Nazionale Trapianti

WHO Collaborating Centre on Vigilance and Surveillance for Human Cells, Tissues and Organs









# History of the NOTIFY Project







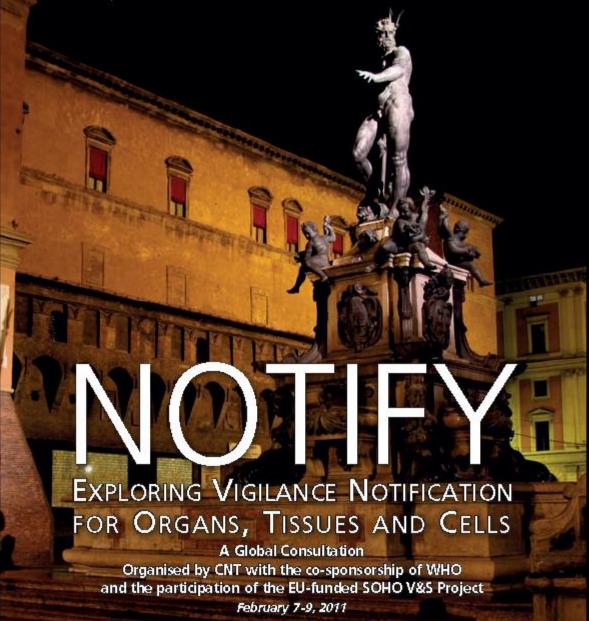
#### The Bologna Meeting Participants

- 116 attendees
- Regulators, government agencies, professional societies, international organisations, scientific and clinical experts in organ, tissue and cell transplantation and in assisted reproduction.
- 36 countries (Bulgaria, Italy, USA, Switzerland, Spain, France, Germany, Netherlands, Japan, India, Argentina, Portugal, Ireland, Denmark, Czech Republic, Lithuania, Slovenia, Australia, Brazil, Norway, Slovakia, Luxembourg, Thailand, Canada, Poland, Belgium, Singapore, Austria, Iran, South Africa, Russia, Croatia, Cyprus, Malta, Romania, Nigeria)















#### The NOTIFY Tools

- NOTIFY Website <a href="http://www.notifylibrary.org">http://www.notifylibrary.org</a>
- NOTIFY Library of didactic cases of events and reactions



- NOTIFY Booklet
- NOTIFY Journal
- NOTIFY Network for horizon scanning ECDC+ USCDC+ ...







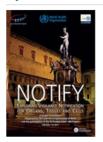
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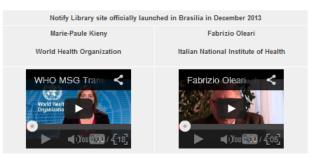


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Click on this image to download the report of the Bologna Notify Meeting and 5 didactic papers developed by the Notify experts





#### THE NOTIFY LIBRARY OF ADVERSE EVENT AND REACTION TYPES

Welcome to the Notify Library site where experts from across the globe collaborate to share didactic information on documented adverse outcomes associated with the application of human organs, tissues and cells. We aim to support continued improvements in safety and efficacy in transplantation and in assisted reproduction.

GENERAL PUBLIC

HEALTH PROFESSIONALS CLICK HERE

HEALTH AUTHORITIES CLICK HERE



NEWS: > Notify Libr

Do you have
Questions?
Corrections?
Additions?
Suggestions?
Please contact us at
notifylibrary@iss.it







A database of all **types** of severe adverse events and reactions that have been reported arising from procurement and processing to clinical application of cells, tissues and organs for transplantation as well as of medical products of human origin used in assisted reproduction technologies.

- 1. A reference for professionals focused on diagnostic and investigation
- 2. but also providing evidence for donor selection,
- 3. A source of information for candidate recipients and living donors
- 4. A database for risk mapping and risk based quality management



Recipient Adverse Reactions -





Mail Calendar Documents Photos Reader Web more ▼ deirdre.fehily@iss.it | Settings ▼ | Sign out Google docs Group 3 Worksheet Private to dmstrong2 + 94 more Saved seconds ago Saved File Edit View Insert Format Form Tools Help D Demonstration of Imputability References Typical alerting signal (i.e. first (how was it confirmed that the **Known Reaction** symptoms/triggers/laboratory findings donation/transplant/application Related to etc.) caused the reaction?) Group 6-10 9 Delayed engraftment delayed hematological graft recovery EUSTITE criteria 9 EUSTITE V&S, 2010 10 11 Infection/Sepsis (product-related) 12 fever; sustained hypotension; nausea; Positive product sterility testing with vomiting; shock; positive surveillance Bacterial infection/sepsis the same pathogen blood culture 6 EUSTITE V&S, 2010 13 fever, interstitial pneumonia, flu-like Viral infection (donor-transmitted) Positive donor testing (same virus) 6 symptoms; positive serology or NAT Sun et al, 2009 14 DNA sequence analysis of Symptoms consistent with acute HBV contaminant matched DNA of 4 bone Hawkins, et al, 1996 (see infection; HBV in multiple recipients of Viral infection (HBV) lab contamination marrow recipients from the Tedder et al 1995 for clinical product from same facility contaminated storage tank 6.8 information) 15 fever, flu-like symtoms, fungal Positive product fungal testing (same septicemia; blood culture positive for Fungal infection (product-related) specie) fungal elements 6 Mele. et al. 2005: 16 Mori T, Kato J, highly suspected with CMV-negative diarrhea, interstitial recipient transplanted with CMV-CMV (new) positive donor, in absence of Civivpneumonia/pneumonitis, fever; positive Over 1,700 CMV PCR in prior CMV-negative recipient positive blood transfusion or other exosures references in total 17 Toxoplasma sepsis, CD34 selected Sepsis at day +69, death FUSTITE criteria cells, autologous Endnote Library 18 BMTx from recipient's sibiling who was serologically positive for syphilis; Syphilis Syphilis seroconversion; day +63 recipient had TPHA that went down with treatment

Donor--Apheresis

References

🚱 Internet | Modalità protetta: attivata

Known Reaction

**100%** 

Donor--Marrow

Adverse Events







Group 2
Lists Reactions
and Events for
Tissues
(non ocular)

Group 3
Lists Reactions
and Events for
HSC

Group 4
Lists Reactions
and Events for
Ocular Tissues

Group 5
Lists Reactions and
Events for
Gametes and
Embryos

Group 6

Master Sheet
Infections

Group 7

Master Sheet

Malignancy

Group 8

Master Sheet
Characteristics
and Handling

Group 9

Master Sheet

Clinical

Practice







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Master Sheet

Clinical

Practice







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Group 1 **List Reactions** and Events in **Organs** 

Group 2 **Lists Reactions** and Events for Tissues (non ocular)

Group 3 **Lists Reactions** and Events for HSC

Group 4 **Lists Reactions** and Events for **Ocular Tissues** 

Group 5 Lists Reactions and **Events for** Gametes and **Embryos** 

Group 6 **Master Sheet** Infections



Group 7 **Master Sheet** Malignancy



Group 8 **Master Sheet** Characteristics and Handling



Group 9 **Master Sheet Clinical Practice Errors** 





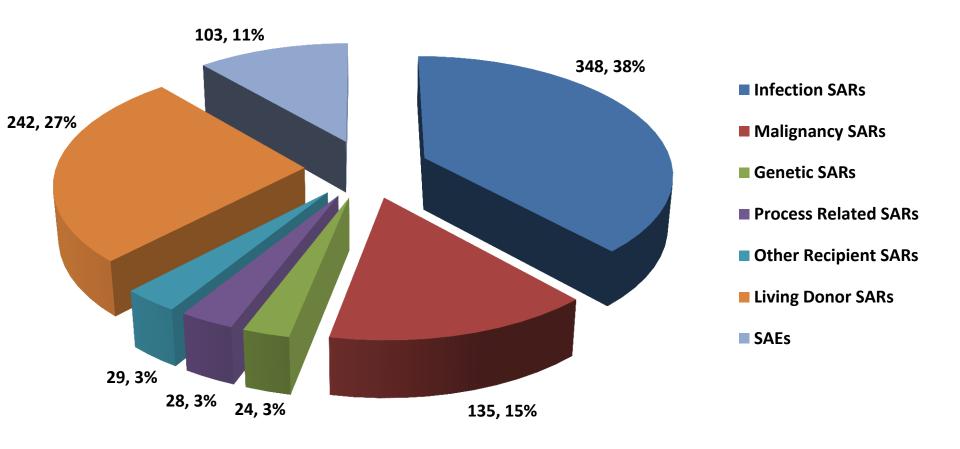






### Uploaded records by INCIDENT type

(n. 909)



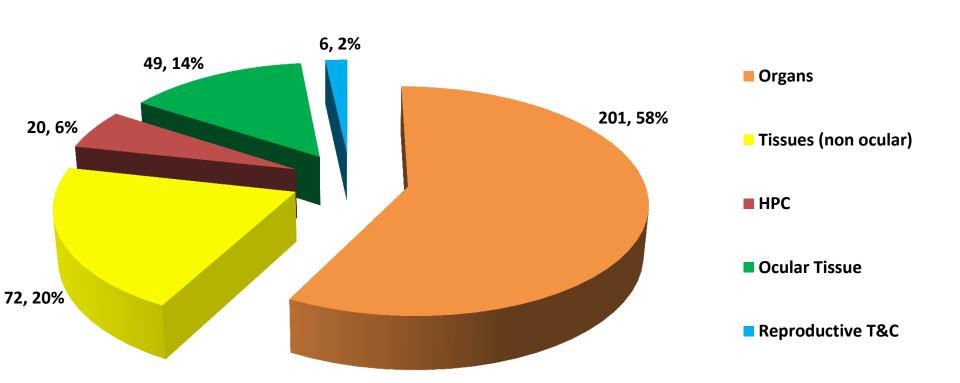






# Donor transmitted INFECTIONS by SUBSTANCE type

(n. 348)



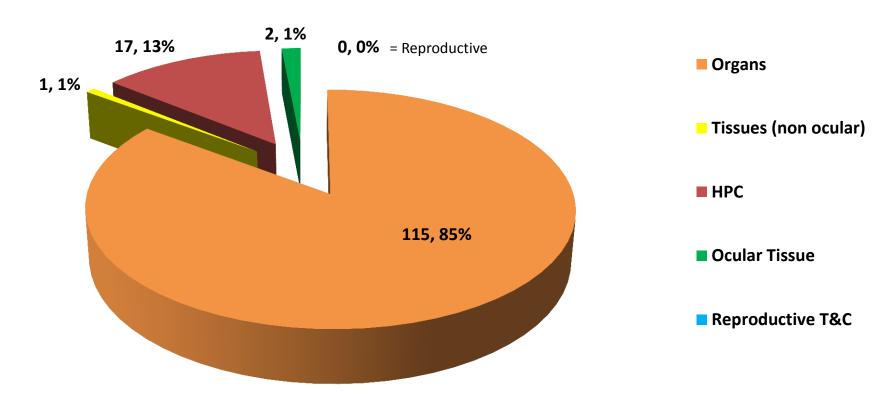






# Donor transmitted MALIGNANCIES by SUBSTANCE type

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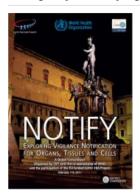
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Click on this image to download the report of the Bologna Notify Meeting and 5 didactic papers developed by the Notify experts



> over 400 new records were uploaded on April 29th. Database now has > 900 records.

#### THE NOTIFY LIBRARY OF ADVERSE EVENT AND REACTION TYPES

Welcome to the Notify Library site where experts from across the globe collaborate to share didactic information on documented adverse outcomes associated with the application of human organs, tissues and cells. We aim to support continued improvements in safety and efficacy in transplantation and is assisted reproduction.



The database is continually updated and to date 100% of the cases collected (until 2010) by the BIG V&S were examined and uploaded. The next phase of the Notify Project will be to collect new cases (from 2010 to present) and increase the database volume. The search engine is accessible without username and password.



#### Centro Nazionale Trapianti



Do you have

Questions? Corrections? Additions? Suggestions?

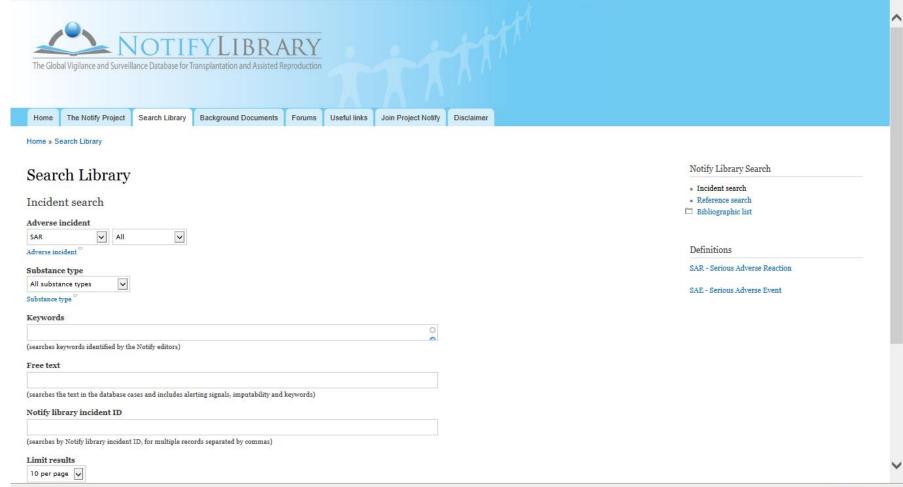
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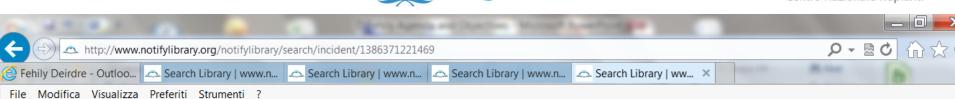












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■ Incident ID	Incident description	Incident type	Substance type	Latency (SAR) When detected (SAE)	Alerting signal (SAR) How detected (SAE)	Frequency data and estimates	Demonstration of imputability (SAR)  Root cause (SAE)	Keywords	References		
<u> </u>	Human immunodeficiency virus (HIV)	SAR => Recipient => Infection => Viral => HIV	Tissues (non- Ocular) => Allogeneio => Musculoskeletal => Bone	3 weeks	Fever, sweats, enlarged nodes, diarrhea, N/V. Frozen femoral head used in scoliosis surgery		Proven. Live donor (Injecting drug user, large nodes predonation) and recipient developed AIDS after 40 months	HIV (human immunodeficiency virus)     femoral head     bone transplantation     AIDS (acquired immunodeficiency syndrome)	1 reference <sup>™</sup>		
☐ 202	Human Immunodeficiency virus (HIV)	SAR => Recipient => Infection => Viral => HIV	Organs => Liver	8 days	Lymphocytopenia/Aplastic anemia/Positive test		HIV p24 Ag/Ab	HIV (human immunodeficiency virus)     liver transplantation     aplastic anemia     lymphopenia	1 reference		
☐ 567	Human Immunodeficiency Virus (HIV)	SAR => Recipient => Infection => Viral => HIV	Organs => Liver	10 - 148 days	Positive test		HIV p24 Ag/Ab	HIV (human immunodeficiency virus) liver transplant donor transmission recipient infection	2 references <sup>C</sup>		







































# 'Inverse' search

Search

Reset

Print/Save selected items

New search

Found 285 records (up to page top).

Reference ID	Reference	Incidents
1119	A new arenavirus in a cluster of fatal transplant-associated diseases., Palacios, G., Druce J., Du L., Tran T., Birch C., Briese T., Conlan S., Quan P. L., Hui J., Marshall J., et al., N Engl J Med, Mar, Volume 358, Issue 10, p.991 - 8, (2008) DOI Google Scholar BibTex RTF Tagged MARC XML RIS	2 incidents
741	Successful transplantation of a liver graft with a calcified hydatid cyst after back-table resection, Jimenez Romero, C., Moreno Gonzalez E., Garcia Garcia I., Loinaz Segurola C., Gonzalez Pinto I., Gomez Sanz R., Hernandez-Gallardo D., and Moreno Sanz C., Transplantation, Oct 27, Volume 60, Issue 8, p.883 - 4, (1995)  Google Scholar BibTex RTF Tagged MARC XML RIS	1 incident
155	Organ selection in intensive care: transplantation of a liver allograft, including calcified cyst of Echinococcus granularis, Bein, T., Haerty W., Haller M., Forst H., and Pratschke E., Intensive care medicine, Volume 19, Issue 3, p.182, (1993) Google Scholar BibTex RTF Tagged MARC XML RIS	1 incident
577	Rapidly progressive hepatic alveolar echinococcosis in an ABO-incompatible renal transplant recipient, Geyer, M., Wilpert J., Wiech T., Theilacker C., Stubanus M., Kramer-Zucker A., Fischer K. G., Drognitz O., Frydrychowicz A., Kern W., et al., Transpl Infect Dis, Oct 26, (2010) DOI Google Scholar BibTex RTF Tagged MARC XML RIS	1 incident
890	Donor Infection and Transmission to the Recipient of a Solid Allograft, Len, O., Gavaldà J., Blanes M., Montejo M., Juan R. S., Moreno A., Carratalà J., De La Torre-Cisneros J., Bou G., Cordero E., et al., American Journal of Transplantation, Volume 8, Issue 11, p.2420 - 2425, (2008)  DOI Google Scholar BibTex RTF Tagged MARC XML RIS	7 incidents
677	Hepatic and intestinal schistosomiasis after orthotopic liver transplant, Hoare, M., Gelson W. T., Davies S. E., Curran M., and Alexander G. J., Liver Transpl, Dec, Volume 11, Issue 12, p.1603 - 7, (2005)  DOI Google Scholar BibTex RTF Tagged MARC XML RIS	1 incident
1339	Donor-to-host transmission of bacterial and fungal infections in lung transplantation, Ruiz, I., Gavaida J., Monforte V., Len O., Roman A., Bravo C., Ferrer A., Tenorio L., Roman F., Maestre J., et al., American journal of transplantation and the American Society of Transplantation and	7 incidents
1723	Fatal pneumonia caused by Panton-Valentine Leucocidine-positive methicillin-resistant Staphylococcus aureus (PVL-MRSA) transmitted from a healthy donor in living-donor liver transplantation, Obed, A., Schnitzbauer A. A., Bein T., Lehn N., Linde H. J., and Schlitt H. J., Transplantation, Jan 15, Volume 81, Issue 1, United States, p.121 - 124, (2006)  Google Scholar BibTex RTF Tagged MARC XML RIS	2 incidents
1326	Strongyloides stercoralis hyperinfection transmitted by liver allograft in a transplant recipient, Rodriguez-Hernandez, M. J., Ruiz-Perez-Pipson M., Canas E., Bernal C., and Gavilan F., Am J Transplant, Nov, Volume 9, Issue 11, p.2637 - 40, (2009)  DOI Google Scholar BibTex RTF Tagged MARC XML RIS	2 incidents
335	Posttransplant malaria: first case of transmission of Plasmodium falciparum from a white multiorgan donor to four recipients., Chiche, L., Lessge A., Duhamel C., Salame E., Malet M., Samba D., Segol P., and Treilhaud M., Transplantation, Jan, Volume 75, Issue 1, p.166 - 8, (2003)  DOI Google Scholar BibTex RTF Tagged MARC XML RIS	6 incidents

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	Reference ID	Reference	Incidents
	1119	A new arenavirus in a cluster of fatal transplant-associated diseases., Palacios, G., Druce J., Du L., Tran T., Birch C., Briese T., Conlan S., Quan P. L., Hui J., Marshall J., et al., N Engl J Med, Mar, Volume 358, Issue 10, p.991 - 8, (2008) DOI Google Scholar BibTex RTF Tagged MARC XML RIS	2 incidents
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	155	Organ selection in intensive care: transplantation of a fiver allograft, including calcified cyst of Echinococcus granularis, Bein, T., Haerty W., Halle 1. For 14 - Enterobacter cloacae - Kidney medicine, Volume 19, Issue 3, p. 182.  (1993) Google Scholar BibTex RTF Tagged MARC XML RIS  18 - Escherichia coli (including Multidrug-Resistant) - Liver  25 - Staphylococcus aureus Methicillin-Sensitive (MSSA) - Lung	1 incident
	577	Rapidly progressive hepatic alveolar echinococcosis in an ABO-incompatible renal transplant recipient, Geyer, M., Wilpert J., Wiech T., Theilack r C W., et al., Transpl Infect Dis, Oct 26, (2010) DOI Google Scholar BibTex RTF Tagged MARC XML RIS  188 - Morganella morganii - Kidney 616 - Escherichia coli (including Multidrug-Resistant) - Kidney 618 - Klebsiella - Lung 619 - Klebsiella - Kidney	1 incident
	890	Denoy Infaction and Transmission to the Recipient of a Solid Allowards Len O. Gaveldà I. Blancs M. Montein M. Juan R.S. Morenn A. Carretalà	7 incidents
	677	Hepatic and intestinal schistosomiasis after orthotopic liver transplant, Hoare, M., Gelson W. T., Davies S. E., Curran M., and Alexander G. J., Liver Transpl, Dec, Volume 11, 15 use 12, p.1803 - 7, (2005)  DOI: Google Scholar BibTex RTF Tagged MARC XML RIS	1 incident
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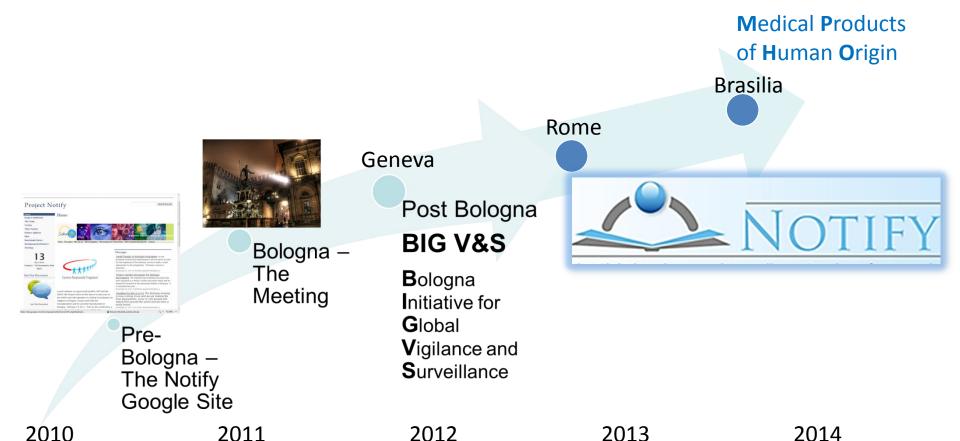
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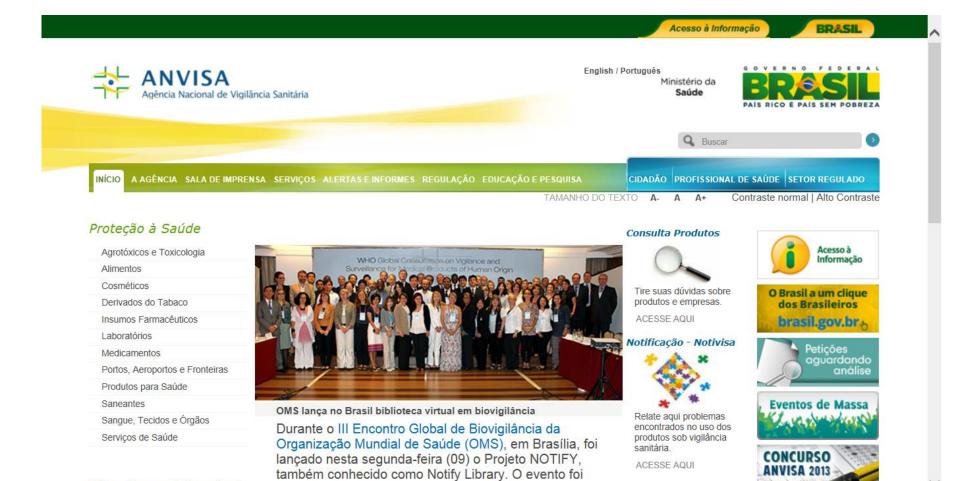
# History of the NOTIFY Project







# Notify Consultation Brasilia December 2013









#### Brasilia Participants (Blood)

- Arlinke Bokhorst
- Ludo Muylle
- Jorge Condeco
- Matt Kuehnert
- Luc Noel
- Mike Strong
- Paul Ashford

- Anuj Sharma
- Ghazi Saleh Saeed
- Geni Camara
- Daniel de Freitas
- Deirdre Fehily
- Barbee Whitaker







# Next steps Blood as MPHO in Notify Library

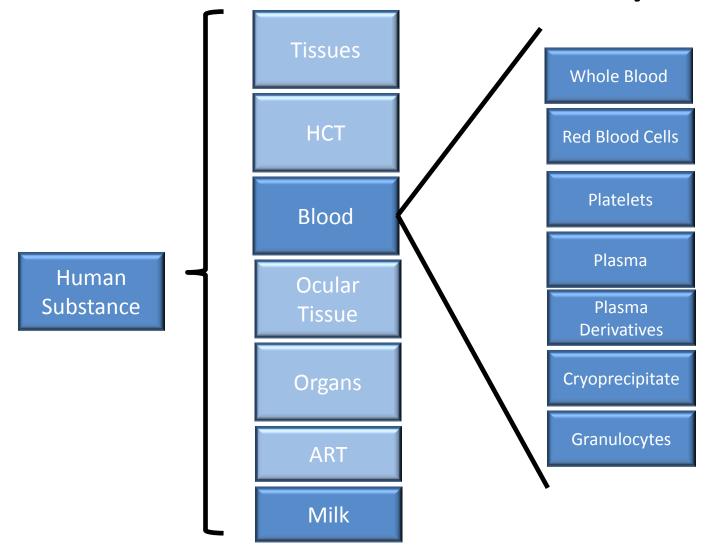
- Share with International Haemovigilance Network and the Working Party of ISBT
- Confirm blood taxonomy
  - MPHO Substance
  - Occurrence/Incident/Event Categories







# **Substance Taxonomy**









# **Blood Taxonomy Attributes**

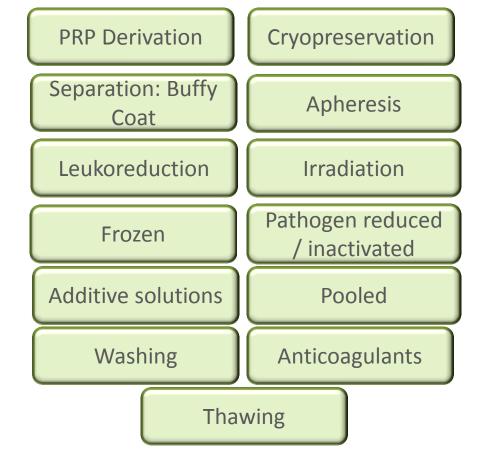
Donor to Recipient
 Relationship Attributes

Autologous

Allogeneic:
Single Donor

Allogeneic:
Multiple Donor

Processing Attributes









#### **Event Categorization**

- Incident or Event
- SAE
- Occurrence
- SAR
- Reaction
- Harm or No Harm
- Recipient or Donor







#### Recipient (Patient) Harm

#### **Transfusion Reaction**

- Allergic Reaction
- Acute Hemolytic Reaction: immune
  - ABO
  - Other alloantibodies
- Acute Hemolytic Reaction: nonimmune
- Delayed Hemolytic Reaction: immune
  - ABO
  - Other alloantibodies
- Delayed Hemolytic Reaction: nonimmune
- TRALI
- TACO
- TAD

- Delayed Serologic Reaction
- Post Transfusion Purpura (PTP)
- Transfusion Associated Graft versus
   Host Disease
- Febrile Reaction
- Hypotensive Reaction
- Hypertensive Reaction
- Hemosiderosis
- Transfusion Associated Sepsis
- Under transfusion
- Other (e.g. air embolism, hyperkalemia, other metabolic reactions)







### SARE Taxonomy: Donor Harm\*

#### Vasovagal Reactions

- No Loss of Consciousness (LOC)
- LOC
- LOC (complicated)
- Location on site
- Location off site

#### Allergic

- Local
- Systemic
- Anaphylaxis

#### Local Injury related to needle

- Nerve Irritation
- Hematoma/Bruise
- Arterial Puncture
- Painful Arm
- Major vessel injury
- Infection
- Bleeding

#### Apheresis Infusion Reactions

- Citrate
- Hemolysis
- Air Embolus

Other

<sup>\*</sup>Harmonized Definitions







### Adverse Occurrences, eg.

- Loss of highly matched or autologous material
- Gamete or embryo mix-up
- Loss of suitable organ
- Loss of large quantity of MPOH (unmatched tissues or cells)
- Unsuitable tissue or cells released for clinical use and/or applied clinically







#### Adverse Occurrences: Blood

- Wrong blood in tube or Incorrect Blood Component Transfused
- Unsuitable <u>Blood</u> released for clinical use and/or applied clinically
- Loss of highly matched or autologous material
- Loss of large quantity of MPOH (unmatched tissues or cells): equipment failures
- Others...







# Next steps Blood as MPHO in Notify Library

- Share with International Haemovigilance Network and the Working Party of ISBT
- Confirm taxonomy
- Develop a reporting form
- Pilot test with experts
- Invite Participation
- Establish editorial groups
  - Published literature
  - Other instructive or exemplary cases
- Incorporate into Notify using agreed upon taxonomy







#### www.notifylibrary.org

### Thank you!

Barbee Whitaker, PhD
Director Center for Patient Safety
AABB