WHO CONSULTATION ON VIGILANCE AND SURVEILLANCE FOR MEDICAL PRODUCTS OF HUMAN ORIGIN

Strategy for the NOTIFY project as a global V&S supporting system

REPORT

1-2 DECEMBER 2015

FOREWORD

FOREWARD

This report summarize the discussion and decision taken during the NOTIFY Project Strategic meeting held in Bologna (Italy) from December 1st to 2nd 2015. The meeting was convened by the World Health Organization (WHO) in collaboration with the Italian National Transplantation Centre, “Centro Nazionale Trapianti” (CNT), the WHO Collaborating Centre on Vigilance and Surveillance for Cell, Tissue and Organ Transplantation.

We wish to express our gratitude to Organitzcaó Catalana de Trasplantaments (OCATT) and the Organización Nacional de Trasplantes (ONT) for their support as Competent Authorities collaborating in this project.

The objective of this Strategic meeting was to share with the six WHO Regions the aims and challenges of the Notify Project in order to develop V&S systems worldwide, building a global network to detect, prevent and register any adverse event related with the use of MPHO. The scope of the meeting was also to define the strategy, roadmap and work plan of the Notify Project as a main part of the WHO initiative in MPHO.

This Strategic meeting was prepared with the invaluable help of the CNT team.

This report represents the views of the participants and not necessarily those of WHO. All the participants in the consultation should be thanked for their active participation and their will to achieve consensus. The Secretariat owes special thanks to Alessandro Nanni Costa, who judiciously chaired the meeting, to the rapporteur, Elmi Muller and Deidre Fehily, and to the whole operational team for their thorough work.

José Ramón Núñez Peña
HIS/SDS
WHO Headquarters

1. Introduction

1.1 Welcome collaborating centre: CNT

The meeting is opened by J. R. Nuñez (WHO) and Alessandro Nanni Costa (CNT). Dr Alessandro Nanni Costa welcomed the participants to the meeting: Strategy for the Notify project as a global V&S supporting system highlighting the importance of having together editorial groups members, representatives of the different WHO regions and the operational team working on the Notify Project.

1.2 Introduction of participants, election for Chair and Rapporteurs

For the full list of participants, and excused see appendix 1.

Dr. Luc Noel was elected chair of the meeting; Elmi Muler and Deirdre Fehily were elected as rapporteuses.

2. Vigilance and Surveillance as a key element of the EB 136 decision.

Jose Ramon Nuñez presented a presentation based on MPHO mandate, Notify Project role and general outcomes that should be achieved during this meeting.

2.1 Objectives of the meeting. Jose Ramon Nuñez

The objective of the meeting is to share with the six WHO Regions the aims and challenges of the Notify Project in order to develop V&S systems worldwide building a global network to detect, prevent and register any adverse event related with the use of MPHO. It's also a priority during the meeting to define the strategy, roadmap and work plan of the Notify Project as a main part of the WHO initiative in MPHO. In order to achieve these challenges it will be important to analyse the regional's situation of MPHO and which are the key elements in each WHO region to launch MPHO and V&S worldwide, including the competent authorities, professionals and individuals that should be involved. Summary of the objectives per meeting day:

2.2 The MPHO mandate roadmap. **Jose Ramon Nuñez**

MPHO include all the substances derived wholly or in part from the human body and intended for human application. MPHO have common ethical, safety and risk concerns to take into account. The fundamental ethical criterion for all these substances is respect for the human being, to their inalienable rights and the to the person's dignity.

MPHO initiative is a new cross-organization aiming to recognize the singularities of MPHO and to explore self-sufficiency and the non-commercial nature of tissue of human origin and build Member States consensus.

Roadmap mandate:
May **2013** Programme Budget 2014–2015. Headquarter deliverable: "Conduct global consultations to explore self-sufficiency and the non-commercial nature of tissues of human origin and build Member State consensus "
On **2013** also ISBT/TTS/ WBMT associations met in Geneve to join the initiative.
September **2014**: First expert meeting in Bologna to develop principles for safe practice with MPHO.
On **2014**, Experts meeting: Italy, Lithuania, Malta, Slovenia and Spain had a meeting on the principles of global consensus on donation of blood and other products of human origin.
2015 EB 136 decision: Request the Director-general to convene consultations with Member States and international partners to support the development of global consensus on guiding ethical principles for the donation and management of the mentioned MPHO, good governance mechanisms; and common tools to ensure quality, safety and traceability, as well as equitable access and availability as applicable, to result in a document to be submitted, to the WHA for consideration.

Work to be presented in 2017 (17th WHA):
- Member states and international partners need a global consensus document
- It needs to address good governance, vigilance and surveillance as well as equitable access
- It needs to be a draft decision by all countries using the guiding principles to recognize the dignity of a donor and the safety of both donors and recipients
- This document is to be presented at the 17th World Health Assembly
- It needs to be at the Executive Board by Jan 2017 which means all documents need to be submitted by Nov 2016

Document outline:

1. Global consensus on ethical principles
2. Good governance (Global overview of vigilance systems)
3. Quality and safety (Role of Notify project could be addressed and how to maximise this now to public/professionals as well as a marketing strategy)
4. Equitable access

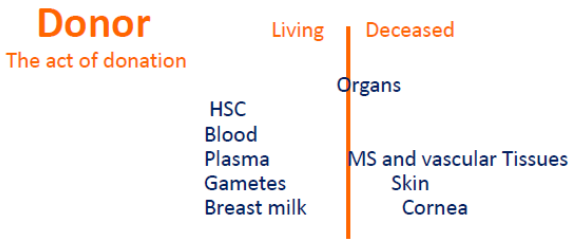
2.3 V&S, a key to the effective implementation of the MPHO consensus. **Luc Noel**

Luc Noel started off thanking Dr Nanni Costa for his work on this project.

2.3.1 What is Medical Products of Human Origin (MPHO)?

Include all substances derived wholly or in part from the human body and intended for clinical application. MPHO have a common origin and destination: human bodies destined to recipients patients. MPHO require Donors.

There are some commonalities to MPHO: risk inherent to human origin and destination and societal responsibility necessary for enough donations.
The act of donation defines the product as a medical product of human origin (MPHO)



Society has one hand the act of violence and on the otherhand the act of Health which involves:

1. Dignity
2. Human Rights
3. Global Human value
4. "Caring"

Global Human values are safety as well as ethical risk: MPHO EPITOMIZE GLOBAL HUMAN VALUES

Global
Global circulation of people and MPHO
Safety Risks (transmissible diseases, lack of access but also human errors) and
Ethical Risks (abuse and exploitation of individuals and society) are universal

Values
Self Sufficiency in MPHO at Global level to meet all needs and protect donors can only be based on solidarity and equity through a societal commitment involving the public at large

MPHO, an exceptional class of medical products reflecting conceptions of humanity, an opportunity

- to demonstrate human values and
- to contribute to the beterment of societies

2.3.2 Vigilance and Surveillance (V+S)

V+S is a cooperative system with a wide endeavour that aims for identifying as well as anticipating adverse event (AE) occurrences from donor to recipient follow-up of products and practices, therefore contributing to the improvement of individual and public health.

We learned a lot from blood Transfusion (BT). BT has AE's and this driving force for a lot of this transmissible disease.
Haemovigilance shaped V+S for MPHO:

- brought together production + clinical application
- shaped triangle relationship between the operator, health authority and clinician
- include clinical monitoring of recipient and donors
- extended to near-misses and AE without harm /revealing risk
- inspired Risk Management
- unearthed diversity of AE's

- interface with other vigilances: pharmaco device
- diversity of natural heamovigilance systems.

WHO AIDE-MEMOIRE

Haemovigilance is a set of surveillance procedures covering the entire transfusion chain, from the donation and processing of blood and its components, to their provision and transfusion to patients and their follow-up. Haemovigilance includes the monitoring, reporting, investigation and analysis of adverse events related to the donation, processing and transfusion of blood, as well as the development and implementation of recommendations to prevent their occurrence or recurrence.

Hemovigilance vector of progress in low income countries because structural deficiency, fragmentation, lack of oversight is more prevalent in these places. V & S helps by getting:

1. reliable data
2. roles
3. responsibilities
4. enhance communication

↓

Need for global development – Tool needs to be better used internationally

↓

This is a national responsibility also for developing world:

1. Laws change from country to country
2. Legislation in Africa
3. Policy
4. Plans
5. Governmental oversight
6. Dialogue clinical/oversight/pt

2.3.3 Notify and MPHO

The concept of Medical Products of Human Origin, underlining their exceptional nature, has the potential to renew the understanding of issues associated to MPHO and streamline their management at national level.

It will strengthen Member States' commitment to meet national responsibilities to satisfy all needs, protect donors and recipients and participate in the global effort for safety and quality through V&S.

The WHO EB136(2) Decision is a significant opportunity which was made in Jan 2015 Request Director General to convene consultation with members status/international partners:

2 Global consensus on ethical principles at donation/management MPHO
3 Need to review guiding principles
4 Strongly supported by professional societies who are in official relation to WHO
5 Recognition of MPHO with their requirements
6 Global legally binding instruments – is reachable if carefully explored

Good Governance Mechanisms and Existing Tools

1. Legal - Council of Europe Convention against trafficking Human Origins

2. Research/Education – International Professional Societies and International Scientific Journals
3. Nomenclature/Coding – ICCBBAA and code ISBT 128
4. Global Observatories – held by WHO
    - Blood safety
    - Donation & Transplant
    - Hematopoietic Stem cells
5. Ethical monitoring/advocacy – Declaration of Istanbul (DICG)
6. V & S – Notify project

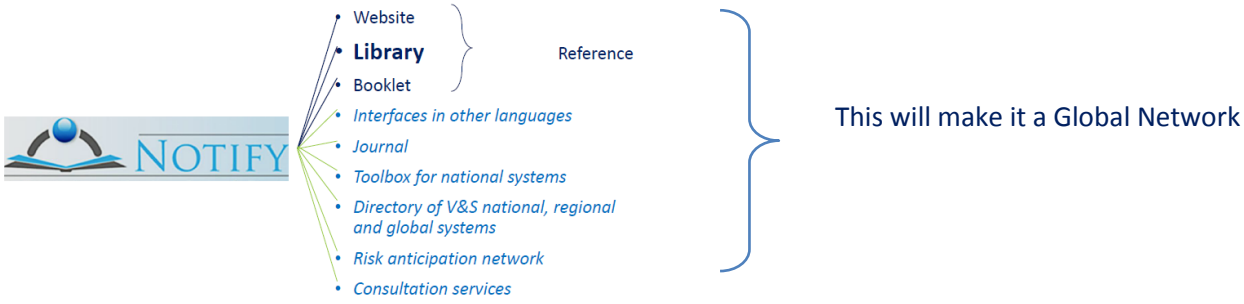
The challenge is to find resources. Current funding comes from Government Organization, by sources of income like Journals and Scientific Society. WHA will need to be advised on resources for funding.

ICCBBA is a model of funding for a global tool and service:

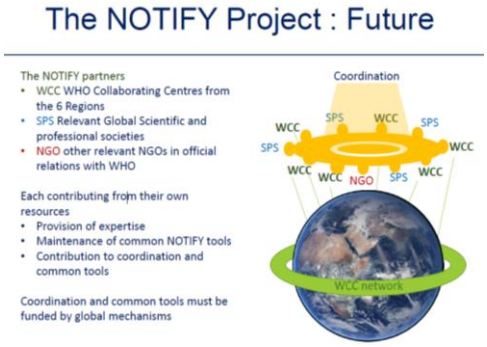
- ISBT128 is a global nomeclative and codes that trace in >4600 facilities and 75 countries
- Has >250 volunteer experts
- ICCBBA has 9 people on staff
- Funded from fees chartered for use of ISBT128
- Annual budget USS 1,4 million

Notify currently consists of the following:

To promote the use of V&S in the provision and clinical application of medical products of human origin and to maximize at global level the benefits to be realized through effective V&S.



A global network of collaborative need to join the current Notify group. This will mean that regulatory agencies, national MPHO operators, public health CDC's networks for risk detection etc can all come together with their own specific expertise and funding. Also structured collaboration with global relevant scientific and Professional societies coordinated through teleconferences.



2.3.4 Communication

Notify must continue strengthening its role of reference but also develop a role of communication promoter across MPHO stakeholders through Networks of Notify partners and news sharing through website, journals and updates in congresses.
Notify could become a brand identifying communication on adverse occurrences translating in opportunities to progress.

The Gains for the Global Community are:

- Transparency V & S extending into clinical trials/allogeneic cellular therapy
- Global registry of pharmacovigilance safety through better communication and alertness quality of MPHO and related services
- Opposition to trafficking, exploitation and inequity with MPHO
- Trust of the public and therefore donations
- Boost to the development of MPHO services in LMIC through a renewed global dynamics, data, advocacy, access to models
- Transparency and V&S sharing inherent to activities with MPHO extending to clinical trials e.g. allogenic cellular therapies and advanced therapies with collaboration with pharmacovigilance

2.3.5 Regional Consultation

Preparation of regional consultations to make the best of the opportunity given by Decision EB136(2)

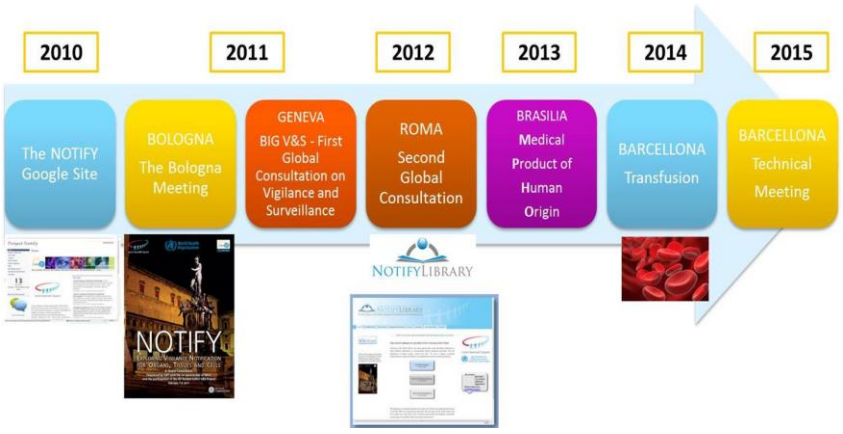
- Regional contexts and specificities to influence proposals on principles and tools
- Regional participation in NOTIFY as a support to bringing together the various stakeholders in MPHO and progress at regional level
- Conversely identification of the most relevant regional partner(s) for NOTIFY to ensure global covera

3. Update Notify project

3.1 The Notify project as global V&S Supporting System: main components and objectives–Fehily /Petrisli

Objectives of Notify Project: To promote V & S in provision of clinical applications of MPHO and to maximize global level of benefits to be realized through the lessons of vigilance

3.1.1 History



2010: Notify Google site
2011: Bologna – International Exploratory Meeting – gathering to produce a publication
2011: Geneva - Big V & S (Bologan initiative for Global V & S): organs/tissues/cells (No blood)
2012: Rome website launched – decided to do a searchable database
2013: Brazilia: Became MPHO (Medical products of human origin)
2015: Barcelona: Notify library started
2015: Bologna: MPHO also moving ahead under initiative of Luc/José at WHO

3.1.2 Why vigilance?

To talk about need of safety and quality is not enough. Vigilance is a didactic tool for safety and quality system for:

1. Process of validation (design qualification, installation qualification etc.)
2. People respond better if they hear something that happened for instance – this happened in Ireland last week
   - Device to check Hb used but was not validated for low Hb
   - 2x *donors* with Hb < 7 → both got reading > 12 → both donors needed blood
   - Device was not validated if Hb < 10

Practical example of vigilance which gives people opportunity to understand this better.

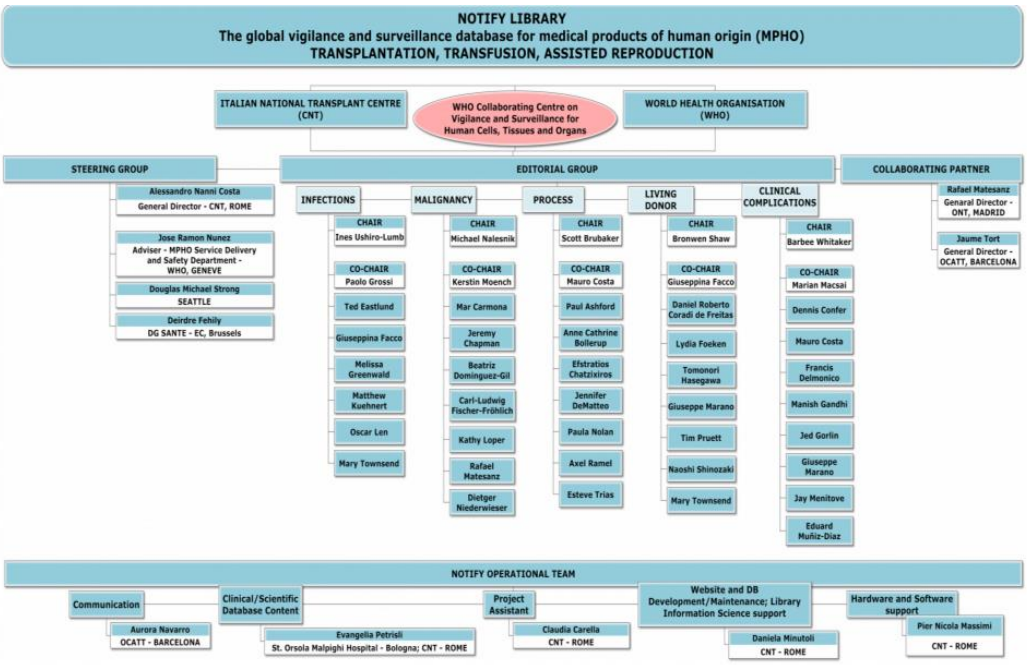
3.1.3 Partners

The NOTIFY project relies on collaborations with institutions, national health authorities and relevant scientific and professional societies, as well as with individual experts. The NOTIFY Partners are promoting the use of V&S for MPHOs and contribute to the development and management of tools for global V&S.

3.1.4 Components: Website, Library, Booklet

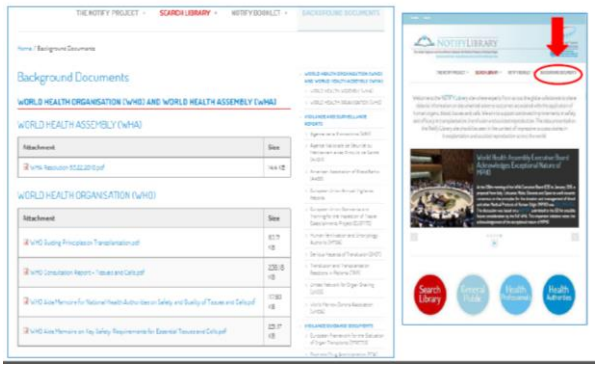
Website components:

- Front page (news), interviews, useful links, global consultations information.
- Organigram



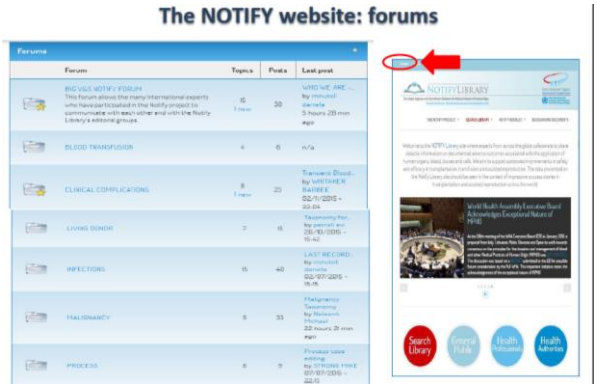
- Background documents: Vigilance Reports and Guidance Documents

The NOTIFY website: Background documents



- Forums in order to increase in activity levels, exchange ideas and make decisions

The NOTIFY website: forums



- Public information: Concerns that it's too negative. This should be explained to public (This part of the Library needs to be improved)

The NOTIFY website: general public section

The website is currently laid out according to taxonomy – there are two different ways to do this. It can be done according to adverse events or according to MPHO classification (Figure 1).

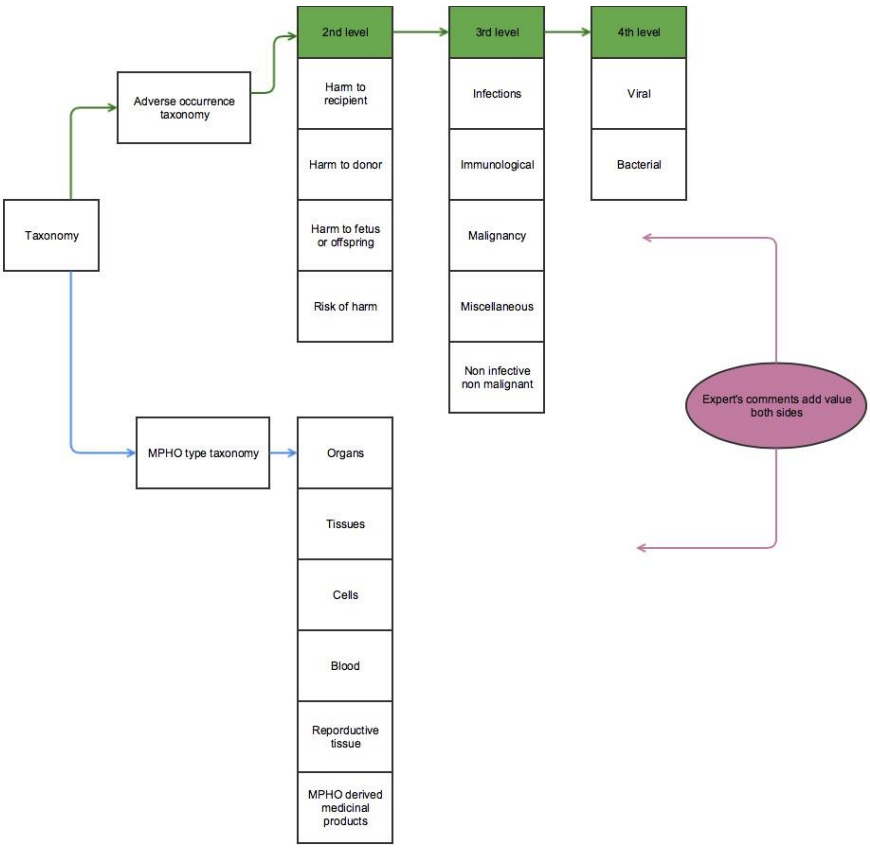
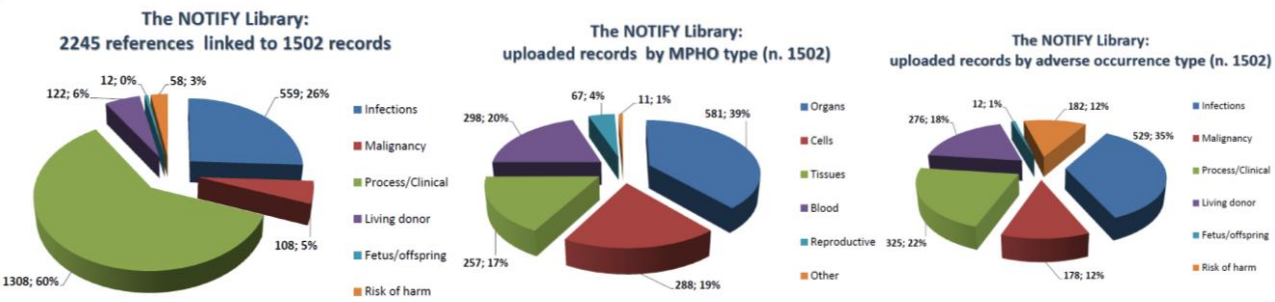
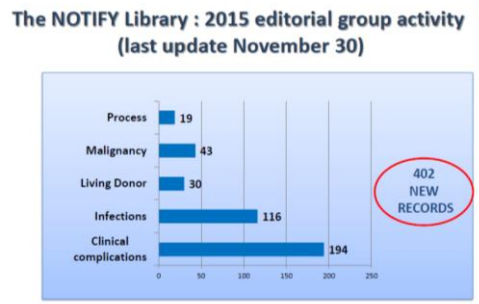


Figure 1: Current website layout options according to taxonomy

<u>Current website library hits (dec 2015)</u>:

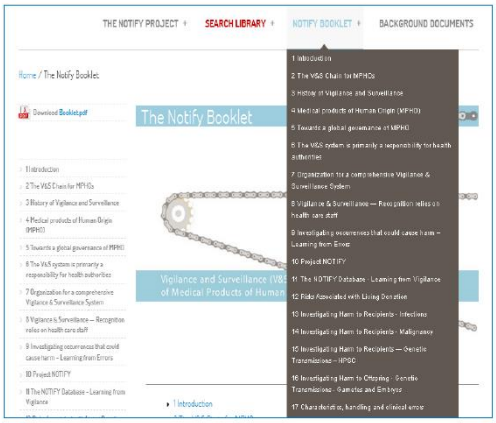


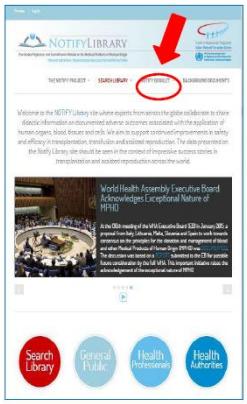


- Library

  Online publically accessible database of **didactic cases of adverse occurrences** collected and analyzed by dedicated editorial groups of international experts, regulators and clinicians. From **procurement** and **processing** to **clinical application** of blood, organs, tissues and cells used in transfusion, transplantation and assisted reproduction. **Linked to their source reference**: literature review (published articles in scientific journals and/or books), case reports from regulatory or professional vigilance programmes (grey literature). It covers all the MPHO – definition of issues still a problem because different organizations use different categories

- Booklet

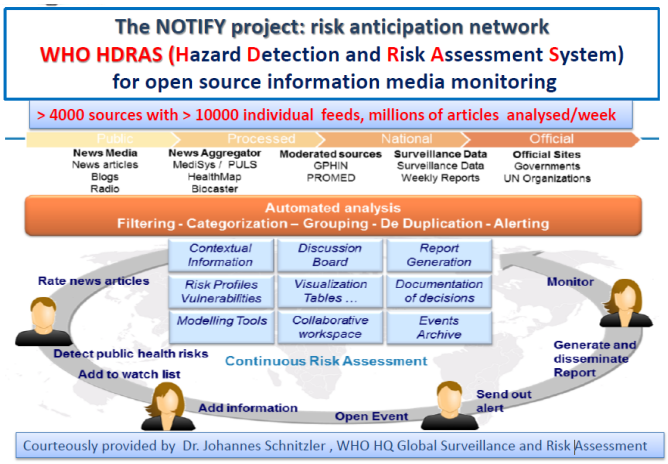




Interactive Booklet through an index

3.1.5 New Initiatives

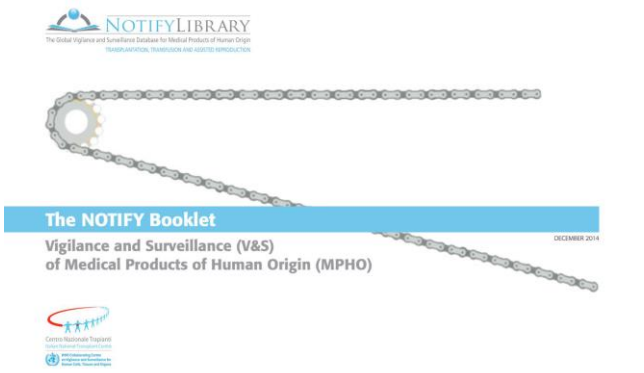
1. Website other languages & translation
2. Adding ethical breaches as 5th type of occurrence
3. e-Journal on V&S
4. Donor disease without documented transmission highlighted
5. Intense Dissemination of activities
6. Evidence of Usefulness of library
7. Terms of reference Editorial groups
8. Establishment of Consultation group
9. Notify Risk anticipation network. WHO - HDRAS (Hazard detection + risk assessment system)



10. VISTART: 3 years EU Joint Action (Grant Agreement 676969 – https://vistrat-ja.eu) since Oct 2015. The main objective of the action is to increase the sharing of vigilance and clinical outcome information between Member States to achieve higher standards of safety and quality across blood, tissues and cells. **Work-Package 5 – Part A** aims to increase the participation of EU Competent Authorities for blood, tissues and cells in the WHO Notify project's vigilance didactic tool, the NOTIFY Library (www.notifylibrary.org) **Projects Input:** Transfer of information from EU CA annual SARE reports. **Projects Output:** Development of a guidance document on selection and analysis of case types with didactic value for insertion in the NOTIFY Library. Conduct of a pilot scheme for Inter-MS support between network of vigilance officers, specialist experts and professionals managing and investigating individual suspected or real SAREs

3.2 Notify Booklet: a guide for health authorities and professionals. Mike Strong

The booklet is a work ongoing since 2011. It has been a challenge to build on a single document for such massive information and convert into document of less than 50 pages, deductive and advocacy strength of a flyer. Now is one year old, because it was launched on December 2014.



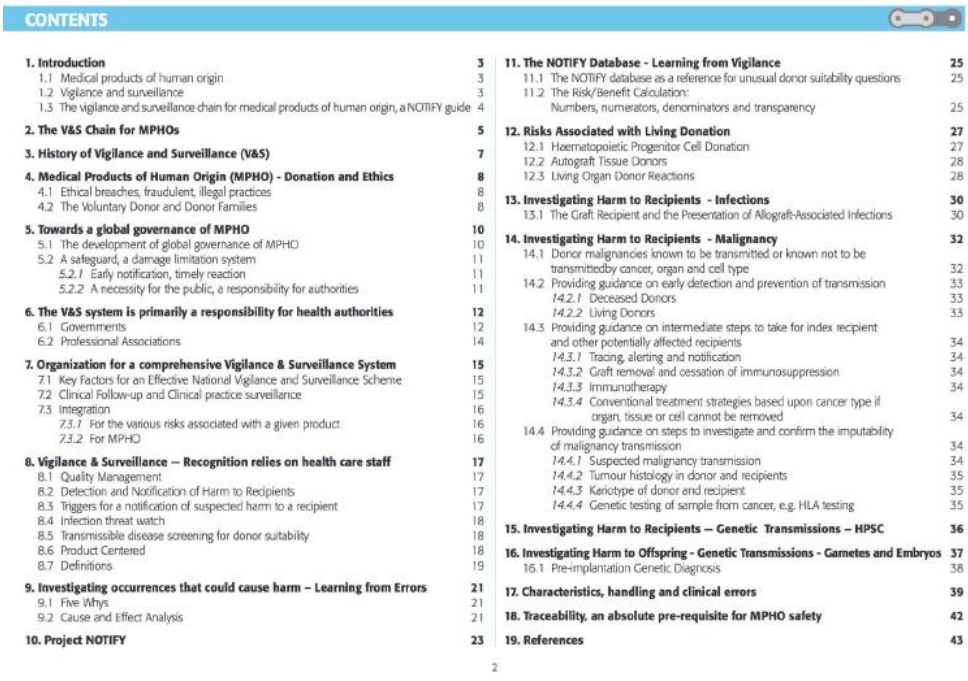
3.2.1 The Clinical booklet - what is in it?

Targets healthcare professionals to:

- Justify and encourage participation in V&S
- Globally harmonize concepts
- Globally share outcomes
- Fit within the NOTIFY project
- Provided to National Health Authorities (NHA) in WHO Member States to promote V&S for MPHO
- To be customized to meet national specificities

Concept of the booklet: Explain, synthesize, comment and guide with "chapters" that can be downloaded or printed individually. Has the potential to meet the needs for communication inherent to the novelty of the NOTIFY project.

Table of Contents



CONTENTS

2

3.2.2 What is missing?

1. Chapters: Specific to type of MPHO (Organ, cell, tissue, **blood**, ART, breast milk…)
2. Using the NOTIFY Website resources
3. Introduction of and links to well established national V&S systems
4. Introduction of and links to supporting Scientific and Professional Societies
5. Links with NOTIFY interfaces in other languages than English
6. A mechanism for updating e.g. Definitions

3.3 Use of the Notify Library-data from Google Analytics and information directly from user questionnaires Daniela Minutoli /Claudia Carella

Notify Library website www.notifylibrary.org was published in 2012 and since the very beginning it was foreseen to collect traffic information of the website through Google Analytics.
In 2013 during the Brasilia Global meeting some preliminary statistics have been presented with positive trend on the use of the website. A through analysis on the research performed by users on the Notify Library was request by NOTIFY project experts' during the technical meeting held in Barcelona (February 2015) in order to demonstrate the importance of the Notify Library as supporting tool to the Vigilance and Surveillance of MPHO worldwide.

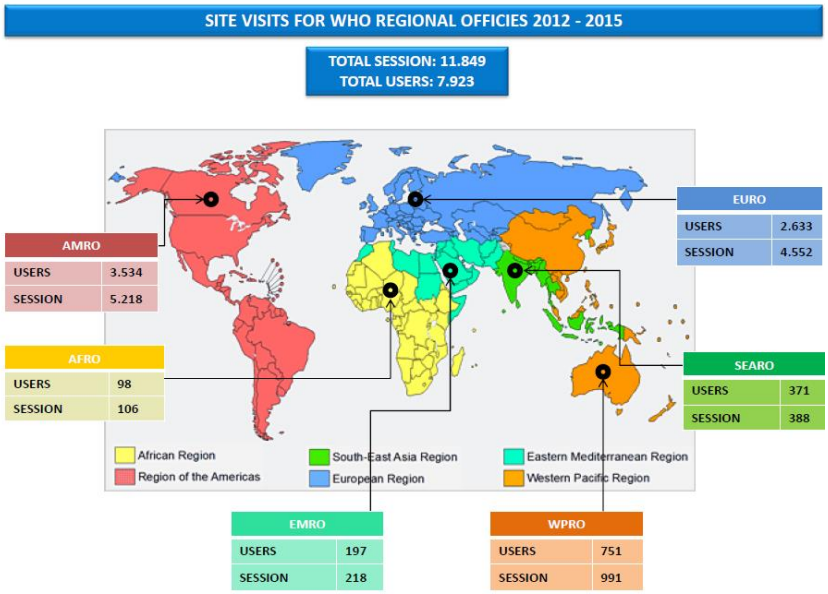
Used web analytics technologies: Google analytics
Parameters to be analyzed: time range, inclusion/exclusion criteria, number of users, geographical coverage, number of sessions, type of content page.
Database: design of a relational DB with Microsoft Access
Visualization by Occurrences type or MPHO: The Notify Library Taxonomy was used in a Micorsoft Access Query to identify the type of arguments searched on the Library

3.3.1 Definitions:

Web analytics definition: is the measurement, collection, analysis and reporting of web data for purposes of understanding and optimizing web usage. However, Web analytics is not just a process for measuring web traffic and is generally used as a tool for assessing and improve the effectiveness of a website. It helps to estimate how traffic to a website changes, providing information about the number of visitors to a website and the number of page views.
Visit/Session: A visit or session is defined as a series of page requests from the same uniquely identified client recognized by an IP address.
User: The uniquely identified client that is generating page views within a defined time period (e.g. day, week or month). A uniquely identified client (IP address) is usually a combination of a machine (one's desktop computer at work, at home) and a browser (Firefox, Safari, Chrome etc., on that machine).
New User: A visitor that visit a given website for the first time.
Bounce rate: Is the duration of session, expressed in percentage, of a single-page visits (i.e. visits in which the person left the website from the entrance page without interacting with the page). If the Bounce rate is low the data is positive because the user remained on the website for a longer period; if the percentage is high, the data is negative because it means that the user left the website without making any interaction with it.
Pages/Session: (Average Page Depth) is the average number of pages viewed during a session. Repeated views of a single page are counted.
Avg. Session duration: The average length of a Session.
Visualization by Occurrences type or MPHO – argument searched by users on the Notify Library.

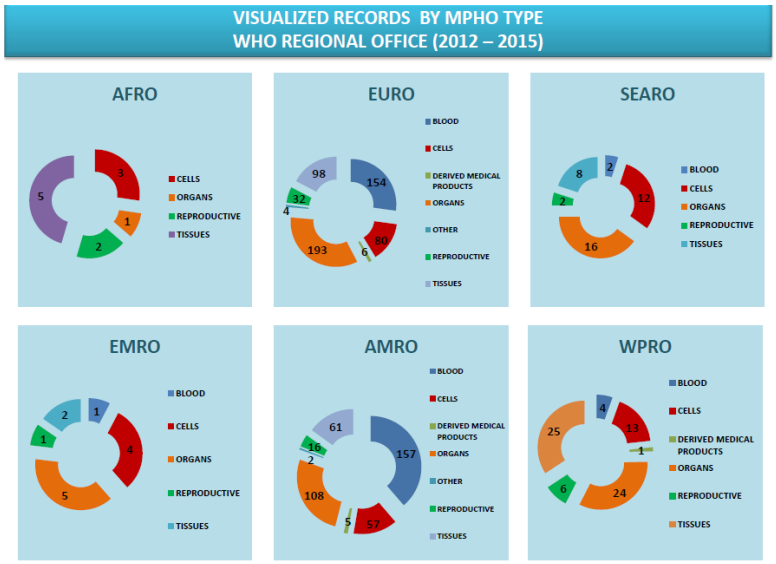
3.3.2 Users

New user bounce rate has gone up from 49% in 2013 to 54,13% in 2015. But session duration has also gone up although the average pages per session is still 4,29-4,29. Currently the total amount of users are 7.923 and the total amount of sessions are 11.849.



So the bounce rate did go up but it is important to note that the users also went up so if you look at the ration users: bounce rate it has probably been stable. If you look at the total visualized pages it is now 48.876. By occurrence type the immunology pages had been visited the most and after that infections.

In terms of geographical area the worst area is Africa and the best is Europe. If you look at the didactic cases the section on Blood gets used the most.



3.3.3 July 2015 Online Questionnaire

As decided during the Barcelona technical meeting it was decided to investigate with a feedback questionnaire (to be filled on a voluntary basis) the type of audience and satisfaction of users about the library. The questionnaire was launched on the Notify Library as a popo-up that appear soon after the research is started on the LIbrary, last July 2015. Data will be collected for at least one year and consolidated information shared during a future Global meeting.

3.4 Notify Consultation Group: Draft Proposal Nanni Costa

3.4.1 Why have this group?

Provide a 'top level' advice via the website in order to engage people on a regular basis with the site and the Library, involving new people contributing to it.
Stimulate routine use by those people that could benefit from it.

3.4.2 How to contribute?

Support to those establishing MPHO vigilance programmes. The group could:

- Advise authorities worldwide on how to establish and manage vigilance systems.
- Disseminate the use of the Notify Booklet already available on the website as the basis of that advice building also some practical instructions and a regular dialogue with those requesting support.
- Contribute as experts to the WHO regional consultations on MPHO on behalf of the project encouraging and supporting local and regional vigilance programmes.
- Encourage the authorities that they are supporting to share their reports with the Library.
- Support to authorities investigating serious adverse occurrences.

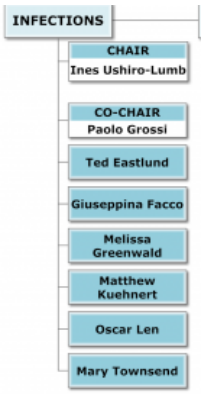
The group could nominate an appropriate expert to give support and advice when an authority is dealing with a specific serious occurrence. This advice could include topics such as:

- how to treat a possibly infected individual
- where to find a laboratory that is expert in a particular an unusual test
- how to establish imputability for a particular case of harm to a recipient
- how to prevent an error that has implied serious risk
- General involvement in the dissemination of the project, the library and its objectives.

The group would aim to ensure that as policies and programs are developed and presented worldwide that the Notify Library is incorporated in those policies and programs as an integral part of Vigilance Communication
Review library content as a contribution to the medical literature
Place the NOTIFY library issues into national/regional context by developing a series of "guidance" documents on relevant risks and benefits of MPHO utilization from specific donor types

4. Review of progress in the Notify Library – Specifically looking at Infections

4.1 Infectious Group. Ines Ushiro-Lumb



February 2015, meeting in Barcelona: approximately **121** old records waiting to be edited, including blood product-related
Post-Barcelona, consolidation of records to eliminate non-Notify material and to merge similar publications into single records. **89** records remained/ 12 to 15 records assigned to 6 group members. Re-assignment of a reduced number of cases to 5 members. Over **60** cases still in editing by early November 2015. Another consolidation exercise: 25 cases in editing by 24th November. Completion of work on 27th November, **all cases reviewed**

4.1.1 Future Work: Provenance of new cases

- Submission by user via website
- Project NOTIFY peers
- Automated continuous search run by CNT operations
- HDRAS

- Criteria of entry of new cases
  - Check if paper already in database
  - Check if paper is unique and if similar one is already in database
  - Submit a lot to Chair and co-chair
  - Generate record
  - Chair /co-chair assign to group to review case

4.1.2 Systematic search

- Literature search programmed by Daniela Minutoli

- Dry runs being performed and optimization in progress
- Automated search runs in continuous mode
- Search query designed to look for individual pathogens and individual MPHOs
- **Period: 2012 onwards**, except prions
- 484 records listed and scanned, assigned green or yellow status
- Sub-groups of organisms: bacteria, fungi, parasites, viruses, prions
- Green- on the basis of title and abstract, suitable for Notify
- Yellow- possible, need to read the paper to decide

Organism group	Total	Green	Yellow
Bacteria	199	16 (8%)	10
Fungi	22	4 (18%)	1
Parasites	70	19 (27%)	
Viruses	175	16 (9%)	6
Prions	18	0	5

Fine tuning and optimizing search strategy → shoved example CANDIDA.

- Debska-Slizien, A., et al(2015). "Candida arteritis in kidney transplant recipients: case report and review of the literature." Transpl Infect Dis 17(3): 449-455.
- Levesque, E. et al (2015). "Fungal complications after Candida preservation fluid contamination in liver transplant recipients." Transpl Int 28(11): 1308-1316.
- Rathnasamy M, et al (2015). "On Candida arteritis in renal transplant recipients." Transpl Infect Dis

4.1.3 Next Steps

70 – 90 cases must still be entered to bring us to date for 2015.
Need to look at cases in real time – would like to be up to date by March 2016.
Suggest consideration for a call for volunteers from other working groups to help bringing us up to date to the end of 2015 asap, and no later than March 2016. Called for volunteers to help with this work preferably:

- Already familiar with NOTIFY concept
- Already familiar with the tool
- Members with an interest or expertise in infection
- New cases from Jan 2016 – enter "real time".

Process definition:

Assignment
↓

Accept review of entry within 3 weeks

↓

Discussion

↓

Completed case reviews from each member

↓

Current membership sufficient to deal with incident cases, provided stable activity,monitor.

Responsibility to disseminate and emphasize the principle of a balanced and proportionate approach, aligned to the medical procedure being performed and the local reality

4.2 Malignancy Group: Michael Nalesnik

Issues facing malignancy analysis:

- Many changes in clinical practice regarding use of donors with malignancy over the years
- Terminology used in reporting cases varies; tumors described by organ (e.g. "lung cancer", "brain tumor"), specific tumor (e.g. "lung adenocarcinoma") or not at all (e.g. "metastatic carcinoma")
- Tumors may arise de novo in allograft ("donor-transmitted vs. "donor-derived")
- Many reviews from voluntary registries (e.g. Penn Registry) may skew frequency assessment, risk assessment

Editorial Group methods include:

Literature search: Records obtained from Project NOTIFY, supplemented by review of personal libraries
51 additional reports not included in NOTIFY found from 1971-2011 (to be incorporated)

Case Distribution: Spread evenly among members according to availability; Each record reviewed by at least two reviewers

Case Revision: All cases revised as necessary by Chair/Co-Chair

Group Communication: E mail distribution list, NOTIFY Forum, Google website of uploaded pdf files of individual publications

Records successful reviewed and published:

1. 192 total
2. 177 "Malignancy, harm to recipient"
3. 15 "Malignancy, risk of harm" (includes 3 tissue)

Records reviewed and rejected: 37 total Undergoing re-review for possible incorporation

Records in editing: 0

Other Editorial Group Specific Issues:

Estimated Frequency/ Taxonomy / Keywords/ Report types

For example estimated frequencies:

Frequencies cannot be estimated from individual reports, disparate reviews

- *Group consensus (Barcelona 2014)*

–Important information to be obtained: If a potential donor has a cancer of this type can the organs be transplanted and what is the risk of transmission (i.e., what is the frequency of transmission)?

–Overall search for cases of transmission and for cases of donor cancer not transmitted not able to be performed at present

- *Even if possible, publication bias would make results questionable*

–Best current information should be provided to guide clinical use and place tumor into context for others

- *Group answer is to use this area to include current Council of Europe summary and recommendations*

–Desirable to report in a standard format

–Standard template devised

4.2.1 Taxonomy

Taxonomy for Malignancies has lagged behind that for infectious diseases.

1. Prior taxonomy a mixture of organs (e.g., breast cancer) and a few specific tumor types (e.g., choriocarcinoma)
2. Revision must be detailed enough for use but not too detailed to make unusable
3. Revision must fit into current number of allowable subcategories on website

•Solution (Barcelona, 2014)

4. Divide taxonomy by organ or system type and list specific relevant tumors

Allow for cases in which specific tumor is not described + Allow for cases that describe unusual or rare tumors + Allow for entities that do not fit neatly into these categories e.g., metastatic tumors of unknown primary site, carcinoma in situ, benign tumors of relevance to transplantation

4.2.2 Keywords

Keyword list is extensive - reprented as single alphabetical list. Long list invited "fatigue" when trying to apply → multiple terms meaning the same thing (this is a problem for future multiple terms of the same concept which might confuse entry and limit search results).

Revisited keywords and structure them appropriately 2 ways:

Two-pronged approach

1. Keywords relevant to malignancy extracted and grouped by concept, similar terms placed together

->allows for ease of use and more consistency

2. Keyword concepts organized into "superstructure" to cover items in addition to tumor type, includes type of report, donor type, method of imputability, therapy, others-> Allows for complete coverage of potential searches from all starting points

Representative Portions of Keyword Structural Approach

Renal oncocytoma
Upper pole mass
Bone and Soft Tissues/Sarcomas
Bone
Chondrosarcoma
Kaposi's
NF1 (neurofibromatosis type 1)
Osteolytic
Sarcoma
Gastrointestinal
Bowel obstruction
Intestinal metastasis
Tubulopapillary adenoma
Breast
Breast cancer
Breast nodule
Male/Female Genital, Germ cell cancers
Choriocarcinoma
* Placental choriocarcinoma
Germ cell tumor
hCG (human chorionic gonadotropin)
Ovarian cancer
Prostate adenocarcinoma
* Prostate carcinoma
* Prostatic neoplasms
Cervical carcinoma (my addition)
Skin
Melanoma
Non-pigmented mass
Skin nodules
Squamous cell carcinoma
Subcutaneous nodules
Neuroendocrine
Neuroendocrine carcinoma
*Neuroendocrine tumor
Small cell

Topic	Keyword examples
Type of report	Case report Single center series Registry series Subject review
Tumor site	Colorectal Bladder Cervix
Tumor type	Adenocarcinoma Squamous cell carcinoma
Donor type	Deceased DCD Living donor
Imputability	FISH DNA fingerprinting
Etc	Etc

4.2.3 Next steps

Records

- Reviewing previously rejected cases for possible inclusion: Incorporate subject reviews, identify report types
- Merge "missing" reports from personal library with central database to provide information for more complete searches if necessary
- Continue to update records for comprehensive database: Taxonomy

- Updating entire database to new taxonomy: Keywords
- Standardizing use of keywords to enhance search capabilities; include all similar terms or one term to search all?

4.3 Living donor - recent work and future challengers: Bronwen Shaw

This group is further in some regards - almost all living donor cases were added as part of early "ethics" work, but restricted to solid organs and stem cells.

- Very few outstanding cases
- Systematically updated since then
- No "group" method defined for this reason

Now Blood = added - even then only about 40 cases listed often from large reviews rather than individual cases.

Since Barcelona 30 successful reviews of records and developing taxonomy which can also be used for blood.

4.3.1 Prospective process

1. Blood cases
    - need to catch up on a huge literature
    - how far back to we go?
2. Diversity of members of group and activity of members

- How do people want to work?
- 10 people on the group
    - 4 people active
    - 3 people inactive, but wants to be more active
    - 3 people didn't reply
- Need to separate advisory /supportive members versus those that do the work.

People feel we should add more people to the group.

4.4 Clinical complications (CX) - Mike Strong Substituting for Barbee Whitaker

Historically clinical CX separately from Blood group - many reactions for instane ABO mismatches - has got something to do with BLOOD. Clinical CX is about Non-Infectious AE's following transfusion or transplant.

Status Barcelona: Next Steps

- Address questions like Why /audience /purpose /level of art.
- Develop materials.
- Develop /validate TAXONOMY.

Post Barcelona: Mapped transfusion complications to NOTIFY TRALI /TACO /TAD still to be resolved.

- Instructions for entry of new cases.
- 3 SME's added in area of transfusions.

194 records reviewed:

- Only 19 rejected
    - What happens if they're rejected?
    - Will they be removed from management system?
    - Not everyone has 2 reviewers

- This was done in malignancy group.
- 0 records currently in editing process.
- 22 papers in queue for 10 review and entry into NOTIFY.

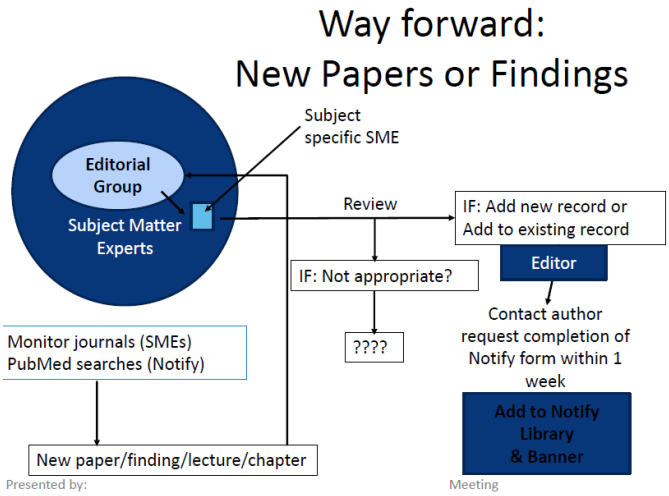
4.4.1. Literature search

There is a need to come up with Process, standardized, there is still a backlog.

Currently:

- Identification of initial cases by editorial group.
- Case review amongst editorial group acc to expertise
- Group communication skype /email.

4.4.2. Way forward



•Primary cases (flagged as NB)

↓

Will need a mechanism to highlight importance.

1. Editorial group issues

- How to communicate
- How to involve Inactive members.

4.5 Process: Scott Brubaker

This group does the evaluation of process failures that affect allograft characteristics /clinical utility /availability for use. Former titles of this editorial group:

"Product Property 2012"

"Process" 2013

"Product Property /Clinical complications" 2014.

Reviewed only 6 records → 1 Blood /5 Organs damaged at procurement.

- 3 "human milk" - Contaminated internet sales.
- 1 Art embryo not preserved put emergency IVF.
- 1 Organ kidney inadvertently discarded.

1. Tissue (bone) because of HBV test it used.

Other EG specific issues

We were advised not to use web-link from FDA for reference to the recall; created Notify document (PDF) from the recall report to maintain perpetuity of record.

Similar issue for a media article (discarded kidney); proper attribution maintained; required accessing newspaper website and following copyright details.

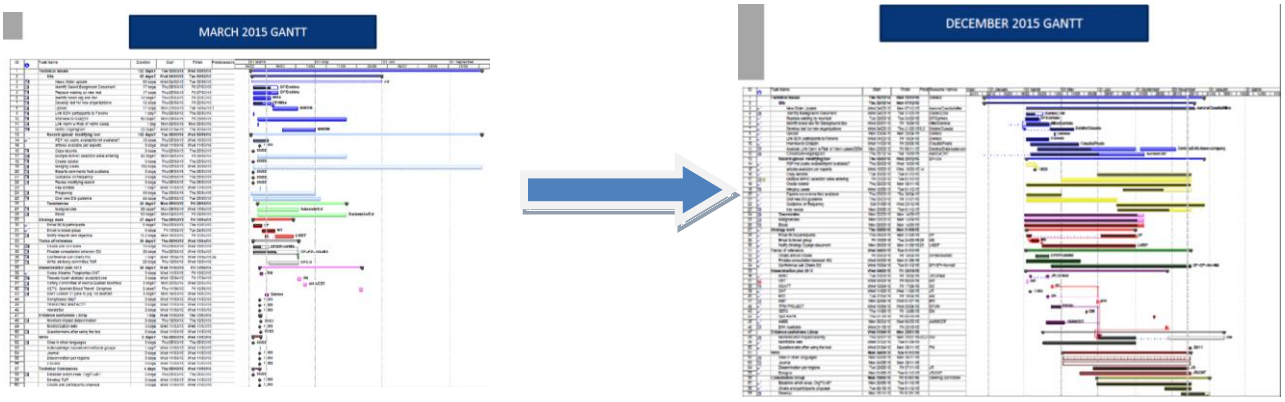
Literature search
6 new articles submitted recently (1 in September; 5 in November)
Case distribution
1 Blood – equipment wear vs. equipment misload during photopheresis

5 Organs – damaged at procurement
Case revision
In "process"
Group communication
It can improve via more involvement Sent email 11-24-15 with 6 pending cases attached

NOTIFY administrators can provide user access information (i.e., the last time a member accessed the Library using their user name/password)

4.6 Dissemination

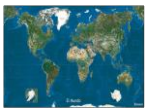
Previously to talk about specifically the dissemination process a Project Gantt table was presented in order to summarise all the actions performed during 2015 calendar year.



The dissemination activities during 2015 have been worldwide, promoting vigilance of all the different MPHOs (organs, tissues, cells, blood and ART). Notify operational team, editorial group members and professionals involved in vigilance programs have been promoting the project.

how

- Oral presentations
- Poster presentations
- Invited speaker
- Worshops
- Online trainning coures
- Fsace to face Courses
- Meetings
- Newsletter

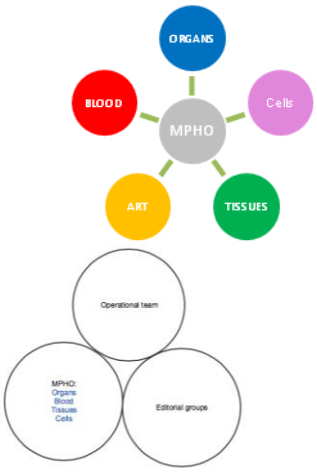


where

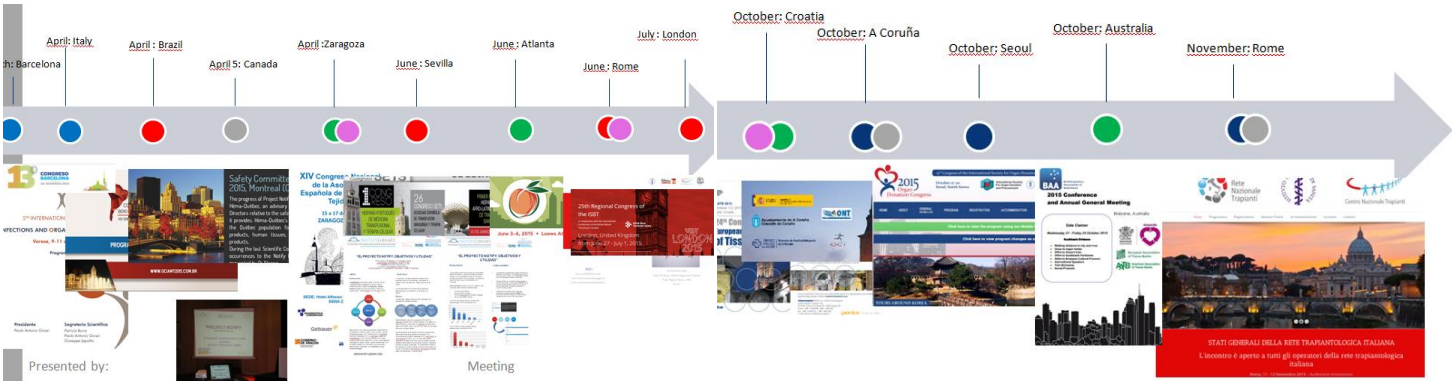
- Australia
- Belgium
- Brazil
- Croatia
- Canada
- Italy
- Korea
- London
- Luxemburg
- Montengro
- Spain
- USA

To whom

- Organ Transplant coordinators
- Tissue transplant surgeons
- Hemthologist
- Competent Autorities



4.6.1 Congress Activity 2015 (each MPHO different color)

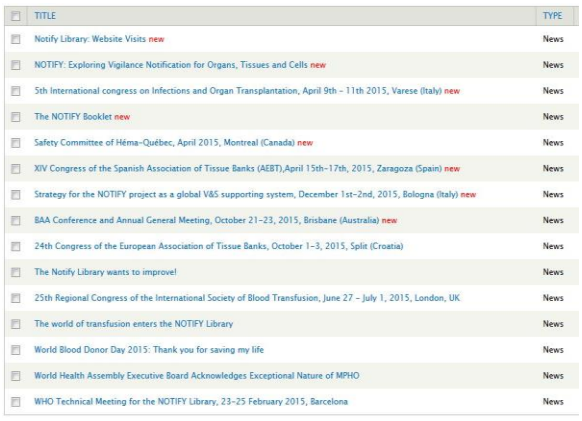


4.6.2 Educational Programs

- The international educational programs have international professionals which is a great opportunity to interact and explain the Notifylibrary tool specifically highlighting its advantadges and benefits of using it.

4.6.3 Newsletters: AABB, WHO, WUTBA

4.6.4 Web site news (15 different news posted in home page/news slider)



TITLE	TYPE
Notify Library: Website Visits new	News
NOTIFY: Exploring Vigilance Notification for Organs, Tissues and Cells new	News
5th International congress on Infections and Organ Transplantation, April 9th – 11th 2015, Varese (Italy) new	News
The NOTIFY Booklet new	News
Safety Committee of Héma-Québec, April 2015, Montreal (Canada) new	News
XIV Congress of the Spanish Association of Tissue Banks (AEBT),April 15th–17th, 2015, Zaragoza (Spain) new	News
Strategy for the NOTIFY project as a global V&S supporting system, December 1st–2nd, 2015, Bologna (Italy) new	News
BAA Conference and Annual General Meeting, October 21–23, 2015, Brisbane (Australia) new	News
24th Congress of the European Association of Tissue Banks, October 1–3, 2015, Split (Croatia)	News
The Notify Library wants to improve!	News
25th Regional Congress of the International Society of Blood Transfusion, June 27 – July 1, 2015, London, UK	News
The world of transfusion enters the NOTIFY Library	News
World Blood Donor Day 2015: Thank you for saving my life	News
World Health Assembly Executive Board Acknowledges Exceptional Nature of MPHO	News
WHO Technical Meeting for the NOTIFY Library, 23–25 February 2015, Barcelona	News

4.6.5 General Public- there is still the question of how much the project should emphasize the public section. Right now is generic and with a limited information.

5.Vigilance and Surveillance in the 6 WHO regions

The day started with a summary of 1st day meeting by Luc Noel.

Yesterday we reviewed to the interaction and requests for medical products of human origin. We found consensus along the principles of blood transfusion, resolution around the WHO guiding principles for cell, tissue and organ transplantation. We listed to the existing global tools for medical products of human origin. We established Notify as a key to promote global alliance and for the necessary national requirements. These are illegal, structural, etc.

The Notify library had made enormous progress in both tools and content. Small backlogs are present, for instance in the infection group.

In terms of process: it is possible that the Notify corresponding partners i.e. institutions with ongoing events of vigilance and surveillance, share anonymous reports of advert events because they had a didactic value. These reports could be posted by Notify.

Considerable work at standardization of nomenclatures is to be emphasized and commented on in Notify news. News of the medical products of human origin global community has two appear on the Notify website. It is important to note which countries have not provided information.

Questions and Discussion:

Frank: Should complications be reported? These complications could be accessible and used by clinicians and individuals. We can explore the use of concrete cases.

Luc: another important point is the standard of work on nomenclature especially in blood transfusion areas: this should appear in the Notifying news.

Consultation groups – how can we be to use global expertise?

1. Members of the Notify community may **agree individually** to provide advice to institutions in order to facilitate progress. This is informal and a directory will be available on the Notify website.
2. The future **global directory of and vigilance and surveillance systems** with in formation provided on each organization, will focus on potential value as a reference tool. This will be an important support for new and developing systems.
3. Theory is a proposal for a WHO experts committee: "**Donor dignity and donation safety** for medical products of human origin"

5.1 WHO AFRO region – Dr Andre Loua

This region has 47 countries, 892.696.000 people (13% of the global population). It carries 25% of the global burden of disease, 69% of the global HIV, 29% of the global TB, 80% of the global malaria, 42% of the global anemia and 8% of the global's hepatitis B and C. It has an increasing rate of non-communicable disease in this region like hypertension and diabetes.

In terms of medical products of human origins like cells, Tissue, blood, organs,

assisted reproductive technology, there is little data available. Transplantation takes place in Algeria, Ghana, Kenya, Mauritius, Nigeria and South Africa. Haemodialysis also takes place in some places. Although screening is available, there is very little data.

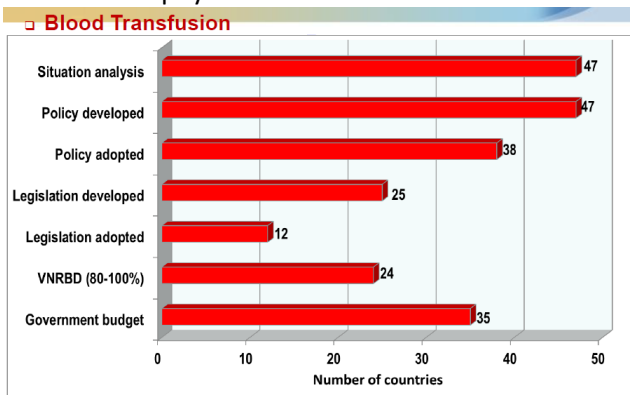
5.1.1 Key factors for national vigilance and surveillance will be:

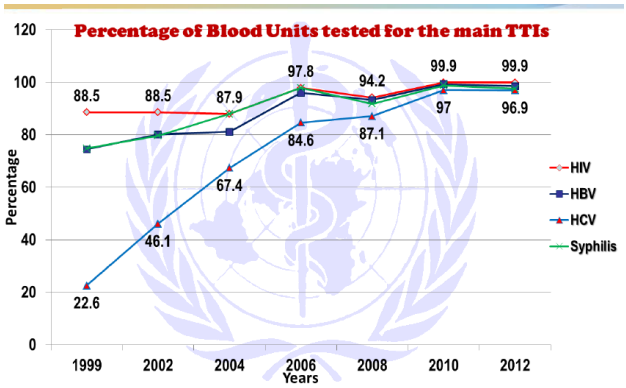
- Traceability
- Standard reporting systems
- Rapid alert systems
- Cooperation between authorities and clinicians
- Link to overseeing bodies

Not all countries in Africa have dialysis or a budget for this. Kidney transplantation is only available in a few countries in Africa. Furthermore screening for chronic renal failure is a problem. They are now quite a few countries with transplantation have been identified as a priority and where legislation exists as either a draft policy or policy. The declaration of Istanbul is known in a few African countries.

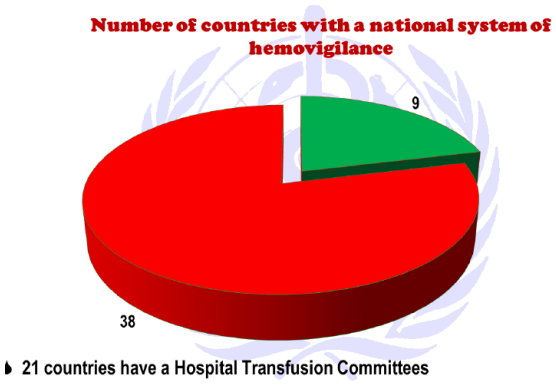
If you look at blood transfusion the situation is quite different. In about 47 countries policies exist or are being developed. In 38 countries these policies had been adopted already. In 25 countries legislation around blood transfusion exists. In 12 countries this legislation had been fully adopted.

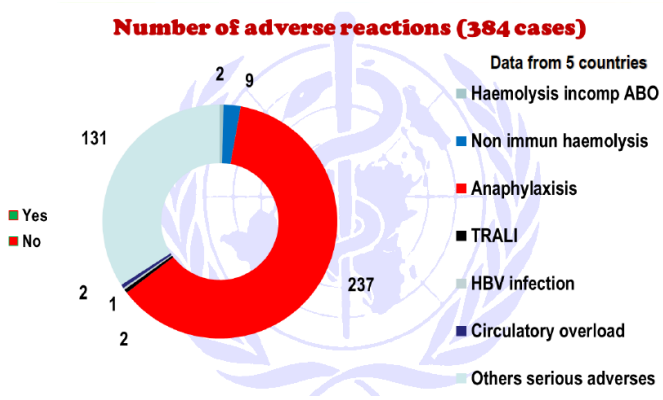
Testing for HIV, hepatitis B and C, as well as syphilis existed in 40 African countries in 2012. The prevalence of infections transmitted by transfusion is decreasing. Nine African countries have full hemovigilance programs. 21 countries have a hospital transfusion committee in place. In 2012 five African countries report it serious at these events to the WHO. In total there were 384 adverse events reported, of which 237 were anaphylactic reactions.





A pilot project was launched in Bobo Dioulasso between 2005 and 2009 to look at the rate blood transfusion reactions and forms were used with each unit of blood distributed. A total of 34,000 blood products were distributed to just more than 23,000 patients. Transfusion incidents were noted in 1.1 to 16.1 / 1,000 units transfused. 0.35% deaths, 0.26% hyperthermia, 0.1% allergies, 0.03% nausea, 0.03% tachycardia and 0.2% acute pulmonary edema were reported.





5.1.2 Issues in Africa

- The transplantation is not a priority and is not yet taken into account in the health system in the most of countries
- The appropriate legislative environment in which transplantation and blood transfusion can operate is not yet in place in all countries
- The insufficiency of regulatory oversight and coordinating authorities
- The dispersal of expertise and facilities in the existing centre
- The high cost and sustainability to support the transplanted patients
- The tissue typing laboratories not established in Africa
- Insufficiency of the good pathology training programs
- The weaknesses of hemovigilance system in the Region

5.1.3 Perspectives for the future

- It might be useful to carry out a survey across the region
- A regional consultation to develop guidelines in this region should be organized
- There is an urgent need for haemo vigilance systems
- That government in Africa and need to make a commitment
- Africa needs more regional and international cooperation

5.2 The American Region with specific focus on Latin America (AMRO/PAHO)Maria Dolores Perez Rosales

There are 42 countries in Latin America and the Caribbean. The population is 630.115 and the number of whole blood donations in this region round about 9 million and almost 7 million transfusions.

Sub-region	Availability of Red Blood Cells	Red Blood Cells Discarded	Total Transfused
CAM and Spanish Speaking Caribbean	888,223	44,061	871,615
Caribbean	57,680	3,935	52,020
Andean Community	1,214,594	105,763	1,197,541
Southern Cone	1,105,759	252,113	1,053,859
Brazil	3,231,788	308,229	3,222,948
Mexico	1,321,413	113,597	1,264,536
Total	7,819,457	827,698	6,991,759

World Health Organization

5.2.1 Discard rate

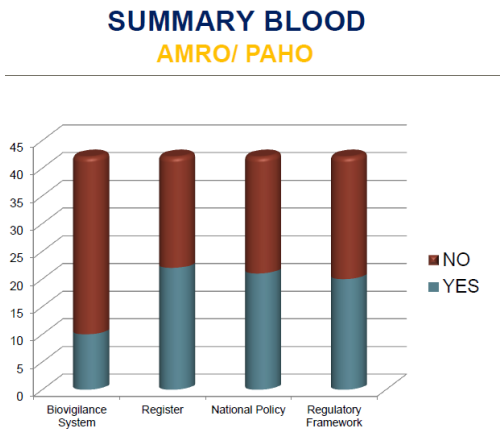
One of the problems in this region is the discard rates for blood products. This is costly, and can be improved by vigilance and surveillance.

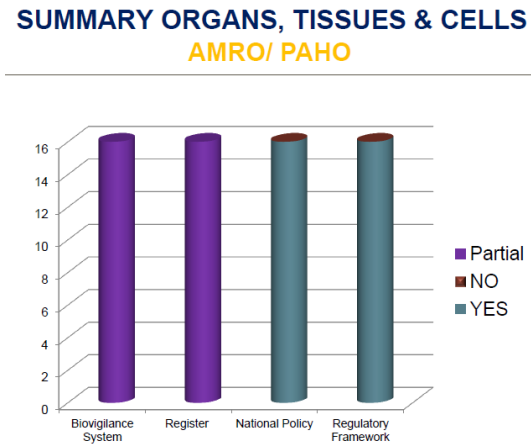
1.2.2 Activity on blood, organs and tissues

They are only 10 countries in this region where they are national vigilance and surveillance systems (245); they are no national vigilance and surveillance systems in 32 countries (76%). Some of these countries with no national system, have regional or local programs. But today are many countries where there is no registration of adverse events nationally. There are 10 countries in this region with a national program, five with a local program and 7 where vigilance and surveillance programs are based in local hospitals only.

In 21 countries vigilance and surveillance is available for blood. In 20 of these countries legislation and regulatory framework exist. However they are not always vigilance advisory committees or some equivalent to this body. Often biovigilance systems for blood, organs, tissues, cells include professional societies like RCIDT, TTS, STALYC, SLANH. The problem is a fragmented health system. Vigilance and surveillance is sometimes only partial and in many places adverse events are not reported. There are 16 countries with vigilance and surveillance systems, most of them for living donors. Deceased donation and tissue adverse events are only reported in 11 countries. However sometimes registration on a local level or in a hospital exists.

A problem in Latin America is that blood groups and organ transplant groups don't work together. Medical products of human origin need to be grouped together. Argentina is starting to work on this but there is nowhere else way this is currently the practice.



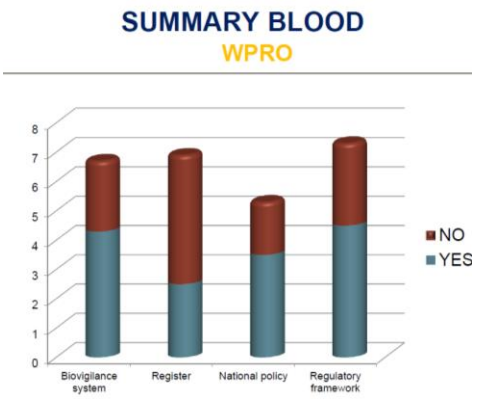


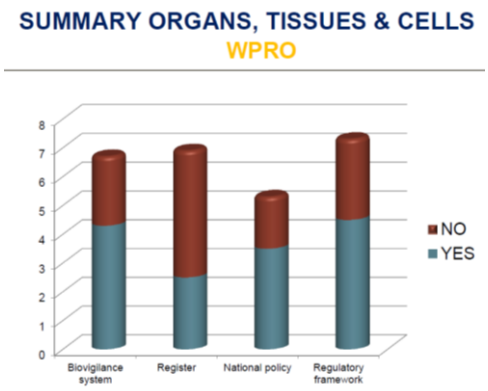
5.3 Western Pacific Region: Mamila and the Phillipines – Klara Tisocki

5.3.1 Overview and activity

This region has 37 countries and a population of 1.8 billion. Involves Australia, China and lots of small island countries which only have about 10,000 people. It's a very diverse area. It has some very developed various like Australia, Japan, Korea, South Korea, Singapore and New Zealand. But it also has emerging economies like China, Malaysia and Vietnam.

The number of blood donations collected in this region is close by 4.756.622 and this involves data from 10 countries. There are seven countries with vigilance Systems. In these countries donor related adverse events are also reported. In 20 countries they are no vigilance system. Seven countries have registries which are either local or hospital-based, there are no national registries. In nine places there are national blood policies and in five countries there are legislative frameworks. In these five countries they are also advisory committees.





5.3.2 Institutions

The key institutions are the Asia Pacific lads and narrow transplant group known as APBMT. They are also WHO collaborating Centre is for blood transfusion services based in Australia, Korea and Singapore. Professionals in this area work with professional societies like TTS, AST, TSANZ, Malaysian society, Hong Kong Society, Korean society as well as the International Society for Pharmacovigilance (ISOP).

5.3.3 Needs in this region

- National legislation frameworks
- Definition of roles and responsibilities of national authorities, institutions, National professional societies to ensure compliance with legislative frameworks.
- Adoption of global norms and standards, ethical principles and capacity building to operationalize rules and requirements.
- National quality assurance mechanisms
- Transparent resource allocation and distribution mechanisms

2. Plan of action for the Notify Project

- The issues that came out of this meeting are summarized as follows:
    a. There is a shared responsibility between notify and the WHO;
    b. Theory is a real need for the notify system;
    c. There is a common solution for tissues, cells, organs and blood.

- This project could be the basis of something we can work on through the professional societies. Three societies affiliated with the WHO would be possibly help: WBM ass. TTS and blood transfusion ICCDA. The societies can put together a document on ethical principles which can extend beyond all medical products of human origin. There has already been extensive consultation in all the societies and I think it is really to be published.

- If we cannot have regional meetings one option would be to have online consultations - many elements can be discussed online. After an online draft document had been designed, discussion can take place in smaller groups. It is possible to have a process that is partly online with only one or two big meetings. Technically the document can be available online for comment. We need the experts to make the draft documents and then people can comment. If you want to consult with lower middle income countries, it might not get the great people if you go through the ministries of health. A small technical advisory group is necessary. To document can then be drafted and the paper can be available online. I still suggest we have the consultation based on this paper.

- The consultation process should involve each and every member state. It needs to address the health authorities: the attendees will have to be designated people by the ministers of health. This meeting needs to be the result of multiple conversations between the Departments of Health and formal regional consultations. A draft document does not need much consultation. Discussion can be done after the draft document had been circulated. There is no draft document yet. The document must be concise, crisp, and sharp. A resolution that needs to be discussed by the World Health Assembly. The assembly wants to know about guiding principles, tools. We need to stress how communication tools look. The level of health system development needs to be taken into account for each country. This sequence is as follows: drafting of the document, sharing the document with governments, use it as a working document for regional consultation. A consensus paper will allow the WHO to understand what professional societies' roles and responsibilities are, and what is happening at country level. This will have to be run through many regional meetings. It needs to be finished by September 2016.

- WHO needs to increase also what is the guidance and how to deal with ethical problems. The documents needs to address safety and good clinical practice. WHO consultations should be planned during this meeting; we should define where, how many, which notify experts, which member states will be involved. The WHO will draft letters to countries to look at how many countries can be involved with Notify: we will ask whether they need help and we do they need expert group advice. I want to stress the importance that the WHO is committed to Notify. It was the requests from the director general of the WHO that there should be global consensus by consultation. We do need to involve the member states. The new document needs to be developed after all the checks had been done. The idea is to do an update of the guiding principles.

- The document needs to be written by the experts, the WHO will use this. It's a document of international agreement. We then take this document to the member states to define these services. Consider web based meetings. Considered videoconferencing. Funding is a problem. Representation by the minister of health as well as a technical person is important. We also need to look at institutional partners.

3. General Group discussion

- It is important to look at 4 things:

a) The use of the library
b) Reporting adverse events – there is currently no direction to the clinicians;
c) We must not forget about guidance documents that have been created before;

d) We need to build on our relationships with the WHO and the Council of Europe – there are guidelines on the WHO website for organs and blood which can serve as "aide memoire" documents to medical products of human origin.

- The library is the way forward. A huge amount of work was done, and the momentum needs to be maintained. We need more volunteers specifically in the infection group. Phase 1 is the literature and phase 2 is using vigilance systems specifically from annual reports. Broader issues that need to be addressed are the fact that the aide memoir documents were based on blood and this needs to be re-looked at. We need to support challenges in other parts of the world: the library is probably not the best thing for them, but the booklet is good guidance document for medical products of human origin although it is still missing blood. The consultation groups will be a really valuable tool and we need to rely on our experts. We need to look at other languages - this might come from regional meetings. We need to think of the journal.
- Journal would be very valuable especially if it could publish reports. It can be an electronic medium to process incidents. It can also be used to generate reports.
- Ophthalmologist has a journal that is open access and free but this is a huge undertaking. The notify library website is already a free and open access resource. Duplication is a problem.
- The concept is a good one but the journal is logistically not easy.
- The proposal for the journal is to have case studies, all submissions will have to be submitted in a specific format. The second type of article would be reviews of the content of the library. The idea is to have a journal that has both reviews plus case studies under the auspices of the WHO.
- This could be an electronic journal. The advantage would be that we can group together medical products of human origin. This will specifically be valuable if we setup guideline documents.
- Countries who do not have a sufficient reporting system will need this summary. A lot of this work is already available in the Council of Europe guidelines. It is very important to add expert comments at the bottom of each review.
- For developing countries, the most important thing would be ethics, governance, allocation, resources. Malignancy probably falls on the higher end - we need to rather raise ethical issues for instance coercion/ using very ill patients to get a transplant done. The malignancy contribution is quite narrow in scope at the moment.
- It is very important to provide feedback to people who provide information. Different users and in different stakeholders use the tool differently. The positive impact is if this tool benefits the community and if results are communicated back to the people who are reporting. There is a fundamental fear about vigilance which needs to be addressed.
- We don't have data on all fertility issues. Donor derived adverse events needs to be disseminated better. The library is a very good tool, but we need to keep on thinking how to use it better. Then member states need to use it more.
- We need to link the journal to patient safety and vigilance, we need to create reports. This will be a huge challenge.
- Many regions have no registry. Only 3.7% of users lived in Africa. We have different situations in each region. We need to try and have more contacts and dissemination in Africa.
- In Europe reproduction is under the same umbrella as medical products of human origin. There is a limited number of cases elsewhere. Notify is a tool to these people, we should include them in more reports and involve them as stakeholders.
- Let's see how we can organize the means in front of us. How many people are able to read the library? The link with the WHO needs to be emphasized with institutions. Notify is the vigilance arm of the WHO. What is the use in developing countries and how is this different to developed country? I would think it is on the label of the professional. Communication and dissemination of the tool is so important.

- Dissemination is very important. We need to reinforce the vigilance and strength of medical products of human origin.
- The priorities are:
    a. Revise the booklet and add blood, the initial draft of 2010 needs to be revisited and possibly revised, new definitions needs to be added;
    b. Consider global issues that had not been addressed before and also some new technology for instance in assisted reproduction technology;
- Actions to be considered:
    - We need to look at the operational team: Give editorial group work at certain times and with certain intervals. This needs to be streamlined.
    - We need to revisit to the templates.
    - We need to look at the consultation group and who will be involved.
    - How do we present the tools? Perhaps not in the same way as before. My workshops? How do people need to receive this information? What is our marketing strategy?
    - We need to translate a booklet into Spanish and some other languages.
    - Protocols need to be developed. They are many protocols and guidelines available, but these are not always published and publicized in the right way.
    - A journal could be a feedback mechanism to contributors. Cace reports could be considered.
    - If we want the public site we need more material for this.

- The data base search needs to be done in a standardized way. We need standardized terminology for reviews. We could consider a wiki page. A standard review would be to reviewers on each entry and a comment space.
- Each editorial group works in a different way. The risk assessment exercise needs to be done. We need to identify and evaluate risk and vigilance systems in the same way.
- We should not take for granted that things are okay as we have very few users. We need more expert comments. We need standard operating procedures that could be derived from the website.

4. Group Discussions

Open discussions happened at every session and there was a final discussion on the last day. Some issues featured more prominently are summarized here.

Discussion on Notify consultation group: draft proposal

- Who will be on it? For unusual infection (for instance) a committee needs to be able to review national policies rather than a particular incident? (Single case versus overview type of advice.)
- There is a benefit of having experts to review these cases. These people need to be responsible for organizing things as well. We need single experts to drive official documents.
- A committee can make a general recommendation/ review to national V&S systems with and objective to advise. It's not "we have this person - could he be a donor? NOTIFY, can't handle these individual queries. Committee can make general recommendations/review national V+S systems/ Objective advice.
- This needs to be used by Competent authorities in places where systems are not strong like developing world of smaller European countries.

- The topic POLICY vs ON GROUND ADVICE was also addressed. Ideally, it needs to be both – ideally we need more widespread use. There is no vigilance in some Eastern European countries as well – Need to help developed world and also with countries that start – Needs advice on many levels.
- Investigation of specific cases implies several aspects and categories. Example of living donor that died: he was involved in groups that "investigated" this. NOTIFY could do this.
- The library should produce guidance PAPERS – info in library needs to be assessed and published. Tim Pruett made these points before:
    - national regional service
    - public health service guidance doc
    - 35% of donors in Frank's area fall OUTSIDE this guideline
    - NOTIFY should change these guidance docs → can consider new guidance docs from specific donor types

This is something the library can provide to the international community. Not currently enough to affect policy docs. Publication of standards is whatwe need: Periodic publications (Good practice guidelines). PREDICT TRANSMISSION RISKS (Good Practice Guideline and not only seeing deficiencies)

- WIKI website: List of things donor could have – page shows if this is risk to recipient or donor. Based on NOTIFY library. Communicative Tool → can ask individual questions - can get special answers.
- Provide through the project not specific advice but rather broader advice. Needs translation for Latin America.
- Porposal to send abstracts to TTS Congresses to promote discussions also at conferences.
- Advisory group (voluntary people) for WHO – to Competent Authority. Mechanism can be simple – email address? Usefulness → Documents /something close to library, but not exactly the library.
    1. Library – used by Professionals for AE's etc.
    2. Consultation Group – different role – LAYERS:
        i. Specific case by ministry or health authority
        → reach WHO /consult groups to get advice for particular cases.
        ii. Higher role – Role to help member states to get the V+S network that they do not have.
        → Consultation groups then becomes more as a group who advise in place
- Are the WHO Regional offices the transmitters for requests for groups to provide support?
- Vigilance is about OVERVIEW. Possibility for special requests should be there. Should not be too restricted. NB POINT – Is the question asked from Official Authority??
- Competent Authorities asked NOTIFY to advise on V+S systems. We need to figure out how we should address these needs. Sometimes info is confidential – active Specific consultation. Sometimes it is competent authorities asking advice. Think this group should start this systems and requests → to advise them.
- Organize support around the globe /mechanism or resource for professionals. Real time response → WHO would be liable? Individual experts? That's where WHO comes in as they provide response to, member states support level. Funding for countries who can't meet their needs? Channelled through WHO. We have to promote the "will to serve /to help". Brand NOTIFY with different types of services because it's MPHO.
- Liability is inside group → It has to be "experts" with specific duty.
- It cannot be exclusive
- Have to be inside or outside WHO
- It is important to have a written proposal on which make an agreement. The Consultation group is needed. To work at where we want to go.

Discussion on Review of the progress Notify Library

Discussion on Infections

Strong asked: What happened to subgroups – bacteria /fungus. Ushiro-Lumb answered cross over is happening – didn't work so well to have these subgroups. Strong emphasize the chairs needs to think how we go forward learning from different subgroups because members sometimes don't do much – need to define process. Also there is a need to think about disease without transmission and disease that's been treatable without transmission

Discussion on Malignancies

Delmonico asks how do we categorize risk? Nalesnik explains that through the use of the Council of Europe guideline - minimal /medium /high. To be able to search with keyword will also help this. Strong's Question: How much is comment section used? Answer: Comments are now used more to be able to put expert comment in.

Discussion on Living

Fehily asked: Are you capturing donor reactions from reproductive egg donors? Answer: No.
Comment from Reproductive Group: A lot of these are captured in reproductive group.
Mike Strong: Haemovigilance for BLOOD DONORS not well established.

Discussion malignancies

Petrisli: Website has process available for new references. Can also look at adding KEYWORDS to add references. Fehily: This group probably deals with "RISK OF HARM", so they don't get published. Cases might become more now with change of collecting systems → working with Authorities might pick up more DIDACTIC cases. Work in future will increase. Kidney was discarded case - was reported on Audit report from hospital - REF isn't available. Noel: Difficulty of providing substance to report.

Delmonico: At Organ Bank they report damaged organs and he reports them to Board. Can you take Vigilance to the level where you report damage of every organ?

Discussion end first day

- It is time to include public, but unrealistic at the moment.
- What we have in our hands:
    - Unique library
    - Sufficient filtered
    - Substantial (we have the tool)

Question is how to disseminate this? Potential Clients

- Professional people
    - Official professional societies like CNT should be used
- Institutions
    - WHO dissemination through institutions.
    - This needs to be developed now by this group.
        - We "sign" product is working.
        - And we confirm that ground level info is good (good quality)
- Public part of the website:
    - Living Donors use website, they search the risks of donating.
    - Links to specific donation website like solid organs etc.
    - Sign of transparency /warning patients, but we treat patients as experts

- Qualitymust be good to do this
- Funding mentioned – are podcasts /Apps potential funding?
- Dissemination - developing world. WHO Africa needs to think of African presentations.
- Objectives of Regional meeting to get NOTIFY used /quoted. Database needs to report notification from low and middle income countries. Opportunity to health authorities to create Spirit of "confidence" "truthful" "honest" - DIDACTIC PROCESS - regional consultation is part of this.

Dissemination and Brain Storming (tools and future strategies)

Discussion on V&S 6 WHO's regions

AFRO

- The bad news is that there are multiple problems in Africa. The good news is that the WHO and project notify would both be in a position to help. The aim is to grow things and Africa needs support.
- Only a few countries are doing transplants. We need to make sure that the vigilance and surveillance systems are in place for these countries.
- There is a blood transfusion service in Africa. We need these national transfusion services to cooperate better.
- We need vigilance in all African countries. We can begin with a more 'medical products of human origin' approach and later extend this to include more organs. I think notify experts could be useful.
- Haemo vigilance is probably the place to start.
- The African region is improving. How far are we though? When we look at statistics we should not include countries like South Africa as this skews the results. An important principle in Africa is the principle of free donation.
- Blood donors are available in 23 countries. This is a underrepresentation for continent. Is a serious lack of donors.
- When you had an activity of blood transfusion or transplantation, immediately the question of vigilance comes to mind. We should question with the Notify is a useful tool here, as both blood transfusion as well as transplantation is happening on the African continent. All doctors need to have this information when they are giving patients blood or organs.
- Africa is such a big place. It is very complex to make universal comments. Most countries on the continent would aspire to transplant program. However, blood service is the first step: how they screen /how they set the system up.
- One of the big problems is the lack of reporting and the fact that information is not disseminated well.
- Blood transfusions services and dialysis was both available in Mali, but transplantation was impossible in this area because of a lack of surgical expertise and medical facilities. Blood transfusion services do not always mean that the clinical facilities to do transplantation are suitable.

- This example is relevant. There is a discrepancy between the national budget for dialysis, and a health system unable to cope with clinical transplantation. You also need a comprehensive report of the shortfalls in each country. Another issue is the surprising allocation of resources. An end stage kidney patient is much more likely to get dialysis rather than a transplant. It is important to note that vigilance and surveillance can only be linked to a government – this is a very important structural issue. I don't believe it can be driven by clinicians.
- One of the problems in Africa is the limited access to the Internet. If we want to get closer to Africa we will have to print our booklet.
- Here are currently a lot of transport services between the tissue typing laboratories in the UK and Africa. This is often based in the private sector. In Africa many patients receive cash surgery, and there is no vigilance or surveillance.
- Here is an example in Ethiopia where Alan Leichtman Annie's team is doing transplantation. Other examples are Kenya, Zambia and probably more African countries were Europeans or Americans go in to do transplants. I believe the opportunity to have vigilance and surveillance programs exist because of these systems.
- Gathering data on Africa is a problem. The knowledge about medical products of human origin is crucial. Notify could be used to point out errors and also to rationalize oversight.
- We all know the problems and that they exist. Should we approach all the experts in this region? I would like to make people conscious that this program can be used.

AMERICAN

- Only 16 countries out of 42 have vigilance and surveillance systems if you also consider hospital level systems. We need to stress the importance of vigilance. We need to create the need, and then provide the solution. It is worried that blood transfusion still have so many discarded units. The question is why.
- Many countries don't do a proper needed assessment. Systems of fragmented, they are so many blood banks. There are also private blood banks. They don't want the service network, they prefer to work separate.
- Brazil has an unrelated donor bone marrow registry and they report adverse events to national organizations. My question is whether these participants have provided information to Maria's survey. It looks like they were not be presented in this presentation.
- Perhaps Notify also needs to provide a network of professionals and the support to encourage people to use these vigilance systems which are in place.
- Latin America has submitted haemodialysis vigilance systems to notify. It would be good to see what this entails and whether it is in Spanish.

WESTERN PACIFIC REGION

- The question is, could Notify be the Indy point for some of these important needs? It seems the skin cells or not represented - they do report regularly to international bodies.
- It is difficult to analyse all countries. There is a large variety in economical situations. Often countries are not compatible.
- What we consider the best system – the best registry – comes from Australia. Medical education is very strong in these places.
- Sometimes it's hard to get things disseminated. It's difficult to help. For instance: Indonesia has an enormous surface area. They don't see the need for a system. Part of the problem is for people to acknowledge that they need some help to set up the assistance. Vigilance and surveillance will need to be set up in future in these places and it needs to be done effectively. I believe the WHO might be able to help.

- Medical products of human origin are a national resource. Governments need to understand this. The private sector off and feel that they are free from oversight. The WHO needs to play a role in all these places, also in the private sector. We need data. Health authorities should chair and share these initiatives.
- Legislation is taking place in many places for instance in the Philippines. This is another opportunity to bring this to the attention of ministers of health. I believe the WHO would need to get involved here: correspondence and sitting aside and infrastructure and some resources. We need to the WHO backup. TTS and DICG do not cut it on its own. The stature of the WHO is what is needed.

8. List of participants

Strategy for the NOTIFY project as a global V&S supporting system

Dr Mohamed Salah BEN AMMAR Tunis, TUNISIA msbenammar@gmail.com	**Mr Scott A. BRUBAKER** Chief Policy Officer American Association of Tissue Banks McLean, VA, USA brubakers@aatb.org
Dr Chiara BORRELLI Ospedale Evangelico Internazionale Genova, ITALY chiaraborrelli@hotmail.com	**Dr Claudia CARELLA** NOTIFY Project Assistant Italian National Transplant Centre Italian National Institute of Health Rome, ITALY claudia.carella@iss.it
Dr Mar CARMONA Organización Nacional de Trasplantes Madrid, SPAIN mcarmona@msssi.es	**Dr Jeremy R. CHAPMAN (EXCUSED)** Clinical Professor Medicine, Westmead Clinical School Westmead Millennium Institute for Medical Research - C24 - Westmead Hospital The University of Sydney Sydney, AUSTRALIA jeremy_chapman@wsahs.nsw.gov.au
Dr Mauro COSTA	**Dr Francis L. DELMONICO**

Head of Department of Medically Assisted Reproduction Ospedale Evangelico Internazionale Genova, ITALY mauro.costa@oeige.it	Professor of Surgery Harvard Medical School DICG- Director francis_delmonico@neob.org
Dr Antonia DERRICO Professor of Pathology Chief, Pathology Unit, "F.Addarii" Institute of Oncology S.Orsola-Malpighi Teaching Hospital, Bologna University School of Medicine Bologna, Italy antonietta.derrico@aosp.bo.it	**Dr Paola DI CIACCIO** Italian National Transplant Centre Italian National Institute of Health Rome, ITALY paola.diciaccio@iss.it
Dr Dragoslav DOMANOVIC ECDC Stockholm, SWEDEN Dragoslav.Domanovic@ecdc.europa.eu	**Dr Giuseppina FACCO** Italian National Blood Centre Italian National Institute of Health Italian National Blood Centre Rome, ITALY emovigilanza.cns@iss.it
Dr Deirdre FEHILY DG SANTE European Commission Brussels, Belgium Deirdre.fehily@ec.europa.eu	**Dr Paolo GROSSI** Full Professor of Infectious Disease Medical Clinical Department - University of Insubria Ospedale di Circolo - Fondazione Macchi Varese, ITALY paolo.grossi@uninsubria.it
Dr Marian MACSAI Chief Ophthalmology Eye Bank Association of America Glenview, USA mmacsai@northshore.org	**Mr Piernicola MASSIMI** Italian National Transplant Centre Italian National Institute of Health Rome, ITALY piernicola.massimi@iss.it
Dr Daniela MINUTOLI IT Manager Italian National Transplant Centre Italian National Institute of Health Rome, ITALY daniela.minutoli@iss.it	**Dr Kerstin MÖNCH** Deutsche Stiftung Organtransplantation Mainz, GERMANY kerstin.moench@dso.de
Dr Elmi MULLER Southern African Tranplantation Society Cape Town's University Cape Town, SOUTH AFRICA elmi.muller@me.com	**Dr Michael NALESNIK** Division of Transplantation Pathology Pittsburgh University Pittsburg, USA nalesnikma@upmc.edu
Dr Alessandro NANNI COSTA **Director, Italian National Transplant Centre** **Italian National Institute of Health** **Rome, ITALY**	**Dr Aurora NAVARRO** BST- OCATT Notify Project Servicio Catalan de la Salud

cnt@iss.it	Barcelona, SPAIN anavarro@bst.cat
Dr. Luc NOEL WHO Consultant Annency le Vieux, FRANCE lpjnoel@gmail.com	**Dr Philip O'CONNELL** President Transplantation Society Sydney, AUSTRALIA philip.oconnell@sydney.edu
Dr Evangelia PRETSILI Saint Orsola-Malpighi Hospital Bologna, ITALY e.petrisli@yahoo.com	**Dr. Bronwen SHAW** Anthony Nolan Foundation London, UK bshaw@doctors.org.uk
Dr Naoshi SHINOZAKI Executive director of the Cornea Center Tokyo Dental College Ichikawa General Hospital Chiba, JAPAN naoshi@eyebank.or.jp	**Dr Douglas Michael STRONG** NOTIFY Working Group Coordinator Edmonds, WA, USA dmichaelstrong@mac.com
Dr Jaume TORT Organización Catalana de Trasplantes Director Barcelona, SPAIN jtort@catsalut.cat	**Dr. Ines USHIRO-LUMB** Head of Transfusion Microbiology NHSBT London, U.K. Ines.Ushiro-Lumb@nhsbt.nhs.uk
Dr Duc VU Natural Health Products Directorate CEO Health Canada duc.vu@hc-sc.gc	**Dr Barbee WHITAKER EXCUSED** AABB Center for Patient Safety Bethesda, USA bwhitaker@aabb.org

WHO OFFICIALS	
Dr Marie-Charlotte BOUESSEAU (EXCUSED) Ethics, Equity, Trade and Human Rights Health Systems and Innovation World Health Organization Geneva, SWITZERLAND bouesseaum@who.int	**Dr José Ramón NUÑEZ** Adviser Medical Product of Human Origin Service Delivery and Safety Department World Health Organization Geneva, SWITZERLAND nunezj@who.int
Dr Junping YU World Health Organization Geneva, SWITZERLAND yuj@who.int	
REPRESENTATIVES OF WHO REGIONAL OFFICE	
Dr. Yetmgeta Eyayou ABDELLA World Health Organization Regional Office for the Eastern Mediterranean Cairo, EGYPT abdellay@who.int	**Dr Jean-Bosco NDIHOKUBWAYO (EXCUSED)** World Health Organization Regional Office of African region Brazzaville, CONGO ndihokubwayoj@who.int
Dr Maria Dolores PEREZ-ROSALES	**Dr Juan Eduardo TELLO (EXCUSED)**

Advisor Blood Services and Organ Transplants World Health Organization Regional Office of the Americas Washington, USA perezmd@paho.or	World Health Organization Regional Office for Europe Copenhagen, DENMARK jet@euro.who.int
Dr Klara TISOCKI World Health Organization Regional Office of Western Pacific Region Manila, PHILIPPINES tisockik@wpro.who.int	**Dr Gunasena Sunil SENANAYAKE (EXCUSED)** SE/HSM Health Systems Management World Health Organization Regional Office for South-East Asia New Delhi, INDIA senanayakes@who.int