

Management of a Biological Resource Center

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Biobanking Chair - Siena 2010 - Slide set #10

Biological Resource Center (BRC)

"A service provider and a repository of living cells, genomes, organisms and information relating to heredity and the functions of biological systems".

The Organisation for the Economic Cooperation and Development (OECD)

OECD has proposed to establish a global BRC network.

AIM

To promote a rational use of resources and to facilitate the exchange of biological materials among different countries

The book 'Biological Resource Centres' Underpinning the Future of Life Sciences and Biotechnology', (www.SourceOECD.org), describes a program for the implementation of a global BRC network, based on 5 recommendations:

1. to establish national BRCs;
2. to develop an accreditation system for BRCs based on international criteria;
3. to create international linkages among BRCs;
4. to co-ordinate standards, rules and regulations taking BRCs into account;
5. to establish a global BRC network.

Crucial BRC issues

1. 'Preservation and provision of biological resources for scientific, industrial, agricultural, environmental and medical R&D and applications';
2. 'Performance of R&D on these biological resources';
3. 'Conservation of biodiversity';
4. 'Repositories of biological resources for protection of intellectual property';
5. 'Resources for public information and policy formulation'

At the 'Policlinico' hospital in Milan, the mission of exploiting the potentials of cellular therapy and of performing biobanking research was given to a BRC named:

"Center of Transfusion Medicine,
Cellular Therapy and Cryobiology"
(CTMC)

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Building

The foundation diploma of Hospitale Maggiore, Milan, Italy, issued by Duke Francesco Sforza on April 1st, 1456





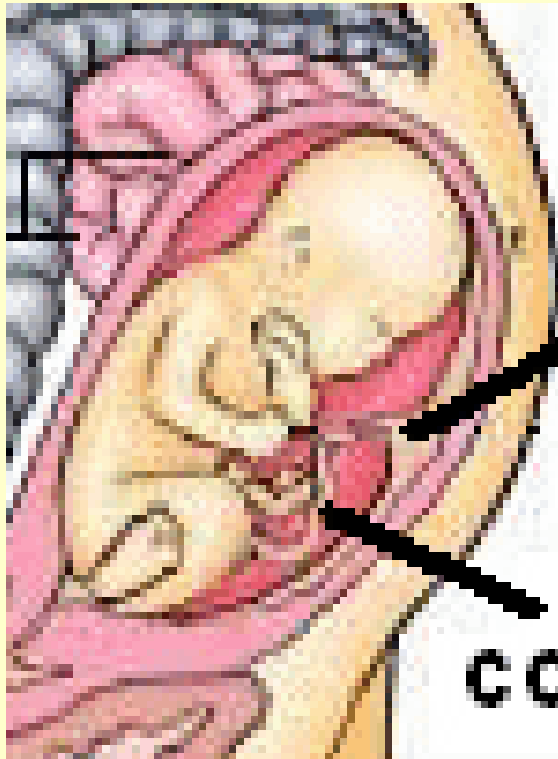
The 'Ospedale Maggiore' in Milano
Anonymous, oil on canvas, XVII century

Foundation
Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena
Milan, Italy



CTMC sections

1. the Milano Cord Blood Bank & Cell Processing Lab
 - inventory of 8,500 cord blood units
 - 450 cord blood transplants
2. the Italian Biobank
3. the 'Franco Calori' Cell Factory (GMP cellular manipulation)
4. the Flow Cytometry and Experimental Hepatology Lab

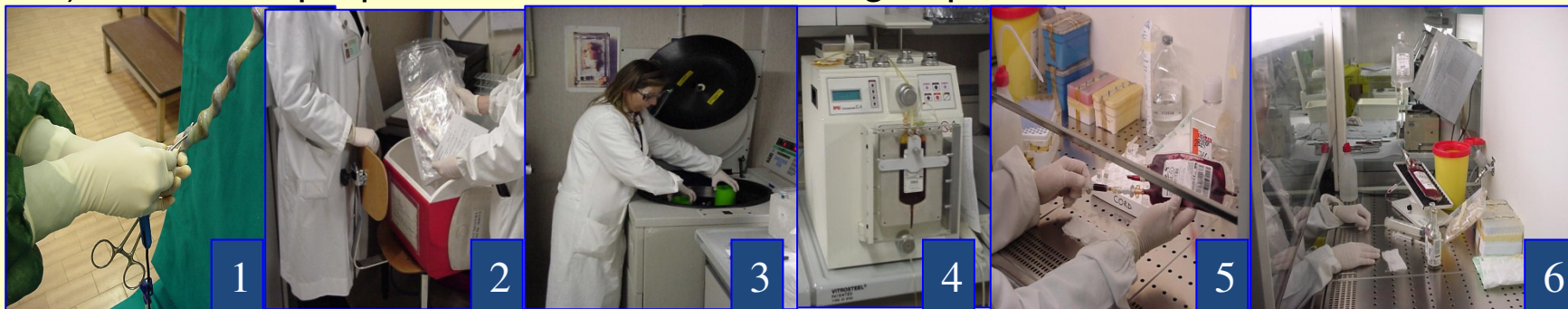


placenta

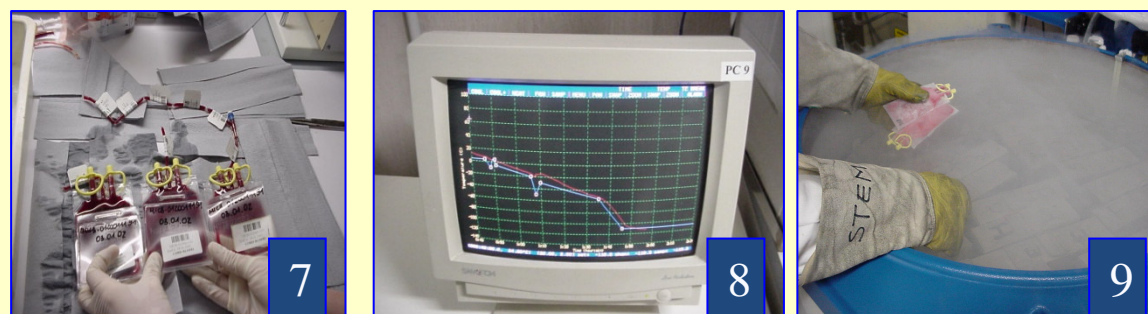
cordone ombelicale

Milano Cord Blood Bank - Il processo

A) Prelievo e preparazione dell'unità di sangue placentare



B) Congelamento a discesa controllata della temperatura

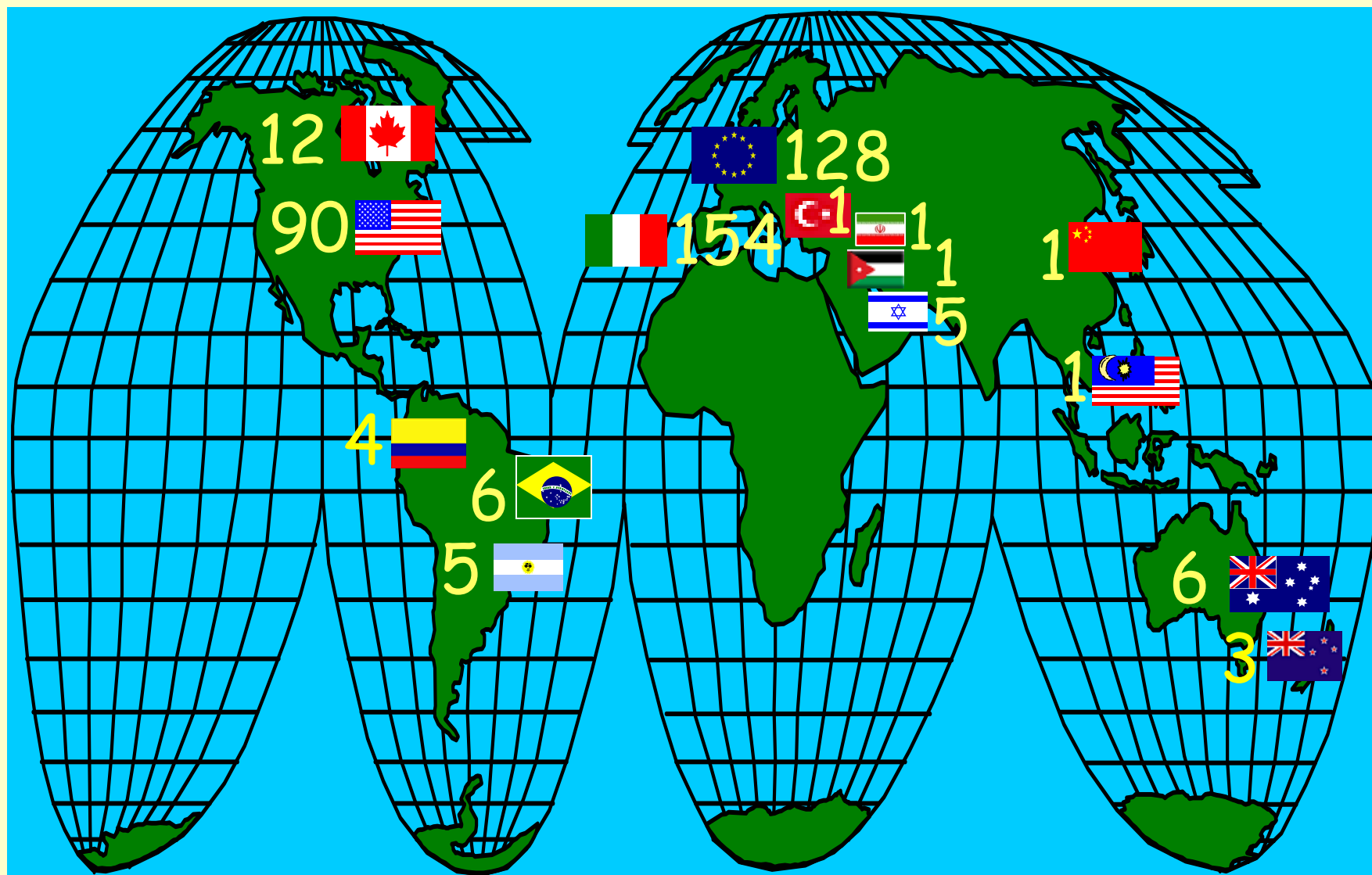


C) Controllo di qualità e trasporto al Centro Trapianto

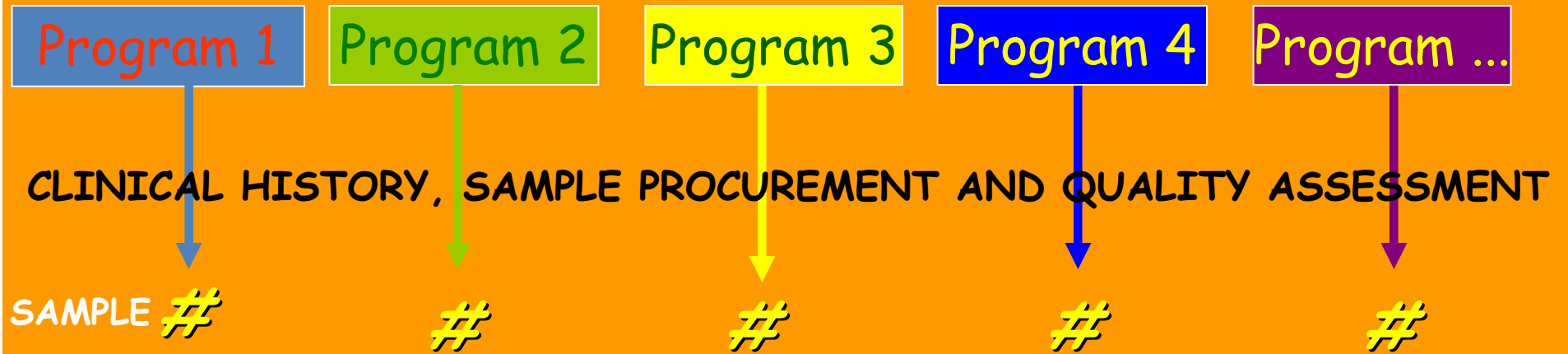


Milano Cord Blood Bank

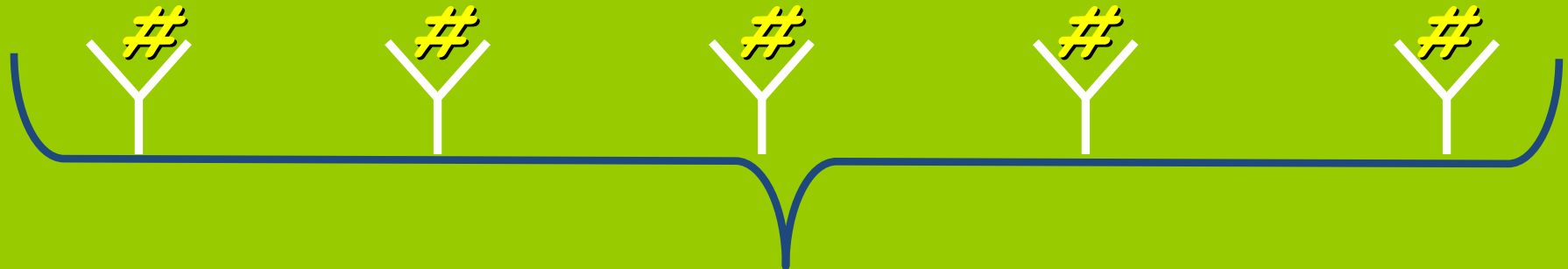
Country of transplant of 418 unrelated units released from 1995 to 2009



CUSTOMERS



BIOBANKING



Contract ("property", rules, fee, tutor)

1. Reception (date, #, type, QA)
2. Processing (aliquotation, labeling)
3. Storage (-80°C, LN)
4. Release
5. Transportation
6. Communication ('marketing')
7. Research
8. Cost

CTMC numbers

- 55 liquid nitrogen tanks and
- 9 mechanical freezers at -80°C
- 1.2 million 2-ml tubes theoretical global capacity
- 8 permanent and 22 research staff
- 2 million euro annual cost

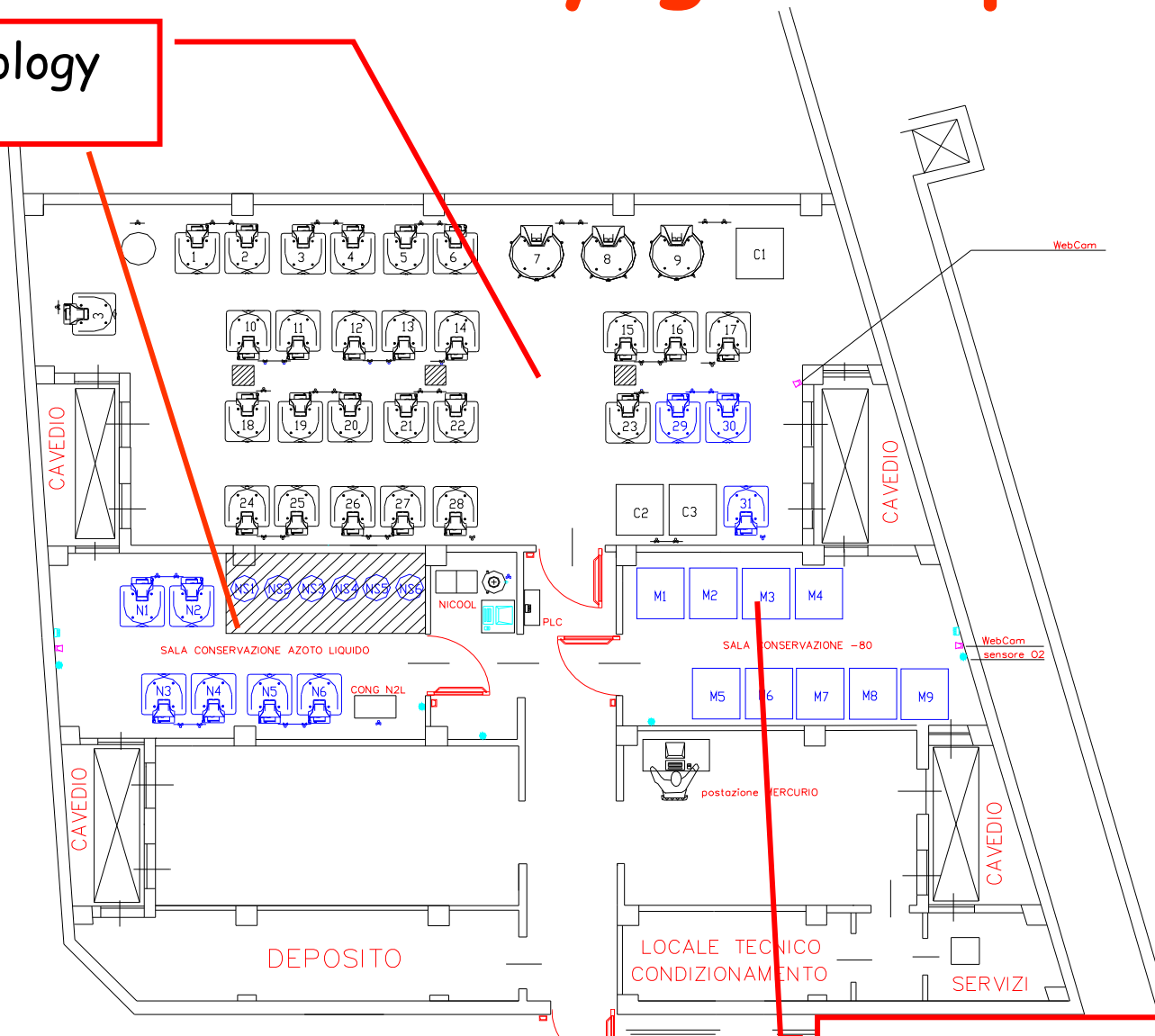
The '3 one' rule

1 euro 1 tube 1 year

... as biobanking costs 1 Meuro and we have the capacity of 1 million tubes...

The CMTC cryogenic space

LN Cryobiology
Area



- 80°C Cryobiology
Area

Inventory of the MHB-Milano Aug-2010 (I)

<i>Type of sample</i>	<i>No.</i>
1. Ancillary samples, Milano Cord Blood Bank (Lecchi)	84,936
2. Ancillary samples, non-GMP cell processing (Lecchi)	3,686
3. Whole blood samples, Rare Donor Bank (Marconi)	12,260
4. Cell culture samples, Cell Factory R&D (Lazzari)	2,101
5. Cell culture samples, Cytometry & Liver lab (Porretti)	953
6. Cell culture samples, Ist. Nazionale di Genetica Molecolare (Abrignani)	916
7. Left over tissues, Clinical Pathology (Coggi)	478
8. Cell culture samples, Genetics Laboratory (Coviello)	19
9. Tissues & cell lines from neurologic conditions (Moggio – Theleton)	1,495
10. Whole blood samples from obst & gynaecol conditions (Fedele)	222
...	...

Inventory of the MHB-Milano Aug 2010 (II)

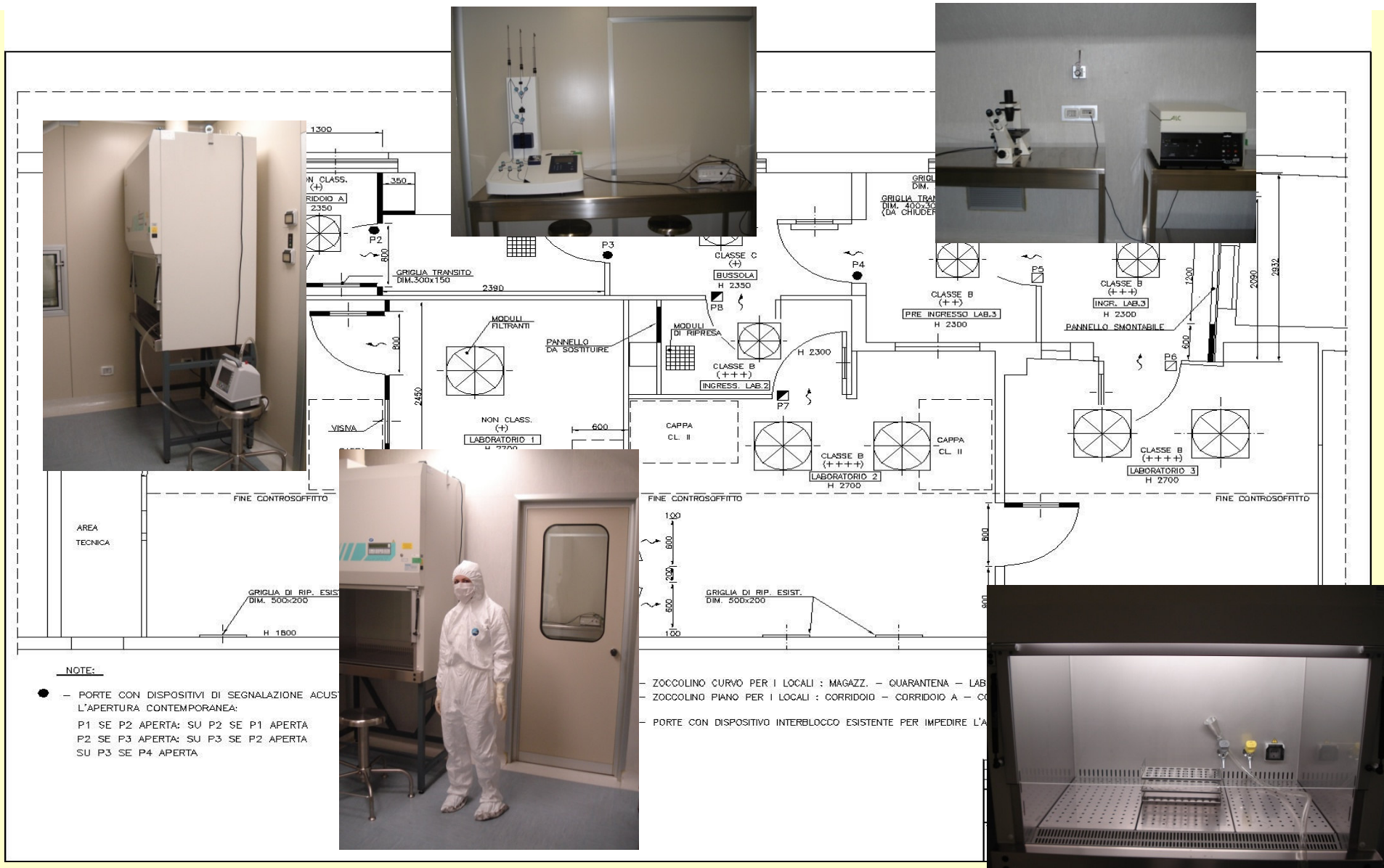
<i>Type of sample</i>	<i>No.</i>
11. Serum samples, Blood Component Lab (Marconi)	27
12. Serum samples, Emergency Medicine (Monzani)	3,013
13. Serum & buffy coat samples, Hematology (Zanella)	5,672
14. Serum samples, Oncoproteomic project, Italy-US (Poli)	10,446
15. Cell culture samples, Medical Genetics (Lalatta)	721
16. Serum from celiac disease patients (Bardella)	6,926
17. Serum & buffy coat, lung cancer patients (Santambrogio)	514
18. DNA, RNA, whole blood, serum, Occupational Medicine (Bertazzi)	29,829
19. Biopsy left-over samples (Catania)	1,958
20. Serum, thalassemic transfusion recipients (Marconi)	10,715
TOTAL (I + II)	176,887

Cell Factory 'Franco Calori'

(camera bianca per la preparazione di cellule staminali per uso clinico)

- **Protocolli clinici sperimentali 2000-2010**
 1. Espansione di cellule staminali da sangue placentare
 2. Trapianto autologo di cellule staminali muscolari
 3. Trapianto autologo di cellule CD133+ nell'infarto
 4. Riparazione della corda vocale
 5. Terapia cellulare dell'insufficienza epatica

The 'Franco Calori' Cell Factory Production area



The CTMC operates with several reference quality standards, including:

- ISO 9000 (Vision)
- Netcord/FACT (Foundation for the Accreditation of Cellular Therapy)
- JACIE (Joint Accreditation Committee- ISBT & EBMT)
- GMP (Good Manufacturing Practice)
- GAMP (Good Automated Manufacturing Practice)
- OECD Best Practice Guidelines for BRC

GMP production of products for cellular therapy

Somatic cell therapy: "Administration to humans of autologous, allogeneic or xenogenic living non germline cells, other than transfusable blood products for therapeutic, diagnostic or preventive purposes"

(Guidance for Industry - Guidance for Human Somatic Cell Therapy and Gene Therapy - FDA 1998)

CELLS ARE DRUGS

2

Managing

Cornerstones of Management

=

1. Definition of objectives
2. Regular monitoring of activities
 - Biomedical 'facts' → measurable outcomes!
 - Cost analysis: who pays?

Annual CMTC budget:
about 50% staff
about 50% operation

Table 1. 2008 objectives of the CTMC
(and related primary responsible person)

1. CTMC (Director)

- 1% CTMC cost reduction in 2008 vs 2007
- Re-training of 5 junior staff on safety-on-the-job rules and procedures
- Release of at least 40 cord blood units for allogeneic transplantation
- Research training abroad for at least 3 months for one junior staff
- At least 6 peer reviewed publications registered by Pubmed



Available online at www.sciencedirect.com



Biologicals 36 (2008) 79–87



www.elsevier.com/locate/biologicals

Special report

Development of a biological resource center for cellular therapy and biobanking in a public polyclinic university hospital

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Banking together

A unified model of informed consent for biobanking

Elena Salvaterra, Lucilla Lecchi, Silvia Giovanelli, Barbara Butti, Maria Teresa Bardella, Pier Alberto Bertazzi, Silvano Bosari, Guido Coggi, Domenico A. Coviello, Faustina Lalatta, Maurizio Moggio, Mario Nosotti, Alberto Zanella & Paolo Rebulla

During the past 10 years, human biological material—body fluids, cells, tissues, intracellular substances or DNA—and the related data have become an important resource for academic medical research, and for the industrial development of diagnostics and therapeutics (Godard

Europe (COE; Strasbourg, France) described as the “increasing cross border flow of biological materials of human origin and data” (COE, 2006), and the interests of third parties, such as the pharmaceutical and biotechnology industries (Elger & Caplan, 2006; Anderlik, 2003).

The research tasks included: a comparative review of international, regional and national requirements for biobanking (Table 1)—laws, guidelines and ethical statements—to identify definitions of informed consent (Table 2); an analysis of articles about the ethical and legal aspects of biobanking research, which

Table 1. 2008 objectives of the CTMC
(and related primary responsible persons)

2. the Milano Cord Blood Bank

- Confirmation of FACT/NetCord accreditation (bank's Technical Director)
- Participation in the JACIE accreditation program of the local bone marrow transplant clinical unit (bank's Technical Director)
- Validation of a new cord blood unit volume reduction protocol (junior research fellow)

Table 1. 2008 objectives of the CTMC
(and related primary responsible persons)

3. the Italian Biobank

- Development of ≥ 2 new biobanking programs (Biobank Coordinator)
- Review of cryogenic rooms standard operative procedure (senior staff)
- At least 1 peer reviewed publication registered by Pubmed (junior research fellow)

Table 1. 2008 objectives of the CTMC
(and related primary responsible persons)

4. the 'Franco Calori' Cell Factory

- At least 4 peer reviewed publications registered by Pubmed (R&D director, senior staff)
- Signature of at least one contract for the supply of cellular therapy services to other hospitals (Cell Factory Technical Director)

Table 1. 2008 objectives of the CTMC
(and related primary responsible persons)

5. the Flow Cytometry and Experimental
Hepatology Laboratory

- Update of the electronic data processing system (junior staff)
- Processing of at least 10 human liver cancer samples (junior research fellow)
- Harmonization of SOPs structure in compliance with the hospital quality system (senior staff)
- At least 2 peer reviewed publications registered by Pubmed (senior staff)

Table 2. Annual (2008) plan of monthly meetings of the CTMC. Items 6-14 from the first meeting (February) represent a set of 'constant' items to be updated at each subsequent monthly meeting and registered in the minutes but not necessarily discussed, in addition to and following those specifically listed each month.

Month	Agenda (and discussion coordinator)
February	<ol style="list-style-type: none"> 1. Presentation of 2008 approved objectives previously discussed with staff (CTMC Director) 2. Discussion and approval of 2007 activity reports (Section Heads) 3. Cord Blood Banking process review (Cord Blood Bank Director) 4. Renewals of research contracts for junior staff (Administrative Officer) 5. Three-monthly paid leave plan (Administrative Officer) 6. Budget analysis of research projects (Administrative Officer) 7. New publications (Staff) 8. New research grant applications (Staff) 9. New research grant approvals (Staff) 10. Allogeneic and related cord blood inventory (Cord Blood Bank Director) 11. No. of cord blood units distributed for transplant (Cord Blood Bank Director) 12. No. of GMP products distributed for clinical use (Cell Factory Technical Director) 13. Inventory of the Italian Biobank (Biobank Coordinator) 14. No. of flow cytometry assays (Flow Cytometry Laboratory Director)
March	<ol style="list-style-type: none"> 1. Three-monthly review of data management and backup responsibilities and formal authorizations (Director) 2. Review of Cell Factory processes (Cell Factory Technical Director)
April	<ol style="list-style-type: none"> 1. Approval of 2008 training needs and plan (Training Coordinator) 2. Internal audit review of last semester (Cord Blood Bank Director)

Table 2 (cont'd).

May	1. Review of Flow Cytometry processes (Flow Cytometry Laboratory Director)
June	1. Three-monthly review of data management formal authorizations and backup responsibilities (Director) 2. Renewals of research contracts for junior staff (Administrative Officer)
July	1. Review of biobanking processes (Biobank Director)
August	1. Budget analysis of the CTMC (Director) 2. Audit review of informed consent procedures to the collection of biological materials (Biojurist)
September	1. Three-monthly review of data management formal authorizations and backup responsibilities (Director) 2. Renewals of research contracts for junior staff (Administrative Officer)
October	1. Review of training needs (Training Coordinator) 2. Last semester internal audit review (Quality System Supervisor) 3. Discussion of objectives for next year (Staff)
November	1. Next year estimated budget (Director)
December	1. Approval of next year objectives (Director) 2. Review of appointments of quality system and training supervisors (Director) 3. Approval of draft of 2008 annual report, to be completed in Jan 2009 (Director)

Format of monthly reports of the CTMC.

In addition to the specific items reported in the table shown in next slide, each CTMC section reports also the following:

- No. of scientific publications
- No. of research grant applications
- No. of active research projects
- Staff variations
- Non conformities/corrective actions
- Other, as deemed relevant by the section coordinator

Report from the Milano Cord Blood Bank

1. No. of collected cord blood units
2. No. of banked cord blood units
3. No. of cord blood units released for transplantation
4. No. of cryopreserved peripheral blood stem cell (PBSC) apheresis units
5. No. of PBSC apheresis units released for transplantation
6. No. of cryopreserved bone marrow units
7. No. of bone marrow units released for transplantation

Report from the Italian Biobank

1. No. of biological samples in inventory
2. No. of biological sample donors in inventory
3. No. of active storage programs
4. No. of distributed samples, by program

Report from the 'Franco Calori' Cell Factory

1. No. and type of clinical products released
2. No. and type of new validated cellular products
3. No. of active cellular products preparation contracts with other hospitals

Report from the Flow Cytometry and Experimental Hepatology Laboratory

1. No. of performed flow cytometry assays, by type
2. No. of processed liver samples

Report from the Biojuridical Laboratory

1. List of formally approved documents
2. Audit of informed consent procedures to biological material collection and use

...and from now on?

- Integrated Quality System(s)
- Integrated Information Technology
 - open to 'outside' → global network
- Specific (BRC) staff training
- Intellectual Property rights
- Harmonized Material Transfer Agreements
- Global Unique Sample Identifier
- Promote academic value of networked publications
- Involvement of public community (consent)
- Professional Business Plan
- The Biobank **Impact Factor** (*Cambon Thomsen*)

... our vision ...

