EPPOSI
European Platform for Patients' Organisations, Science and Industry

EGAN
European Genetic Alliances' Network

BIOBANKS: *THE ENTREPRENEURIAL ROLE OF PATIENT ORGANIZATIONS*

EPPOSI Conference DATA- AND BIO-BANKING FOR RESEARCH
European Society of Human Genetics (ESHG) Congress, Amsterdam, May 6 – 9, 2006

and the

EGAN Symposium THE ROLE OF PATIENT ORGANISATIONS IN DATA/BIOBANKING
Eurobio 2006 Congress, Paris, October 25 – 27, 2006

Colophon

Report written and edited by Cees Smit

Every effort has been made to ensure that these proceedings are an accurate reflection of contributions made by the speakers during the conference, bearing in mind that this is not a verbatim report but rather a summary. Relevant sections of the draft were forwarded to each speaker for verification, and the final text has taken into account comments received. EPPOSI does not accept responsibility for eventual errors that were not communicated to the rapporteur.

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GENERAL INTRODUCTION
Dr. Cees Smit

The European Genetic Alliances' Network (EGAN) organized two meetings in 2006 on current developments in biobanks and data registries. The first meeting was in Amsterdam on May 7, during the Congress of the European Society of Human Genetics (ESHG). The meeting entitled 'Data- and Bio-Banking for Research: towards joint-ventures of patient organisations, science and industry on the road to validated expertise and new therapies' was a co-production with the European Platform for Patient's Organisations, Science and Industry (EPPOSI). In the evening, a dinner-debate closed this event with an informal exchange of ideas about the future of biobanks.
The second meeting took place in Paris on October 26 during the EuroBio 2006 Congress.
The overwhelming impression of both meetings is the increasingly dominant role that patient organizations are going to play in organizing their own biobanks and data registries. This new emerging, entrepreneurial role of patient organizations and the people's faces that are leading this, are described in this report.

Just a dad
Patrick Terry was one of the speakers in Paris during the EuroBio 2006 Congress. On his first slide his name was mentioned Patrick Terry, JaD. After that the JaD was highlighted '*Just a dad'.*
About ten years ago, just before Christmas 1995, the two children of Patrick and Sharon Terry were diagnosed with a very rare genetic disease called: pseudoxanthoma elasticum (PXE). This is a disease in which the body's elastic fibres calcify and lose their elasticity. It spreads throughout the body and shows up in the skin, in the heart and blood vessels, and in the eyes. In about thirty years, the disease normally leads to blindness and at the age of fifty there is a high chance of heart-attacks (1). It can often take some thirteen years after the first complaints before the right diagnosis is made. Just like many other parents with a rare disease, the Terry's went to the library to gather as much information about PXE as possible. Patrick ran a construction company at that time and his wife Sharon had studied theology. They found about 250 articles on PXE that were written in the last one hundred years. Most contradicted each other. Contact with scientists also made them feel rather disappointed. They did not seem really interested in looking for the causes of PXE and the road to a treatment.

The American 'can do' mentality
As a consequence of this, the Terry's founded a non-profit research company called PXE International that commissions and coordinates scientific research. In the beginning, Patrick and Sharon Terry send kits to parents to take blood samples of their children and stored that in the freezer of a neighbour. Nowadays, PXE International owns a professional blood- and tissue bank in Arizona and the company grew to a multinational group with 57 offices, mostly located at the homes of other parents of patients, and 19 labs all over the world. Finally, together with scientists from the university of Hawaii and the inter-university ophthalmologic institute in Amsterdam, they succeeded to find the gene for PXE, which they patented in 2000. Finding and cloning the PXE gene costed about half a million dollars. Soon, a diagnostic test for PXE, developed by PXE International in cooperation with the biotech company Transgenomic, will come on the market. This test will cost about 800 dollars, but PXE International is going to subsidise the test so that as many patients as possible can access it. For Patrick Terry, all this is a logical step in his life: "First I was the boss of a construction company, now of a disease. I'm determined to tackle the condition that my children suffer from. That's all" (a phrase taken from the book 'It's my life: a new revolution patient power' (1) by the Dutch science journalist Simon Rozendaal, who portrays Patrick Terry therein).

All parents of sick children have passion and dedication
To get familiar with scientific research, Patrick Terry worked for three years in a lab to learn how to 'read' the DNA to identify genes. Patrick and Sharon organized their own fundraising from the beginning to get a critical mass of money for research. To speed up the discovery of the PXE-gene, they worked with two competing scientific groups. The money that will be earned with the test for PXE, will be put in further research for PXE. To generate more money for research, the Terry's also set-up other companies. One of these is Genomic Health, that recently marketed a clinical genomic test for early-stage breast cancer. The Terry's are trying to spread their way of working all over the world and invest a lot of time to speak at conferences and to work for IGA, the International Genetic Alliance. Other patients and parents are impressed and never think they could do it. But Sharon and Patrick Terry don't agree with this "Anyone could do what we have done. It's all about passion and dedication. Those are things that all parents with sick children have'."

The French Généthon
One often hears that the developments described above are only possible in a country like the United States. But those who think so are absolutely wrong. At the end of 2005, there was a congress in The Netherlands, jointly organized by the Dutch national research council for health research ZonMw, the European Patients' Forum (EPF) and the Innovia Foundation founded by Stuart Blume (Science and technology professor at the University of Amsterdam). One of the speakers at that congress was Bernard Barataud of the Association Française contre les Myopathies (AFM), the French Society for Muscular Diseases. At the moment, this society is one of the most important financial sponsors of scientific health care research in France with its own laboratory, the Généthon. The money for this research lab comes from a large, yearly television programme called Téléthon. Thanks to the money from this programme, the AFM has substantial influence on research policies in France. In the past AFM gave the money directly to the researchers and left decisions how to spend this money to the researchers, nowadays AFM chooses its own research goals. They now have scientists on their payroll who judge the quality of the proposals from their colleagues and give advice to AFM how to spend the money. In his summary at the congress, Stuart Blume characterised this phenomenon as: "The boundaries between 'science' – the realm in which scientists claimed authority – and 'non-science' were blurred". The man who initiated this all is Bernard Barataud, the father of a child with a serious muscular disease.

A European networking grant for a parent
Tsveta Schyns is a Bulgarian biologist who got a doctorate in genetics at the University of Wageningen. Her husband is a Belgium-Dutch micro-biologist. Eight years ago, their daughter was born with Alternating Hemiplegia in Childhood (AHC). AHC is a rare neurological disorder in which alternately, and sometimes with extreme regularity, first one half of the body and then the other is paralysed. In 2003, Tsveta Schyns founded a scientific network on the disease via internet called ENRAH (European Network for Research on Alternating Hemiplegia). She also tried to obtain a research grant for a European study project on the disease. For that, she registered herself as a research organisation in Austria, the country where she and her family now live. Much to her surprise, after an initial refusal, she succeeded, in getting a substantial grant from the 6th European Framework Programme. The aim of the network is threefold: to understand the epidemiology of the disease better, to formulate better clinical criteria and to improve the education about the disease and its consequences. At the moment, nine countries are participating in the network.

The EuroBioBank
Another example of how patient organisations perform an entrepreneurial role is the EuroBioBank. This is a project from AFM and Eurordis, the European organisation for people with rare diseases. The aim of the EuroBioBank is to provide human DNA, cell and tissue samples as a service to the scientific community to enhance research in rare diseases. Within the EuroBioBank, thirteen research laboratories are co-operating, together with two ICT-companies and a biotechnology company.

Eurordis and AFM are taking care of the infrastructure needed for the EuroBioBank and the fundraising. They succeeded to get a substantial grant from the 5th European Framework Programme.

The patient as a entrepreneur

The examples above are a source of inspiration for many patients and parents of children with a serious disease. There is a trend towards globalization in the world of patient organisations. On the internet, everyone can take notice of developments which also get serious attention from science. In a recent editorial of Nature Genetics, several other examples are mentioned. The overall conclusion is that an increasing number of patient organisations are working to create their own databank or biorepository. The examples also show that it will be impossible to neglect patient organisations as a stakeholder in further initiatives which involve the collection of body material or the storage of medical data. In the United Kingdom, patient organisations have responsibility in organising the national biobank. For most patient organisations, the primary objective for their involvement is to find the cause of their disease or to improve their treatment options. People like Patrick Terry, Bernard Barataud and Tsveta Schyns play an important role as both role models and passionate professionals.

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I. EPPOSI CONFERENCE & Dinner Debate

Data- and Bio-Banking for Research TOWARDS JOINT VENTURES OF PATIENT ORGANISATIONS, SCIENCE AND INDUSTRY ON THE ROAD TO VALIDATED EXPERTISE AND NEW THERAPIES:

EPPOSI Conference

Organised in conjunction with the European Genetic Alliances' Network (EGAN) at the occasion of the European Society of Human Genetics (ESHG) Congress Amsterdam, May 6 – 9, 2006

The EPPOSI Conference 'Data- and Bio-Banking for Research: TOWARDS JOINT VENTURES OF PATIENT ORGANISATIONS, SCIENCE AND INDUSTRY ON THE ROAD TO VALIDATED EXPERTISE AND NEW THERAPIES' WAS ORGANISED BY THE THREE CONFERENCE CO-CHAIRS: JEAN-JACQUES CASSIMAN, DETLEF NIESE AND COR OOSTERWIJK WITH THE ASSISTANCE OF YSBRAND POORTMAN AND JOSÉ STAALSTRA

The EPPOSI Conference & Dinner Debate was organised in conjunction with the European Genetic Alliances' Network (EGAN) at the occasion of the European Society of Human Genetics (ESHG) Congress in Amsterdam, May 6 – 9, 2006

The Epposi Conference has been sponsored by IBM, Novartis, Amgen, Biogen, Genzyme and Cryo-Save

Introduction

The EPPOSI conference on 'Data and Bio-Banking for research', held in Amsterdam on May 7, 2006, brought together for the first time representatives from patient organizations, research institutions, industry and regulatory bodies. This EPPOSI conference made perfectly clear that if the establishment of bio-banks is stimulated and integrated at all levels of disease-specific, epidemiological and applied biomedical research and health care, progress into health care research can be significantly increased and costs of both clinical trials and daily health care can be significantly decreased. Therefore, it is urgent that European and international regulatory systems for bio-banks used for research purposes, need to be further developed and harmonised to permit appropriate sharing of data and samples to maximise the potential healthcare gain.

It also made clear that the development of biobanks is welcomed, but more importantly, is being led by international patient organizations. Almost at the same time as this conference, the editorial of Nature Genetics (April, 2006) mentioned the advocacy role being played by individual patients and their families to unravel genetic disease. At this EPPOSI conference, representatives of several patient organizations demonstrate how their self-developed bio- and databanks can progress to effective therapies for thus far untreatable diseases. It was also made clear at this conference that patient organizations have to play an important role in telling the public at large what the long-term benefits of data- and biobanks can be for society. To profit from these long-term benefits it is essential that these banks are no longer perceived as a project, but as an essential infrastructural tool in health care. An infrastructure that is a worthwhile investment for society.

EPPOSI will progress the outcomes of this data- and biobanking conference. The second EPPOSI 'Value of innovation' workshop is being planned, which will include messages from the Amsterdam conference. With the European Union Research Framework and Public Health Programmes still under discussion, this conference was also an excellent opportunity to develop views on shared governance and true partnership. These views will certainly further be discussed by EPPOSI with the European Commission.

I would like to thank all of the different stakeholders who contributed to this successful event, especially those at EGAN for their cooperation and organisational work and also those at IBM, Novartis, Amgen, Biogen, Genzyme and Cryo-Save, who made this whole conference possible.

Michael Griffith
Chairman EPPOSI

Executive summary

The European Platform for Patients' Organisations, Science and Industry (EPPOSI) is an EU patient-driven partnership between patient organisations, industry and academic science and clinicians. It was founded in 1994 to discuss and influence policies in human healthcare in Europe, based on co-operative views by its stakeholders. EPPOSI's mission is achieved through a range of activities including meetings, debates and workshops between stakeholder representatives.

Worldwide, patients, science, governments and industry recognize the value of collections of human biological samples and associated data for research and therapy development. Such collections are frequently referred to as "bio-banks". Many (inter)national bio-banks are currently being set up or are already operational. The potential benefits for unravelling the molecular pathology and biology of disease are enormous. For many multifactorial diseases, the relationship between genetic and environmental factors can be studied. For less common genetic diseases, the unravelling of the genetic defect(s) and subsequent clinical research can be accelerated, but only if a sufficient number of patients can be identified who actively contribute to the research.

The EPPOSI conference 'Data and Bio-Banking for Research' dealt with the need for new paradigms for research and development, based on the progress and possibilities in personalized medicine, personalized prevention and health maintenance strategies, fast developments in the field of information technology, diversification of common diseases into several less frequent indications based on understanding disease mechanisms on a molecular basis, and last but not least, the increasing role of patient organizations in (clinical) research based on human biological samples and associated data.

Speakers and presentations

Patrick Terry (whose presentation was given by Michael Griffith, chairman of EPPOSI) started with the example of the Genetic Alliance Biobank and showed that a collective biorepository, set up by US-based patient organizations, can be a lever that allows members to move research.

Veronika Karcagi outlined the working of the EuroBioBank. The EuroBioBank network was established by two patient organisations – Eurordis and AFM – with the support of patients and scientists in France and other European countries. The major aim of the network is to facilitate research on rare diseases by providing quality human biomaterial such as DNA, cells and tissues.

Jasper Bovenberg discussed ownership by patient organisations of their own tissue and data as well as the topic of how patient organisations can manage their tissue and data.

After these three introductory speakers, representatives of patients organisations presented examples of how their organisations started up patient registries and with what aim.

Ria Broekgaarden spoke in her presentation about the development of the Pompe survey, and the possibility that through this type of research the following research questions can be answered positively, namely:

- to use questionnaires to follow the course of the disease over time;
- to categorise patients according to the severity of their disease and;
- to help determine endpoints for clinical trials.

Tsveta Schyns introduced the need of patient registries for research on rare diseases and the value of patients/science partnership when building up a registry. She demonstrated these with the example of the ENRAH Association and the current ENRAH for SME's project that she is coordinating. ENRAH is a non profit organisation focused on support for research on one ultra rare disease, namely Alternating Hemiplegia of Childhood (AHC).

Rod Mitchell mentioned the possible development of the Dutch IBD Warehouse, a biobank for Crohn's disease (and other chronic diseases) as an example of how to target treatment for a disease through personalised medicine. He also referred to the important role that patients' organisations might play in educating society about the importance of the development of biobanks in helping to find causes and cures for many diseases.

The following two speakers went into greater detail about the particular needs of scientists with regard to the development of biobanks.
Alastair Kent spoke about the Public Population Projects in Genomics (P3G), a not-for-profit international consortium to promote collaboration between researchers in the field of population genomics. It has been launched in order to provide the international population genomics community with the resources, tools and know-how to facilitate data management for improved methods of knowledge transfer and sharing. Its main objective consists in the creation of an open, public and accessible knowledge database. The motto is transparency and collaboration.
In his presentation, *Andres Metspalu* started to mention a number of topics that are more relevant for the development of biobanks than he would ever have thought of. After that, he explained more about the Estonian Genome Project.
In the developmental process of biobanks, especially the information technology industry could be helpful in providing the right concept to answer the well-formulated questions of biobanks. Three speakers at the EPPOSI-conference dealt with these issues.

Olivier Cohen made it clear in his presentation that patient registries can be a very useful tool for exchange between researchers. Therefore on different levels, the HC Forum supports researchers with the relevant computer technology to optimize this exchange. This support is both on the national as on the international level.

Michael Hehenberger showed that the emergence of biobanks in many parts of the world is proof that governments, health insurance companies, healthcare providers, patient organizations, bio-pharmaceutical and diagnostic companies are seriously working together on the transformation of healthcare to more 'personalised healthcare'.
The convergence of information technology (IT) with molecular biology, drug discovery and the practice of medicine, has also opened opportunities for science based and patient centric approaches to healthcare. This transformation will require advanced IT infrastructures and information systems, so it is better to speak of 'information based medicine'.

Detlef Niese started with the often overlooked topic that biobanks may serve different purposes. He then discussed ethical and legal challenges and aspects of quality assurance and collaboration.

As last speaker of the EPPOSI-conference, *Jane Kaye* mentioned in her presentation that the current legal instruments across Europe differ in such a way that they provide some principles but no uniform standards and no organisational models for biobanks.

Conclusions
At the end of the EPPOSI conference on bio-banking and research, *Alastair Kent* summarised the main points of the conference. Main points, that struck him as interesting and relevant for further discussions.
In Alastair Kent's words, the contributions from the speakers have contained a wealth of ideas and models of good practice. There has been far too much to attempt to summarise adequately to do justice to the material presented by all who took part. So, what follows is a subjective extract of points which struck Alastair Kent as interesting and relevant, and worthy of further developments when considering biobanks and their scientific, ethical, medical and social possibilities.

1. Patient groups have taken a key role in promoting the need for tissue and sample banks to be set up to explore a wide range of genetic diseases. In some cases (notably some of the very rare conditions) it has been the patient group which has not only identified the need but also taken the lead in setting up and managing the biobank and in controlling the uses to which it is put (e.g. Genetic Alliance, Eurordis, Parent Project Duchenne Muscular Dystrophy in the UK, PPUK).
2. A biobank does not necessarily have to be a discrete entity located in a single repository. Biobanks can be 'virtual' structures, resulting from the creation of a framework and a data sharing mechanism to bring together sample collections in separate locations – which may not even be the same country.
3. Biobanks must be based on a secure funding stream which recognises the time scale needed for them to achieve results. Too short a time horizon will produce unrealistic expectations and

potentially threaten the opportunities and benefits which these resources offer. In this respect it is important to see biobanks as part of the scientific infrastructure. They are a resource on which projects can be based not the projects themselves.

4. Public trust will be secured if biobanks are firmly based in the principles of equity and fairness. Public sector sample collections must indorse transparency of action and decision making, and arrangements for preserving the confidentiality of donors and the security of samples and data must be robust. Ownership of data and samples must be clear, and relationships with other stakeholders (including other government agencies and the private sector) laid out for public appreciation right from the start.
5. The legal and ethical framework governing the operation of biobanks must be logical and proportionate to the risks and benefits these resources offer. Too lax and public trust will be lost. Too rigorous and beneficial outcomes desired by all will be prevented.
6. When constructing sample and data banks (especially for very rare conditions) the experience, knowledge and expertise of patients and families must not be overlooked as a source of valuable information (often that is simply not available from other sources, e.g. Pompe's Disease Association)
7. Data and sample biobanks have many and varied stakeholders (patients, academia, clinicians, government, industry, etc.). These all have different interests and expectations of the biobank, and the overlaps and tensions between them can be likened to a complex eco-system. Keep the balance requires a sensitive governance structure in which no one group has automatic power or control over all the others if stability is to be maintained, and the system is to neither fragment nor fall in on itself under the weight of competing interests.
8. The legal framework for governance of biobanks consists of those things which must be done by statutes (binding principles), and those things which, whilst they may be good practice, or the subject of professional codes of conduct for example, are not legally binding. It is important to be clear what fall into each category, and what the standards for compliance are in each case.
9. The long term sustainability of biobanks will depend on continued trust and endorsement by sample donors and the general public. Active progress of patient and public education and engagement will help to bring this about, as will regular feedback of findings to the public arising from research using the biobank resources – once these findings are reliable enough to withstand public scrutiny!
10. It is important to remember that the reason for creating these resources is not 'scientific curiosity' per se, but a desire to respond to unmet health needs – particularly serious, usually chronic, life limiting diseases. Holding to this purpose will help preserve the integrity of biobanks, and not permit this to be knocked off course by short term opportunism or the exigencies of funding demands.
11. Biobanks must bear in mind the need to secure the maximum possible technical and ethical interoperability given the specific legal requirements of the state in which they are established. This requires an anticipatory framework which will permit their purpose and uses to evolve in the light of new knowledge and new opportunities.
12. Biobanks represent 'big biology'. The regulatory and governance frameworks, and the models of how genetic research is done developed from small scale studies of single gene disorders are not entirely relevant to this new phase in genetic research, so new models, new ways of working and new sets of rules and regulations will be needed to allow the return on the investment (however defined) that these resources represent to be realised as soon as possible, and in ways that reflect the principles on which public investment in basic science and it application for health gains are based.

Recommendations from the EPPOSI Dinner Debate
After the EPPOSI conference on Biobanks, a dinner debate was held at the Rosarium in Amsterdam, where all participants elaborated further on the results of this first biobank conference. Bio-banks are not new, but this EPPOSI conference was the first one where all the experiences from patients, science and industry came together. Collaboration between these three parties is needed.

A first and main recommendation was that a bio-bank must have a clear goal, a research question. To reach that goal, there are many types of bio-banks with many purposes in many sizes. Without a clear research question, a clear goal, it is useless to set up a biobank. In biobanking, several developmental stages can be distinguished, like:
Phase 1: start-ups for a rare disease (example of ENRAH)
Phase 2: first results for a rare disease (example of Pompe's disease)
Phase 3: register for chronic diseases (example of Crohn's disease)
Phase 4: Multi-purpose register (example of the Mayo Clinic)

A second recommendation was that biobanks must be perceived as a needed infrastructure to answer research questions in health care, not as a project. Therefore, short-term funding is a threat for continuity. Non-structural EU-grants should be supported by structural national funding. Sometimes membership fees can be an additional solution for long-term funding.

The third recommendation was on regulatory issues. Harmonization of laws is needed, there are large differences between US and EU laws and within the EU national laws differ tremendously. Harmonization does not mean overregulation. The law must be first of all intelligible with binding and non-binding principles. Also informed consent procedures must be harmonized. Confidentiality and security must be based on principles like equity, fairness and ownership. And finally, when bio-banks are set-up for research, use for criminal-investigations should be resisted strongly.

The fourth recommendation dealt with the role of patients organisations.
Patients organisations are paving new roads when they develop their own biobanks. Added value of involvement from patient organisations can be to convince the public about the usefulness of bio-banks, to raise awareness. There is a need to educate patient organisations in how to start and structure a bio-bank. At the same time it must be realized that there is no blueprint for this. Patient organisations will also be mindful though of the wishes of the patients and families, especially concerning the provision of samples, data, etc; the need for education, an improved understanding of the informal consent process and the myriad of legal and ethical issues.

Biobanking by patient organisations: the USA experience.

Patrick Terry, Genetic Alliance BioBank

Patrick Terry's presentation was given by Michael Griffith, chairman of EPPOSI. The example of the Genetic Alliance Biobank, started by Patrick Terry shows that a collective biorepository – set up by US-based patient organizations - can be a lever that allows members to move research.

At the end of 2003, seven genetic advocacy organizations established the Genetic Alliance BioBank introducing a new age of consumer advocacy and translational research. Members pay an annual fee, and receive all of the necessary training, technical assistance, protocols and documents. The Members of the BioBank are:

- CFC International
- Inflammatory Breast Cancer Research Foundation
- Joubert Syndrome Foundation
- National Psoriasis Foundation
- NBIA Disorders Association
- Noonan Syndrome Support Group
- PXE International

The Genetic Alliance BioBank

The Genetic Alliance BioBank is an advocacy owned repository for biological samples and clinical data. The BioBank offices are in Washington DC, and its laboratory facility is in Wisconsin. It offers a centralized, standardized setting for collection and archiving of specimens, high storage and participant protection standards, and researchers gain access to samples through the member organizations. Advocacy organizations retain control of the specimens banked at the Genetic Alliance BioBank.

The BioBank requires members to be nonprofits with professional advisory boards who agree to use BioBank approved documents and follow BioBank protocols. Each member pays an entry fee and an annual fee, and there are per-sample charges for storage and withdrawal. If groups wish, these fees can be passed on to researchers. The BioBank offers repository services now – DNA, tissue and cell lines. Member groups are not required to make their specimens available for bank-wide research uses, but participation at that level will greatly enhance the value of the BioBank to the advocacy community as a whole.

BioBank members receive specimen kits, training and documentation, technical assistance as needed, peer-to-peer mentoring, and database and data-collection report. Member organizations determine their recruitment strategies and administer informed consent. The BioBank distributes kits (with directions for return), extracts DNA and archives samples. It then records the 'deposits' in a database. Members authorize withdrawals for research projects they approve. The BioBank lab reports deposits and withdrawals to the BioBank office, which bills member organizations for specific activity.

Advocacy run blood and tissue banks

Historically, the research environment has been competitive and fragmented, and blood and tissue collections have been small and inconsistently managed. A collection might contain samples only from individuals with more severe disease, since those individuals might be more motivated to participate in studies. Different collections might have different consent and confidentiality procedures, offering donors inconsistent protections. Samples have often been considered the property of the research entity that collected them, and this has hindered sharing materials with other researchers and has limited reporting of outcome information to research participants.

These limitations can contribute to a sense among individuals and families with genetic conditions that they are 'missed' for their biological material, perhaps without a clear benefit. This impression reduces trust between researchers and participants, especially for individuals affected by a rare disease that is not well understood.

When an advocacy group leads this effort, it can protect its members from potential conflicts of interests among researchers and corporations interested in genetic information. In this way, an advocacy driven biobank or repository is a powerful way to consolidate the power of the members of a patient group. And so, they can play an active role in research that truly benefits affected individuals.

Conclusion
A cooperative blood and tissue bank can speed gene discovery, build mutation databases, and improve the understanding of genotype/phenotype correlations. These cooperatives gather groups together to share the costs of the endeavour while enjoying the reduced overhead of larger-scale operations. And it can do this in a responsible way: by advocating for member groups in interactions with researchers, enforcing protection of specimens used, and protecting the privacy of research participants. A collective biorepository can be a lever that allows members to move research.

For more information:
www.biobank.org and its members:
www.cfc.syndrome.org
www.ibcresearch.org
www.joubertsyndrome.org
www.psoriaisis.org
www.nbiadisorders.org
www.noonansyndrome.org
www.pxe.org

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For the summary of Mr. Terry's presentation, material was used from the BioBank. For the use of this material, written permission was given by the BioBank.

The advocates
The April 2006 editorial of Nature Genetics describes a significant change in how research in human genetics has been conducted over the past two decades. The editorial mentions three examples, where a member of a genetic advocacy group who is not an academic has co-authored a gene-discovery. With regard to the work that Sharon and Patrick Terry did on PXE, Nature Genetics illustrates this tendency. In 1994, Sharon and Patrick Terry's two children were diagnosed with PXE. After that unhappy news 'they raised money, established a registry of more than 2000 affected individuals worldwide, created blood and tissue banks and helped spearhead the research effort that resulted in the gene identification. Without the essential resources they put together, and the focused attention they placed on a disease that had drawn little interest from the scientific community, it's safe to say that the molecular basis of PXE (especially ABCC6, a transmembrane transporter of unknown function) would still be a mystery. Moreover, in an unusual move, the patent rights to ABCC6 were assigned to PXE International, the non-profit organization they established and that still catalyzes research on PXE'. Nature Genetics mentions also other parents that pioneered the advocacy approach to seeking help for their children. Most of the organizations they started are working together within the US based Genetic Alliance. According to Nature Genetics the potential reach of organizations like the Genetic Alliance continues to grow.
In January 2006, the March of Dimes released a comprehensive report on birth defects. The report notes that at least 70% of the more than six million children affected by birth defects each year could be positively affected by intervention. As part of a global effort to address this unmet need, the report specifically calls upon groups like the International Genetic Alliance (IGA) to serve as a lynchpin in the partnerships among governments, scientists, health-care providers and patient support groups that will be necessary to reduce the number of birth defects in developing countries.
The editorial of Nature Genetics ends with the statement that 'the advocates are serving individuals and promoting research into rare diseases. But in addition to providing the first critical insight into disease aetiology, these gene identifications can shed light on more common disorders as well. Regardless, the day will soon be upon us when genetics is better integrated into even routine medical practice, and lay advocacy groups will no doubt be crucially involved in translating research findings for the widest possible range of health-care consumers'.

The role of patients in biobanking for rare diseases in Europe.
Veronika Karcagi, EuroBioBank/Eurordis

*Karcagi outlined the working of the EuroBioBank. The **EuroBioBank network** was established by two patient organisations – Eurordis and AFM – with the support of patients and scientists in France and other European countries. The major aim of the network is to facilitate research on rare diseases by providing quality human biomaterial such as DNA, cells and tissues.*

This positive impact on European people has been acknowledged and EuroBioBank was awarded the *'Newropeans Grand Prix 2004'* prize for best European project in the category Research & Technology. The EuroBioBank project was funded for three years (2003 – 2006) by the EU-Commission (5th FP), and will serve as a platform for various projects and consortia in the future. The EuroBioBank brings together 16 partners from 8 European countries, including:

- twelve Biological Resources Centres (BRC's) storing a total of 165000 documented human biological samples;
- two IT services companies;
- one biotech company and
- Eurordis, the European umbrella organisation for rare disorders.

The **objectives** of the EuroBioBank are to:

- identify and localise biological material of interest to researchers;
- build a critical mass of rare disease sample collections;
- distribute high quality material and associated data to users;
- promote quality banking practices;
- disseminate knowledge and know-how to the scientific community through training
- enhance collaboration with the medical and scientific community in the field of rare diseases

The exchange of samples is now facilitated by the online EuroBioBank catalogue of collections at www.eurobiobank.org, which enables scientists to find specific information about the available samples across the entire network and request them. The network also promotes quality banking practices for collection, preparation, storage, and transport of biological material, and addresses the ethical issues relating to these practices. The EuroBioBank partners have developed harmonised Standard Operating Procedures (SOP's) and a standardised Material Transfer Agreement (MTA) that comply with the OECD's recommendations for Biological Resource Centres (BRC's). These documents can be found on the EuroBioBank website.
Regarding ethics, the EuroBioBank partners published an innovative book on the ethical and legal implications for biobanks. This publication gives an overview of current legislation in the different member states represented at EuroBioBank and can be obtained from their website.
The long-term aim of EuroBioBank is to continue facilitating research on rare diseases by providing the appropriate biological samples donated by the patients. This may ultimately contribute to the development of therapies for approximately 24 - 36 million people with rare diseases in Europe. To reach this aim, a solution must be found for the long term sustainability of public BioBanks. This certainly implies recognition of the public health value of BioBanks and of their importance as fundamental infrastructures. Another challenge is harmonisation – a key word in the EU – both at the legislative and the scientific level, to reach high quality standards.

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Patient organizations as owners and managers of their data and tissue.
J. A. Bovenberg, attorney at law

Bovenberg discussed ownership by patient organisations of their own tissue and data as well as the topic how patient organisations can manage their tissue and data.

Introduction
Who owns our DNA? The intuitive answer to this question is readily apparent: you own your own DNA. However, since Watson and Crick discovered its molecular structure, our DNA has gradually evolved from the *Secret of Life* to a potentially lucrative *Commodity*. This development has triggered conflicting perspectives as to who holds legal title to our blood, genes and related health data. While the United Nations have proclaimed human DNA as the Heritage of Humanity, industry claims it to be patentable subject matter. Whereas populations whose DNA is used in national biobanks claim their DNA as their National Property, individual patients increasingly stand up for their Personal Property Rights in their samples. Meanwhile academic researchers claim their collections of biological materials as their Academic Property.

The backgrounds of this discussion are extensively discussed in Bovenberg's book 'Property rights in blood, genes and data', that appeared in 2006.

Do patient organizations own their tissue?
Bovenberg started with giving an overview of arguments contra and pro patient property rights. The more or less final conclusions from this overview are that:
- civil law in the European Union is such that raw tissue is capable of human control as well as the topic of ownership, although it is generally held that body parts, including tissue, should not give rise to financial gain;
- ownership of raw tissue belongs to the individual producing it;
- the individual (patient/family) can transfer ownership to a patient organisation (PO);
- the ownership of a collection of raw tissue provides legal underpinning for a patient organisation to negotiate terms of access by third parties.

But then, there are some complications, like:
- outside the body, cells have limited life-span;
- to enable research, cells must be preserved or immortalised;
- and then the question arises, does ownership of raw tissue extend automatically to tissue as, if and when modified by others?

The answer to this question, can be modified as follows:
- if a person (scientist/industry) creates new material from material owned by some else (patient organization), the new material becomes the property of the owner of the original material (PO);
- if a person creates new material from material owned by someone else (PO) for himself, then the new material becomes the property of the creator;
- but if a person is contracted to create new material from material owned by someone else (PO) for himself, the new material will be owned by the person ordering the creation of the new material.

Do patient organisations own their data?
Patient organisations do collect data from its members. Patient organisations will have a database right in a resultant database if it made a substantial investment (financial, labour) in the collection, verification and presentation of the database. This database right is the exclusive right to authorize or prohibit third parties to extract and/or reutilise the content of the database. This database right in its collection of data provides a patient organisation also with legal underpinning to negotiate terms of access to the database, which means:
- royalties on intellectual property (IP) resulting from research on the database,
- right to control licensing policies and
- right to step in if inventor fails to pursue or exploit IP.

The complications within these general rules, are:

- database right is not an exclusive right in data itself,
- database right does not prejudice any IP or other rights relating to data contained in the database and
- database right is owned by the entity making the substantial investments and risks.

So, multiple parties (subsequently) investing in the database may lead to joint ownership.

How can patient organisations manage their tissue and data?
Patient organisations (PO's) can own their collection of tissue, as well as they can have a database right in collected data. Then, the question arise what legal ways there are for a patient organization to capitalize on these assets. Bovenberg discussed three different options:

1. PO's can start a collaborative research enterprise (CRE), together with scientists and industry under terms of a joint venture (contractual relationship/partnership)
2. PO's can start a CRE, by incorporating a company with scientists and industry as the co-shareholders. PO's could contribute their samples and data to this company as a *contribution in kind*, in exchange for a specific shareholding
3. By way of a donor council to be established within the corporation doing the research and development. In analogy with a workers' council or in analogy with donor involvement in the blood supply. For instance in The Netherlands, the Dutch minister must consult donors and patients for setting policy for the Central Bloodbank Sanquin. Sanquin has instituted a national donor council, representing all donors. This Donor Council gives advice and has to be consulted.

Conclusion
In Europe, in contrast to the United States, patient organisations can claim ownership of collected raw material and database right in collected data. These rights can form legal underpinning for negotiating terms of access by third parties. These rights can be applied in a variety of legal structures to realize control and capital value proportionate to value of the patients' organization contribution to the collaborative research enterprise.

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The Pompe survey: collaboration of science and patients.

Ria Broekgaarden, International Pompe Association IPA

Broekgaarden spoke in her presentation about the development of the Pompe survey, and the possibility that through this type of research the following research questions can be answered positively, namely:to use the questionnaire to follow the course of the disease over time; to categorise patients according to the severity of their disease and to help determine endpoints for clinical trials.

The Pompe Survey Project

In 2002, the International Pompe Association (IPA) and the Erasmus Medical Centre in Rotterdam, the Netherlands jointly started the 'Pompe Survey' project, involving the development and distribution of a collection of questionnaires for patients with late-onset Pompe's disease. The purpose of this study was to describe the 'late-onset' form of Pompe's disease: the natural course, the severity of disease in the patient population, and the use of (medical) care. A second goal was to develop and test measurement scales for the assessment of disease severity and the evaluation of changes over time. Pompe disease manifests as a broad spectrum of clinical symptoms. All patients typically experience progressive muscle weakness and breathing difficulty, but the rate of disease progression can vary widely depending on the age of onset and the extent of organ involvement. When symptoms appear within a few months of birth, babies frequently display a markedly enlarged heart and die within the first year of life. When symptoms appear during childhood, adolescence or adulthood, patients may experience steadily progressive debilitation and premature mortality due to respiratory failure. They often require mechanical ventilation to assist with breathing and wheelchairs to assist with mobility. Pompe disease has an estimated frequency of 1 in 40.000 births. This makes it difficult to obtain an accurate view of the natural course of the disease and to design clinical trials.A recombinant product to treat patients with Pompe disease, became available early 2006, with the market approval of Myozyme in Europe (January 27th, 2006) and in the United Stated (April 28th, 2006).

Mission of the International Pompe Association (IPA)

The mission of the International Pompe Association (IPA) is twofold.
Firstly, to assure that there is early diagnosis and effective, affordable and safe treatment and therapy for all patients with Pompe disease. And secondly, to assure that there is reliable information and support to all patients, their families and other involved parties with Pompe disease.IPA is not an organization of individuals members with Pompe disease, but the members are national patient groups. Currently, there are 33 member-countries of IPA and there are contacts with 5 other countries. For the 'Pompe survey' project, a questionnaire was developed covering topics such as diagnosis, disease history, development in childhood, mobility, respiratory problems, specific symptoms, daily activities and use of care ('Pompe questionnaire'). Further, already existing questionnaires were added for the measurement of fatigue (fatigue severity scale), self care and mobility, the level of handicap (Rotterdam 9-items handicap scale), and quality of life (SF-36 health survey). Currently more than 300 Pompe patients have participated in this project through the IPA-affiliated patient organisations in The Netherlands, Germany, the United Kingdom, France, the United States, Australia and Canada. Some others have participated directly through Erasmus MC.

First results from the Pompe survey

First, results from the Pompe questionnaire in 54 Dutch patients were analysed. An important message from this study was that almost 60% of the adult participants already had mild symptoms as a child related to Pompe's disease. It also became clear that Pompe's disease is a genuine spectrum of disease, with first symptoms possible at every age and with substantial variation in the sequence of respiratory and skeletal muscle involvement. Therefore, follow-up of respiratory function is important for all Pompe irrespective of the age and the level of skeletal muscle weakness of the patient. Another observation from this study was that fatigue and pain were more frequent in Pompe's disease than previously thought. The results of this study have been published in the scientific journal 'Brain'. Meanwhile, follow-up data for the Dutch group have been collected after 1

and after 2 years and are currently being analysed. The international group of patients was sufficiently large to divide into groups based on age and disease duration, and to relate these two variables to disease severity. Furthermore, in 227 patients fatigue was studied in more detail using the 'Fatigue severity scale'. Results were published in the scientific journal 'Neurology'.So far, the Pompe Survey has provided a large amount of information, and newly completed questionnaires are regularly received. More questionnaires are being filled in along with the news that soon a product will be available to treat patients with Pompe disease. It is still possible to participate in the Survey. The questionnaire is available in Dutch, English, French, and German.

Conclusion

The conclusion can be drawn that through this type of research, the development of the Pompe survey, the following research questions can be answered positively, namely:

- to use questionnaires to follow the course of the disease over time;
- to categorise patients according to the severity of their disease and;
- to help determine endpoints for clinical trials.

To predict the course of the disease, extra time is needed for the follow-up of the survey and also more research data should then be included.

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The European Registry of patients with Alternating Hemiplegia in Childhood (AHC): a collaboration of science and patients for research.

Tsveta Schyns, ENRAH Association, Vienna, Austria

Tsveta Schyns spoke on the need of patient registries for research on rare diseases and the value of patients/science partnership when building up a registry. She demonstrated these with the example of the ENRAH Association and the current ENRAH for SME's project, she is coordinating. ENRAH is a non profit organisation focused on support for research on one ultra rare disease, namely Alternating Hemiplegia of Childhood (AHC).

In many rare and newly described conditions such as AHC, it is often the case that research is fragmented and not sustainable: conducted on single cases, results are not published and shared, literature data may appear contradictory. In addition, clinical and genetic research into conditions such as AHC is hampered by the lack of well defined diagnostic (symptomatic) criteria and thus, subsequently, of clinically well defined patients. To address these, sustainable efforts must be made to gather the research resources in the field as well as to reach for the patients. Establishing of a patient registry as a repository of data is a long term investment and can greatly facilitate such efforts. For the needs of the current research on AHC and with the support from the FP 6 Community Research Framework Program 6, ENRAH has commenced (April 2005) to build up a patient registry of AHC patients in Europe. The registry is already set up on line as a repository of clinical and genetic data for people diagnosed with AHC through 9 EU countries clinical centres of AHC expertise – Austria, Belgium, the Czech Republic, France, Germany, Italy, The Netherlands, Spain and UK. The patient data are encoded and the access to these data is secured and protected. At the same time, the web form of the registry (provided by HC Forum France) allows for a speedy uploading of data and access to data by authorised use from any place in the world. The procedures for the use

and access ensure the protection and safety of the data, but also, an open access for researchers expressing interest. In its first edition December 2006, the Registry will include over 120 cases and will be maintained, extended and updated to serve as a foundation for future research into this disease. Thus, not only inspired, but sustainable efforts are needed in order to forward research into rare and, complex and heterogeneous, conditions. The ENRAH model is by building up trusts and providing the necessary support to equally engage science, patients, and industry into a long-term collaboration and partnership on the way of treatment and cure of the disease.
In the report of the EGAN symposium in Paris, a more detailed description of the registry is given, as an example to those patients organizations and their clinicians who want to start with a registry.

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Feasible Science & Industry Collaboration In Bio-banking for Crohn's disease.
Rod Mitchell, EFCCA

Mitchell spoke about the development of the Dutch IBD Warehouse, a biobank for Crohn's disease (and other chronic diseases) as an example how to target treatment for a disease through personalised medicine. He also referred to the important role that patients' organisations might play in educating society about the importance of the development of biobanks in helping to find cause and cure for many diseases.

The European Federation of Crohn's and Ulcerative Colitis Association (EFCCA) works for and with its member national patients associations, primarily at the European level to improve the wellbeing and quality of life and care for patients of all ages. Crohn's disease and ulcerative colitis are non-contagious and non-infectious illnesses, known as inflammatory bowel disease (IBD), which affect over one million people in Europe. It is estimated some 4 – 5 million IBD patients world-wide. At present, there is no known cause or cure. Especially for Crohn's disease, the problem is that it is a complex, remitting and relapsing heterogeneous disease with sub sets of patients. Often, there is repeat surgery, psychosocial dysfunction, extra intestinal complications and for most side effects of treatment, such that it makes travel, working and family life very difficult. Following diagnosis, for many and for total life there are high healthcare costs. So, targeted efforts to treat patients through personalised medicine can not only help the patient and family, but also reduce healthcare costs and improve economies by early return to work.Working towards the goal of personalised treatments, at the Academic Medical Centre in Amsterdam, The Netherlands the concept of a Dutch Chronic Conditions Bio Bank (Warehouse) is being studied, in close cooperation with IBM and with government support. It is planned that the IBD Warehouse will also hold large cohorts of patients through inter hospital collaborations. However, there are a number of legal, ethical, informed consent and other considerations to be addressed as it is planned that the Data Bio bank will contain DNA, serum and faeces, and also biopsy and resection segments in the long term. The available technology means that in time Bio bank facilities will be capable too of collaboration with other centres in Europe and beyond our borders.Importantly society and those directly involved will need education and training, but especially the patients who will become part of the Data Bio bank. Increasingly the patient organisations assist in the education and training of people diagnosed with chronic conditions like IBD and they can assist in dissemination information and in educating about bio banks too. The knowledge to be gained through the Dutch Bio bank feasibility study of the link between genetic susceptibility, environment factors, bacterial antigens and immune symptoms will lead to a better understanding of many complex conditions (including some rare diseases) and in the case of inflammatory bowel disease will help researchers to complete the missing pieces of the jigsaw in their search for cause and cure, provide individualised treatment where necessary and ultimately prevention programmes.

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Note: Rod Mitchell and EFCCA acknowledge the help provided by gastroenterologist, Dr. Daan Hommes of The Netherlands in the provision of background information for the original presentation.

Interoperability and public endorsement for securing quality outcomes from biobanks.
Alastair Kent, P3G

Kent spoke about the Public Population Project in Genomics (P3G), a non-for-profit international consortium to promote collaboration between researchers in the field of population genomics. It has been launched in order to provide the international population genomics community with the resources, tools and know-how to facilitate data management for improved methods of knowledge transfer and sharing. Its main objective consists in the creation of an open, public and accessible knowledge database. The motto is transparency and collaboration.

P3G, at a glance
The Human Genome Project, the International HapMap, and the forthcoming wealth of reports regarding susceptibility genes are creating an urgent need to generate large well-characterized data sets from population samples. These studies will allow the biomedical community to unravel the complex genetic and environmental interactions responsible for most common diseases. P3G) is an international consortium for the development and management of a multidisciplinary infrastructure for comparing and merging results from population genomic studies. P3G will enable the international research community to deliver more effective health care strategies aimed at disease prevention, and at tailoring medicines and other treatment regimens to individuals, families and communities.

Mission
Dedicated to fostering collaboration between researchers and projects in the field of population genomics, P3G develops, in an open and transparent manner, research tools for effective collaboration between biobanks so as to enable the international research community to share expertise and resources and facilitate knowledge transfer for the health of populations.

International Consortium with Working groups
P3G members are leading public organizations partaking in large-scale genetic epidemiology projects and biobanks, (with their own independent governance structure, objectives, etc). In addition to the three founding regular members, CARTaGENE (Quebec, Canada), the Estonian Genome Project, and GenomEUtwin (involving 8 countries), P3G regular membership includes the Centre for Integrated Genomic Medical Research (CIGMR; Manchester, UK), the Western Australian Genetic Health Project (WAGHP, Australia), The Danubian Biobank Foundation (involving 6 countries in central Europe), the National Heart, Lung and Blood Institute (NIH, USA), KORA-Gen (Germany) and LifeGene (Sweden). P3G also includes associate members: Genoma Espana (Spain), Centers for Disease Control (Office of Genomics & Disease Prevention; Atlanta, USA), the Centre de Recherche en Droit Public (Canada), the McGill University and Genome Quebec Innovation Centre (Canada), the National Human Genome Research Institute (NIH, USA) and individual members (scientists, ethicists, etc.). P3G has achieved a critical mass to form the principal international body for the harmonization of public population projects in genomics.
P3G has three international working groups on: technical issues, data handling & storage and ethics, governance & public awareness. The working group on ethics, governance & public awareness is developing priorities for securing interoperability. Another focus is on tool sharing, which includes developing guidelines on: use of information beyond original purpose, semantics/lexicon, access to samples, purposes, ethical review, privacy and property. The third focus is on policy issues, like: political real time, linguistics, legal codes, sensitivity of issues in complex disorders, professional and participants views and prospective informal consent. The meaning of **'political real time'** is that politicians usually have a time-scope of four or five years till the next elections. Most of the issues that are dealt with within the P3G consortium are issues that take a much longer time-period, for instance a cure for cancer might take more than four or five election periods. So, therefore politicians can not easily develop consistent views on these issues.

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The Estonian Genome Project.
Andres Metspalu, EGP, ESHG

In his presentation, Metspalu started to mention a number of topics that are more relevant for the development of biobanks than he would ever have thought of. After that, he explained more about the Estonian Genome Project.

Good law and informed consent
For instance, when Metspalu started to work on the development of the Estonian Genome Project he thought DNA was the most important issue. Now he knows better and it is 'good law' and 'informed consent' that matters. Without a good law and good informed consent procedures, there are too many restrictions from the start to set up a good biobank.
Scandinavia is a good example of an area where there are a lot of good registries. But the actual informed consent procedures are such that there is often a need to go back to the people to ask them for permission to have data or body material included in the biobank.
(Note from the editor: At the EPPOSI dinner conference later that day, a remark was made that the Swedish government will start a public information campaign on biobanks. In this campaign the principles of the Swedish biobank registration procedures will be highlighted. When individuals have objections that their data will be included, they have to say so and then their data will not be included).

Image of biobanks
Now, we are generating biobanks that will be for future generations. In 40 years, the public will see biobanks as a valuable asset for society. But at the moment biobanks have a less positive image. This is mainly because of the preference of the media to bring 'bad' news instead of 'good' news. The linkage of biobanks to criminal (CSI) and terrorist investigations is part of this image problem. If this linkage is made, then your name as a researcher will be 'tainted'. With regard to the future, another problem is that it is difficult to fund a project today with benefits so far in the future.

Financing of biobanks
In the beginning the Estonian government and the EGP was looking for private investors to invest in the Estonian Biobank. This led to good initial results, but private investments went down after the crisis in the stock markets.
Now there is a transition from private to public financing. In May 2006, more definite and stable financing was found for the Estonian Biobank from the Estonian government budget.
The way biobanks are operating and their working standards, is more an issue of the amount of money you can invest in it. Now, a small handling fee is asked from the public research institutions as a way to get expenses refunded. Expenses directly related to sample holding in order to get samples to the scientists. Private companies have to negotiate the price in order to get access to the data and samples of the EGP.

The Estonian Genome Project (EGP)
The goal of the EGP is to develop an excellent population based database with health records and DNA samples for genetic studies of different design. Therefore, it is necessary to have a large collection of health records of high quality together with the DNA, plasma and WBC.
The aim is to have 100.000 individuals in the database by the end of 2010. This will cost about eight million Euro, all inclusive.
The legal framework for the activities of the EGP consists of the Constitution of the Republic of Estonia, the Human Genes Research Act (HGRA), the Personal Data Protection Act, the Databases Act and the Council of Europe Convention on Human Rights and Biomedicine. Phenotype data and the blood sample of voluntary gene donors are collected into the EGP database and biobank. A person who is interested in participating in the Estonian Genome Project has to contact his or her general practitioner (GP) and make an appointment. Upon visiting the GP, the person will be first introduced to the Genome Project. If the person decides to participate, he or she will sign a Gene Donor Consent Form and the GP will give him or her a kit of informational materials. Next, the GP with the gene donor will fill out a questionnaire in the computer. Then a blood sample is

taken. The blood sample and signed consent form are delivered to the EGP by courier. Completed questionnaires are sent electronically to the EGP in the form of authorised and encrypted documents by the GP. Personal data of questionnaires delivered to the EGP are separated and replaced with a 16-digit code in the coding centre. Health data that has been separated from personal data are stored in the database of the EGP. DNA, the carrier of genetic information, is extracted from the blood sample in the laboratory of the EGP. Separated DNA, plasma and the WBC are placed in the storage facility of the EGP. On the basis of DNA preserved in the storage facility, it is possible to prepare personal LD maps of gene donors in the future. Scientists can carry out scientific research in order to find the genes that cause and influence common diseases, using only anonymous data of gene donors.

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Patient registries: a useful tool for exchange between researchers.

Olivier Cohen, HC Forum

Dr. Cohen made it rather clear in his presentation that patient registries can be a very useful tool for exchange between researchers. It's therefore that on different levels HC Forum support researchers with the relevant computer technology to optimize this exchange. This support is as well on the national as on the international level.

HC Forum assist all those who work in the health care sector in establishing common computer based solutions, which enable a coordinated network around the patients and an added value based on the family dimension of the medical information. Because of copyright on the slides, showed during dr. Cohen's presentation there is no summary of this presentation.

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Biobanking: the next step to personalised healthcare.

Michael Hehenberger, IBM

Hehenberger made clear in his presentation that the emergence of biobanks in many parts of the world is proof that governments, health insurance companies, healthcare providers, patient organizations, bio-pharmaceutical and diagnostic companies are seriously working together on the transformation of healthcare to more 'personalised healthcare'. The convergence of information technology (IT) with molecular biology, drug discovery and the practice of medicine, has also opened opportunities for science based and patient centric approaches to healthcare. This transformation will require advanced IT infrastructures and information systems, so it is better to speak of 'information based medicine'.

Information Based Medicine

With the new input from the life sciences (at molecular level a better understanding of the disease & the development of targeted drugs based on genomic insights) and clinical healthcare (the delivery of personalized treatments based upon medical history and genetic predispositions), 'information based medicine' is the link between clinical research and the development of new drugs and diagnostics. In this way, information based medicine is an approach that transforms existing medical and pharmaceutical practices with actionable knowledge generated from the integration of clinical and biomedical data.

Information based medicine requires access to diverse, integrated information about the patient. The challenges are to combine and to integrate: massive volumes of disparate data, data that are often complex, with a need for sophisticated analysis and therefore, there is also the need for growing collaboration across the ecosystem.

For that, IBM has defined three solutions (conceptual architecture) to address the information needs of basic researchers, pharmaceutical research and development and clinical care.

Project examples

In collaboration with academic and industrial partners, IBM is building patient data warehouses and developing query and analysis tools for medical research, bio-pharmaceutical clinical development, and ultimately the care of patients.

Project examples of IT-systems developed so far by IBM are (being) implemented at the Mayo Clinic, Karolinska Institute, iCapture/University of British Columbia, The AMC Dutch IBD Warehouse, The Danubian Biobank and more.

For instance at the Mayo Clinic, data are collected from more than 4 million patients. A typical end user query, like 'How many patients have been diagnosed with acute myeloid leukaemia, while less than 60 years of age, living in Illinois, with normal white blood cell count, male, living, with mention of prednisone treatment in clinical notes and for which good microarray expression data exist?', can be answered quite easily with the developed IT-system.

At the Karolinska Institute, an IT-system for the first Swedish Biobank has been developed to focus much more on complex disease aetiology, where gene-environment interactions and lifestyle information are integrated in such a way that it extends traditional epidemiological studies.

Another example is 'The Genographic Project', developed in collaboration with National Geographic, which provides an atlas of the human 'genetic' journey.

Challenges in healthcare

The aging population in all parts of the world, will lead to a change in disease patterns in the future. So, due to the aging of the babyboomers in the western world we have to deal in the coming years with a sharp increase in coronary heart disease. Not only in US healthcare, but also in other parts of the western world health care systems have to deal with problems with patient safety, compliance, productivity problems (hospital productivity is underperforming compared with other sectors) and through all these problems with substantial unnecessary cost.

All these challenges and rising patient advocacy trends, made that IBM organised the past two years a number of worldwide Biobank Summits where these problems and developments were addressed

and focused to solutions. Extensive summaries are available from these summits and can be found on www.biobankcentral.org/public/index/php.

Summit-conclusions
The summits made clear for IBM that the more traditional healthcare system is rapidly changing to a 'new ecosystem' that has been created through the above mentioned linkage of the life sciences and healthcare. This new ecosystem has many critical interdependencies. Circled around the patients, are a number of other partners in this ecosystem, like: research institutions, government agencies, clinical trial support, drug developers, healthcare providers, solution providers, advocacy groups and payers.
Another conclusion is that a paradigm shift is taking place from the more traditional biomedical enterprise to translational medicine. Traditionally, research, drug development, and clinical medicine were three virtually separate endeavours. Bench scientists, drug developers, and clinical researchers rarely, if ever, met together, shared ideas, or even used the same vocabulary. All this has changed in recent years as a result of the genomics and bioinformatics revolution.
Now, translational medicine is the continuum – often known as 'bench to bedside' – by which the biomedical community takes a focused point of view to move research discoveries from the laboratory into clinical practice to diagnose and treat patients. Translational medicine is often used synonymously with 'molecular medicine' and 'personalized medicine', both of which are used to refer to the process of applying molecular insights from laboratory discovery to clinical care.

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The role of pharmaceutical industry.
Detlef Niese, Novartis

Niese started with the topic that biobanks may serve different purposes. He then discussed ethical and legal challenges and aspects of quality assurance and collaboration.

Biobanks: a definition and its purposes
Biobanks are collections of human biological samples (tissue, cells blood etc) and derived data for research purposes. They may be associated with information on the sample donors with varying level of detail. Biobanks may serve different purposes and can be differentiated as follows depending on the purpose for collection and the research objective. Typically, research is the primary objective of a biobank ('Primary biobank', e.g. Icelandic Biobank project, biobank UK) Samples are often collected for epidemiological studies in defined populations (e.g. country, ethical entity, disease). Such biobanks may contain very large numbers of samples, while information on the donor is often limited. Frequently, however, human biological samples are being collected for other purposes than basic research, e.g. in the context of clinical trials for drug development. They may contain large numbers of samples and are usually linked with extensive medical data on the donor. This type of 'secondary biobanks', is especially relevant for industry and studies from academia directed to drug or therapy development.
Human tissues and other biological materials are also extensively collected in the context of medical diagnostics or therapy (e.g. biopsies, clinical pathology). Such materials are often also used for research purposes and represent another type of biobanks with secondary research purposes. Such collections may contain a few or very large numbers of samples. The extent of information on the donor is variable and usually related to the primary reason for sampling.

Why we need biobanks
Today, biobanks are indispensable research tools. There are a number of questions, where biobanks may help to find an answer. For the pharmaceutical industry, biological samples may help to better

understand diseases mechanisms or to identify novel drug targets. For most diseases, we still do not fully understand their underlying molecular mechanisms or what makes a particular person susceptible for a disease.
Secondly, such research may tell us why some patients react differently to the same treatment than others. Why does a drug work well in one person and has only undesired effects in another? How can we identify patients who will most likely benefit from a new medicine and those who will not? How can we optimally measure the effect of a new drug? This is what we call 'personalized medicine' or 'individualized medicine'. Finally, biobanks may help to make the increasingly time consuming and expensive drug development process more efficient.

Setting up and running of biobanks
Biobanks requires rigorous quality assurance, like: storage conditions, unique identifier, transparent and controlled access, protection of personal rights of donor. Furthermore, all traffic of samples and data should be traceable and comply with regulatory requirements. Only adherence to the highest quality standards as defined by Good Laboratory Practice and Good Clinical Practice guarantee valid research results and justifies the risks associated with any research in humans.

What do patients expect from biobanks?
There are a number of expectations and concerns that are often raised, like:
- research may reveal a deadly or serious illness and this may implicate the donor's right to know or not to know
- unauthorized access to research data, for instance by insurers, employers, neighbours or police/justice may result in disadvantages or discrimination.
- my genetic information may be abused or commercialized.

Such concerns may be based on experience or, they may be the consequences of incomplete information or perceptions. It's therefore that we need an active and open dialogue between patients and scientists to better understand each other. Whatever the truth is, perceptions are realities. Patients organizations could play a much more active role here, to explain to the general public the advantages of biobanks and the way of dealing with the above mentioned concerns.

Ethical and legal challenges
Research on human samples principally represents research in humans and should follow the same rules like requirement for informed consent, protection of privacy and an ethical review of the research protocol. All medical data are confidential and require a high degree of protection. To obtain a truly informed consent, the patient should be able to ask the right questions and obtain full answers. Therefore it is needed:
- to use appropriate language;
- to explain the scope of planned research and future research;
- to describe the planned use of samples, release of study results;
- storage conditions and access to samples and data;
- to inform how data and personal rights are protected (e.g. by coding, anonymisation)
- and finally, allow the donor to say 'no'!

A researcher should not be able to identify the donor of a research sample (use of coded samples). And if possible, research samples should be obtained anonymously or should be anonymized. However, in clinical research, anonymization is often not possible, because:
- there is a need to link bio-samples with related clinical trial data;
- requirements of regulatory authorities;
- research could reveal important health information which needs to be communicated back to the patient (e.g. genetic disease, HIV-infection, etc.).

The sample donor should decide whether his sample is stored in a biobank and whether it remains there. On demand of the sample donor a sample should be removed from the biobank. If a sample was collected in the context of a clinical trial, data related to the sample cannot be removed even if the donor withdraws consent because of regulatory requirements.

Protection of privacy

Confidentiality is an integral part of Good Clinical Practice. All data collected from clinical research participants and all samples are routinely coded (Patient ID). Usually, the key for this (primary) code remains with the investigator and/or treating physician. When simple coding like this is insufficient, secondary coding may take place on sponsor side or the primary key may be destroyed (anonymization). This provides a high level of protection and there is theoretically no possibility to link a sample or related information with an identified person. At the end of an investigation, research participants should be informed about research results (GCP, European Data Protection Directive).

Biobanks and international cooperation

Successful research is rarely achievable by individual researchers. Access to materials stored in biobanks and exchange of information across borders between research teams, are essential for scientific progress.

But while research operates on a global scale, laws and regulations are national. The diversity of existing regulations regarding biobanks is a relevant hurdle for researchers.

Therefore, harmonized guidelines regarding the setup and use of biobanks as well as for the international exchange of samples are essential.

Conclusion

Biobanks offer new opportunities for biomedical research. For an efficient application of new research technologies, a solid level of trust between science and society is essential. This trust depends at large on respect to the research subjects' autonomy and listening to the needs of society. The perceived risks associated with genetic information may be assessed differently by researchers, research participants and other stakeholders. Those differences in perception need to be respected.

Further scientific progress will also depend on avoidance of unnecessary hurdles and the further development of the international regulatory framework regarding biobanks. This will require close cooperation between all involved stakeholders.

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Developing an European framework for BioBanks.

Jane Kaye, Ethox Centre, University of Oxford

Kaye mentioned in her presentation that the current legal instruments across Europe differ in such a way that they provide some principles but no uniform standards and no organisational models for biobanks.

Current practice

The current practice in Europe is that there are collaborative European-funded projects that share samples and data. There are also companies whose activities cross national boundaries. And also across the globe a transfer of samples and information can be seen.

There are at the moment no specific, binding legal instruments that apply to biobanks. This has resulted in considerable variation in the national law that applies to the use of DNA samples, personal information and medical records in the countries across Europe. This could result in a situation where researchers collaborating across Europe may be operating unlawfully if they share research data and samples across borders where different laws are in operation. There are also concerns that the lack of standardised guidelines inhibits cooperating among researchers across Europe but also restricts the sharing of DNA samples and information across national borders, which is problematic for multinational companies and institutions carrying out collaborative research. Ultimately, this lack of a uniform regulatory system may have implications for the viability and long-term competitiveness of collaborative European research (ref.: Eur Journ of Hum Gen, 2005).

Binding and non-binding instruments

Not all legal instruments are binding on the countries of Europe. For example, the Convention on Human Rights and Biomedicine is only binding on those states that have signed and ratified it and the UK and France have not done so as yet. All signatories to this convention are bound also to any additional protocols. The Recommendation of the Council of Ministers of the Council of Europe are not binding but are authorative and should be influential when a country is considering how to approach such issues. In contrast the directives of the European Community are binding on all members states and must be ratified through implementation into the law of the member-states. A member state can have legal action taken against it if it does not implement directives into national law within a certain period of time.

The result of different legal requirements

The final result of this legislative overview is that it is difficult to ascertain what the law is in member states. This is also a time consuming and expensive exercise.
The different requirements across Europe do not facilitate sharing of samples and information. It also raises concerns about the protection in place for research participants and it is detrimental for research in general.

Possible solutions

The trend is to develop international voluntary standards, like the P3G-project and the IHC laboratory standards. As a result of these voluntary standards, for instance all funding of the European Commission could be tied to these or other standards and requirements. It could be imagined also that an independent agency (for instance, like an EMEA model) looks to proposed standards and requirements and gives, if necessary additional guidelines and approves the whole process. At the end, such a process could lead to a legal instrument.

Further research required

It's certainly needed to have a better understanding of current practice in Europe and across the globe. This is done at the moment at the EC Joint Research Centre in Seville, within the P3G Consortium and the EuroGenBank.
There is also a need for an assessment of different regulatory mechanisms used in biomedicine to determine how appropriate they are for biobanks. Then an assessment of the legal framework has to

be made to determine what is possible and also a clear understanding of what regulation of this type is trying to achieve.

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II. EGAN Symposium

The role of patient organisations in data/biobanking
Paris, October 26, 2006

organised in conjunction
with the EuroBio 2006 Congress
Paris, October 25 – 27, 2006

The EGAN symposium 'The role of patient organisations in data/biobanking' was organised by EGAN at the occasion of the EuroBio 2006 Congress on October 26 in Paris

The EGAN symposium was sponsored by IBM and EuroBio 2006

Summary of the EGAN symposium
The EGAN symposium 'BioBanking: the role of patient organisations in data/biobanking' made it once again very clear that the development of biobanks is welcomed, but more importantly, is being led by international patient organizations. Almost at the same time as this conference, the editorial of Nature Genetics (April, 2006) mentioned the advocacy role being played by individual patients and their families to unravel genetic disease. At this EGAN symposium, representatives of several patient organizations demonstrated how their self-developed bio- and databanks can progress to effective therapies for thus far untreatable diseases. It was also made clear at this conference that patient organizations have to play an important role to tell the public at large what the long-term benefits of data- and biobanks can be for society. To profit from these long-term benefits it is essential that these banks are no longer perceived as a project, but as an essential infrastructural tool in health care. An infrastructure that is worthwhile to invest in for society.

Speakers and presentations
In a one and a half hour session, five speakers gave a presentation on the several aspects of the development of biobanks in the medical health care sector.

Brett J. Davis from IBM, USA made it clear in his presentation that the emergence of biobanks in many parts of the world is proof that governments, health insurance companies, healthcare providers, patient organizations, biopharmaceutical and diagnostic companies are seriously working together on the transformation of healthcare to more 'personalized healthcare'. The convergence of information technology (IT) with molecular biology, drug discovery and the practice of medicine, has also opened opportunities for science based and patient centric approaches to healthcare. This transformation will require advanced IT infrastructures and information systems, so it is better to speak of 'information based medicine'. *The report of this presentation is combined with the report of mr. Hehenberger at the EPPOSI conference, and therefore not part of this section.*

Jasper Bovenberg, attorney at law at the University of Amsterdam, The Netherlands, discussed ownership by patient organisations of their own tissue and data, as well as the topic how patient organisations can manage their tissue and data. *The report of this presentation is combined with the report of the EPPOSI conference and therefore not part of this section.*

Patrick Terry from PXE International, USA touched upon two issues in his presentation. The particular way in which PXE International succeeded to find the gene for PXE with the help of patients, who contributed their DNA samples to the researchers. And secondly, the way in which the Genetic Alliance Biobank shows that a collective biorepository, set up by US-based patient organizations, can be a lever that allows members to accelerate patient-centred research.

Fabrizia Bignami from Eurordis, France outlined the working of the EuroBioBank. The EuroBioBank network was established by two patient organisations, the European Organisation for Rare Disorders (Eurordis) and the French Muscular Dystrophy Association (AFM), with the support of patients and scientists in France and other European countries. The major aim of this first operating network of biological banks in Europe is to facilitate research on rare diseases by providing quality human biomaterial such as DNA, cells and tissues.

Rod Mitchell from the European Federation of Crohn's and Ulcerative Colitis Association (EFCCA) spoke about the development of the Dutch IBD Warehouse, a biobank for Crohn's disease (and other chronic diseases) as an example how to target treatment for a disease through personalised medicine. He also referred to the important role that patients' organisations might play in educating society about the importance of the development of biobanks in helping to find cause and cure for many diseases.

Tsveta Schyns chaired the EGAN conference on Biobanking during the EuroBio 2006 Congress. On earlier conferences, she spoke on the need of patient registries for research on rare diseases and the value of patients/science partnership when building up a registry. She demonstrated these needs with the example of the ENRAH Association and the current ENRAH for SME's project, she is coordinating. ENRAH is a non profit organisation focused on support for research on one ultra rare disease, namely Alternating Hemiplegia of Childhood (AHC).

Biobanking by patient organisations 'Innovation: rare disease & orphan drugs'.
Patrick Terry, PXE International & Genetic Alliance BioBank

Patrick Terry's presentation touched upon two issues. The particular way in which PXE International succeeded to find the gene for PXE with the help of patients, who contributed their DNA samples to the researchers. And secondly, the way in which the Genetic Alliance Biobank shows that a collective biorepository – set up by US-based patient organizations - can be a lever that allows members to accelerate patient-centred research.

Patrick Terry's opening slide mentions 'Patrick F. Terry, JAD. And after that the 'JAD' is highlighted and explained as 'Just a dad'. Indeed, Patrick Terry is the father of two children with pseudoxanthoma elasticum (PXE). PXE is an inherited disorder that affects selected connective tissue in some parts of the body. Elastic tissue in the body becomes mineralized, that is, calcium and other minerals are abnormally deposited in the tissue. This can result in changes in the skin, eyes, cardiovascular system and gastrointestinal system. There seems to be great variety in how PXE affects each person. In 1995 - together with his wife Sharon - he started to work on organizing the research to find the cause of PXE and the road to treatment. Therefore they started a non-profit research foundation PXE International Inc., that now has offices in 52 countries. The organization finances 19 laboratories all over the world and they have their own blood and tissue bank, The BioBank. They succeeded together with scientists from the university of Hawaii and the inter-university ophthalmologic institute in Amsterdam, to find the gene for PXE which they patented in 2000. Finding and cloning the PXE gene, costed about half a million dollars. After acquiring the patent and licensing rights to the ABCC6 gene - the molecular basis of PXE, that was the result of their work – their research collaborators also assigned all patent rights to PXE International.
Soon a diagnostic test for PXE will be on the market, that PXE International developed in cooperation with the biotech company Transgenomic. This test will cost about 800 dollars, but PXE International is going to subsidise the test so that as many patients as possible can have access to the test. Based on this gene discovery, PXE International is now working with several companies to see if an intervention and drug treatment for PXE can be developed.

For further reading: see EPPOSI report.

The EuroBioBank Project: The Benefit of Teamwork.
Fabrizia Bignami, Eurordis/EuroBioBank

*Bignami outlined the working of the EuroBioBank. The **EuroBioBank** network was established by two patient organisations – the European Organisation for Rare Disorders (Eurordis) and the French Muscular Dystrophy Association (AFM) – with the support of patients and scientists in France and other European countries. The major aim of this first operating network of biological banks in Europe is to facilitate research on rare diseases by providing quality human biomaterial such as DNA, cells and tissues.*

The positive impact on European people has been acknowledged and EuroBioBank was awarded the 'Newropeans Grand Prix 2004' prize for best European project in the category Research & Technology. The EuroBioBank project was funded for three years (2003 – 2006) by the EU-Commission (5th FP), and will serve as a platform for various projects and consortia in the future. In 2006, the EuroBioBank was cited by the IPTS/ESTO work group on BioBanks as a European model of coordination and of integration of Biological Resources Centers for the organisation and improvement of the use of human biomaterial at European level. Today the EuroBioBank network brings together 14 members from 7 European countries (France, Germany, Hungary, Italy, Malta, Slovenia and Spain) including:
- eleven biological Resources Centres (BRC's) storing a total of 170.000;
- documented human biological samples;
- one IT services companies;
- one consultant expert in BioBanks creation and management and
- Eurordis, the European umbrella organisation for rare diseases.

The **activities** of the EuroBioBank Network are to:
- identify and localise rare disease biological material of interest to researchers;
- process and store a critical mass of rare disease sample collections;
- maintain a centralised website with an online catalogue offering an easy access to the referenced samples available;
- distribute high quality material and associated data to users;
- promote quality banking practices (collection, transport, storage and exchange of biological material) adapted to each type of material (DNA, tissue, cell);
- map ethical issues related to the use of biomaterial samples;
- disseminate knowledge and know-how to the scientific community through training;
- enhance collaboration with the medical and scientific community in the field of rare diseases.

The exchange of samples is now facilitated by the online EuroBioBank catalogue of collections at www.eurobiobank.org, which enables scientists to find specific information about the available samples across the entire network and request them. The network also promotes quality banking practices for collection, preparation, storage, and transport of biological material, and addresses the ethical issues relating to these practices. The EuroBioBank partners have developed 30 harmonised Standard Operating Procedures (SOP's) and a standardised Material Transfer Agreement (MTA) that comply with the OECD's recommendations for Biological Resource Centres (BRC's). These documents can be found on the EuroBioBank website. Regarding ethics, the EuroBioBank partners published an innovative book on the ethical and legal implications for biobanks. This publication 'Outstanding legal and ethical issues on biobanks' gives an overview of current legislation in the different member states represented at EuroBioBank and can be obtained from their website.
Other ethical points of the EuroBioBank project are:
- respect of anonymity in the sample collection;
- respect of the patient's autonomy by using the informed consent;
- form, for collection and use of the biological material for research;
- access to samples: ad-hoc board approval of the projects for which the biological samples are requested, no distribution of samples for cloning projects;
- confidentiality of the data associated with the samples and
- information to the patients on the use of collections and the outcomes of the research projects.

The role of Eurordis within the EuroBioBank Network is to coordinate the work administratively, to apply for grants and find corporate sponsors to ensure the long-term sustainability of the network, to maintain the EuroBioBank website and to serve as the main contact point for the network. The long-term aim of EuroBioBank is to continue facilitating research on rare diseases by providing the appropriate biological samples donated by the patients. This may ultimately contribute to the development of therapies for approximately 24 - 36 million people with rare diseases in Europe. To reach this aim, a solution must be found for the long term sustainability of public BioBanks. This certainly implies recognition of the public health value of BioBanks and of their importance as fundamental infrastructures. Another challenge is harmonisation, a key word in the EU, both at the legislative and the scientific level, to reach high quality standards.

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Collaboration In Bio-banking for Crohn's disease.
Rod Mitchell, EFCCA

Mitchell spoke about the development of the Dutch IBD Warehouse, a biobank for Crohn's disease (and other chronic diseases) as an example how to target treatment for a disease through personalised medicine. He also referred to the important role that patients' organisations might play in educating society about the importance of the development of biobanks in helping to find cause and cure for many diseases.

In addition to his presentation at the EPPOSI conference, Rod Mitchell outlined the Pearl Chain Initiative:

The 'Pearl Chain Initiative'
Since 2003, the heads of the IBD departments of the Dutch Academic Medical Centres in The Netherlands are united in the Foundation Ínitiative on Crohn and Colitis' (ICC). The mission of this group is to improve the quality of life of the IBD patient group. Essential tasks to reach this goal are: innovation of care, education/information and research. To perform these essential tasks well, there is much attention to reach synergy between the IBD-work of the eight Academic Medical Centres. The most important steps to reach this innovation of care-concept is:

- to use a standardised Electronic Patient Dossier (EPD)
- the integration of clinically validated data as well as molecular data from biomaterial of IBD-patients (DNA, serum, faeces, biopsy and resection material)
- the possibility to combine these databanks and ask for data centrally
- (query builder) and
- the returns back from this central data base to the EPD of the individual patient

This whole concept is the IBD-module, and this module can be used as well for other diseases. In 2005 the IBD module was indeed extended to seven other diseases and a grant application was directed to the Dutch Government and its special fund to strengthen the economic structure, the so-called 'FES-money'. This money comes available because of the rising prices of the internal 'gas' reserves within The Netherlands. In September 2006 a positive response came on this request and in total there is now available 70 million Euro, 35 million from the FES-money and 35 million as matching-money form the Academic Medical Centers. The IBD-module is the showcase of this so-called 'Pearl Chain Initiative and the IBD-module should now be operational by the end of 2008.

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The European Registry of patients with Alternating Hemiplegia in Childhood (AHC): a collaboration of science and patients for research.

Tsveta Schyns, ENRAH Association, Vienna, Austria

Tsveta Schyns chaired the EGAN conference on Biobanking during the EuroBio 2006 Congress. On earlier conferences, she spoke on the need of patient registries for research on rare diseases and the value of patients/science partnership when building up a registry. She demonstrated these needs with the example of the ENRAH Association and the current ENRAH for SME's project, she is coordinating. ENRAH is a non profit organisation focused on support for research on one ultra rare disease, namely Alternating Hemiplegia of Childhood (AHC).

Alternating hemiplegia in childhood (AHC) is an extremely rare disease. It is a neurological disorder characterized by frequent, temporary episodes of paralysis on one side of the body (hemiplegia). Symptoms usually begin before the age of 18 months. This syndrome may be characterized by temporary (transient) hemiplegia of varying degrees; temporary paralysis of the muscles that control eye movement (transient ocular palsies); sudden, involuntary movements of limbs and facial muscles (choreoathetosis); and/or excessive sweating with changes in skin colour and body temperature (autonomic nervous system dysfunction). Mental capacity may be affected. The exact cause of AHC is unknown. Some cases of AHC may be inherited as an autosomal dominant trait. Sometimes the symptoms of AHC lead to a diagnosis of epilepsy, but the anti-epileptic drugs can seriously worsen the situation of AHC patients.
Because of the extremely rare character of the disease, there is almost no descriptive data available on AHC as a disease. And where expertise is present in Europe, it is also fragmented. Having heard of the example of Pompe's disease and the way data are collected there, the European network for research on alternating hemiplegia in childhood (ENRAH) was started. The ENRAH network received a grant of 358.000 Euro from the Specific Support Action for small and medium sized Enterprises (SME's) of the 6th Framework Programme for Research, Technology and Demonstration of the EU for a two-year period April 2005 – March 2007.
ENRAH is a non-profit organisation which was founded in 2003 in Vienna, Austria. ENRAH is a partnership of patient organisations, academia and industry in Europe to support the research on AHC. It involves now clinical and academic centres and patient organisations active in the field of AHC from more than 15 EU-countries.

The objectives of ENRAH are:
- forwarding European research on AHC
- partnering of AHC patient representatives, AHC treating neurologists
- and genetic researchers from nine EU countries
- involving industry and SME's in research on AHC and related diseases
- establishing and maintaining a European registry of AHC patients,
- including their disease and family profiles
- facilitating the sharing of clinical data, human biological materials and
- clinical trial data

Data-collection by the European Registry of AHC is:
- clinical data and research results
- retrospective studies with a prospective component
- non-hypothesis driven
- cross-sectional longitudinal
- to provide epidemiological data to enhance the understanding of the
- natural course
- to have a well characterised group of patients, providing a foundation
- for future research and clinical trials
- to have data that can be used to generate hypotheses and test
- hypotheses related to the AHC mechanism and targeted interventions

ENRAH estimates that it must be possible to have at least 120 AHC-patients in their registry at the end of 2007. The data that are collected within the ENRAH registry are personal and clinical data. As well as video recordings and/or photographs and an inventory list of existing human samples from AHC-patients. At the ENRAH website, a questionnaire can be found to identify if a patient is a (possible) typical case of AHC in the opinion of the treating physician, the child neurologist or the data collector. The data collection of ENRAH takes place at the clinical centre as part of patient's regular visits for consultation or treatment or as a special visit to the clinical centre for validation of data or from a referring clinician. At present, only patients at the participating clinical centres will be included into the registry. Participation is voluntary and only with the informed, free, specific and documented consent of the person with AHC or his/her legal representative.
Storage of patient's data is organized as follows: at the clinical centres participating in this project (one per country), each file with patient's data will receive a number according to a unique coding system. To the AHC European registry, personal information leading to the identity of the patient (name, address) will be removed on their files with clinical and other data. photographs, recordings and surpluses. This personal information will be kept separately along with the code identifier. Re-identification will be necessary for follow-up visits in order to update the clinical data and to inform patients about any planned study or trial.
The access to data files is regulated within the following framework: each participating clinical centre can only access its own data project. Participants may have access to other centre's data when they can ensure an adequate level of protection. Access for other users to the original patient files and samples, is outside the limits of the project and must be subject to a separate ethics review at the local committee.
Access for the data in the European Registry is open for research to all project participants during the two years of the EU-project. Subsequently, for as long as the European Registry is securely maintained at the same conditions, any group from the world who can show a legitimate interest, and if its written application is granted by the Steering Board, may have access to the European Registry on alternating hemiplegia in childhood.

Also see EPPOSI report.

APPENDIX A. List of abbreviations

ABCC6	The molecular basis of PXE
AFM	Association Française contre les Myopathies
AHC	Alternating Hemiplegia of Childhood
AMC	Academic Medical Centre
BRC	Biological Resource Centre
CDC	Centers for Disease Control
CIGMR	Centre for Integrated Genomic Medical Research
CRE	Collaborative Research Enterprise
CSI	Crime Scene Investigation
DNA	Deoxyribonucleic acid (double helix)
EC	European Commission
EFCCA	European Federation of Crohn's and Ulcerative Colitis Association
EGAN	European Genetic Alliances' Network
EGP	Estonian Genome Project
EMEA	European Agency for the Evaluation of Medicinal Products
ENRAH	European Network for Research on Alternating Hemiplegia in Childhood
EP	European Parliament
EPF	European Patients Forum
EPPOSI	European Platform for Patients Organisations, Science and Industry
ESHG	European Society for Human Genetics
ETHOX	Oxford Centre for Ethics and Communication in Health Care Practice
EU	European Union
Eurordis	European Organisation for Rare Disorders
FP	Framework Programme of the EC
GCP	Good Clinical Practice
GIG	Genetic Interest Group
GLP	Good Laboratory Practice
GP	General Practitioner
HGRA	Human Genes Research Act
HUGO	Human Genome Organisation
IAPO	International Association of Patients Organisations
IBD	Inflammatory Bowel Disease
IBM	Information Based Medicine
IGA	International Genetic Alliance
IP	Intellectual Property
IPA	International Pompe Association
IPR	Intellectual Property Rights
IT	Information Technology
MTA	Material Transfer Agreement
NIH	National Institute of Health
OECD	Organisation for Economic Co-operation and Development
P3G	Public Population Project in Genomics
PO	Patient Organization
PPUK	Parent Project Duchenne Muscular Dystrophy UK
PXE	Pseudoxanthoma elasticum
SME	Small and Medium-sized Enterprises
SOP	Standard Operating Procedure
UK	United Kingdom
US	United States
VSN	Dutch Neuromuscular Patient Association
VSOP	Dutch Genetic Alliance
WAGHP	Western Australian Genetic Health Project

APPENDIX B. The speakers

Cees Smit was co-founder, board member and co-ordinator of the Netherlands Haemophilia Society (NVHP). He also chaired the Dutch Genetic Alliance (VSOP) and the European Platform for Patients' Organisations and Industry (EPPOSI).
Patrick Terry is the father of two children with pseudoxanthoma elasticum (PXE). In 1995 he started to work on organizing the research with his wife Sharon, to find the cause of PXE and the road to treatment. Therefore they started a non-profit company PXE International Inc., that now has offices in 52 countries. The company finances 19 laboratories all over the world and they have their own blood and tissue bank, The BioBank. The patent rights to ABCC6, the molecular basis of PXE, that was the result of their work, were recently assigned to PXE International.
Michael Griffith is chief executive of Fighting Blindness, an Irish Charity devoted to promoting research to find treatments for blindness, especially retinal blindness. He was co-founder of this group in 1983 and was its first chairman. Since 2005 he is also chairman of EPPOSI.
Veronika Karcagi is head of the Department of Molecular Genetics and Diagnostics at the Fodor Jozsef National Center for Public Health in Budapest, Hungary, a member of the EuroBioBank.
Ria Broekgaarden has a bachelor's degree in Policy and Management. At the moment she is leading the care department of the Vereniging Spierziekten Nederland (VSN), responsible for the Pompe Project within the VSN and secretary of the International Pompe Association.
Tsveta Schyns is, at present, a recognised consultant on European project management and coordination and the Director of ENRAH Association. She has a PHD in Genetics. Her first daughter is affected by the AHC disease.
Rod Mitchell is chairman of the European Federation of Crohn's and Ulcerative Colitis Association (EFCCA). As an early-retired banker he is a member of the boards of the European Genetic Alliance Network (EGAN) and of the European Platform for Patients' Organisations, Science and Industry (EPPOSI) where he has responsibility for financial affairs. He is also board member of the International Alliance of Patients Organisations (IAPO). EFCCA is also a member of the European Patients Forum (EPF) and European Disability Forum (EDF) and has contacts with sister IBD organisations around the world.
Alastair Kent is member of the P3G International working group on ethics, governance and public engagement. In daily life, he is director of the Genetic Interest Group (GIG) in the United Kingdom. The GIG is a national alliance of patient organisations with a membership of over 130 charities which support children, families and individuals affected by genetic disorders.
Andres Metspalu is Professor of Biotechnology at the University of Tartu and Estonian Biocentre, Estonia. He is founder and scientific advisor of the Estonian Genome Project and since 2004 again as a Member of the Management Board of Estonian Genome Project. He is also a board member of the European Society of Human Genetics (ESHG), from 2005-2006 he was President of the ESHG.
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