PROMOTING HARMONISATION OF PHOEBE EPIDEMIOLOGICAL BIOBANKS IN EUROPE

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PHOEBE

Promoting Harmonisation of Epidemiological Biobanks in Europe

Coordination Action

LIFESCIHEALTH

FINAL ACTIVITY REPORT

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Project coordinator organisation name Norwegian Institute of Public Health

Draft 1

PROMOTING HARMONISATION OF PHOEBE EPIDEMIOLOGICAL BIOBANKS IN EUROPE

1 Publishable Final Activity Report

1.1 Project Execution

1.1.1 Background and Objectives

The strength and depth of European bioscience is founded, in no small part, on its rich collection of large population-based cohort studies. Unravelling the causes of complex diseases and translating these efforts into public health and clinical practice is the central focus of medical science. However, tackling these issues transcends the reach of individual studies due to a host reasons ranging from lack of statistical power, the need for multidisciplinary expertise, to issues of geographical variation in genotypes and environmental exposures. It is well recognized that progress will be heavily reliant on access to large-scale biobanks that curate a rich array of data spanning genotypes, biomarkers, clinical measures, environmental exposures, life-style and social factors plus biospecimens.

With this in mind the FP6 project entitled '*Promoting Harmonisation of Epidemiological Biobanks in Europe*' (PHOEBE) (http://www.phoebe-eu.org) was designed as a coordination action (CA) to promote the harmonization of European population-based biobanks so that they achieve maximal interoperability.

PHOEBE started March 1, 2006 and ended August 31, 2009. Its long-term aim was to establish and maintain a cost-effective and "harmonised" network of population-based biobanks and longitudinal cohort studies across Europe and in Canada to optimise the ability of biobanks to: communicate with one another, share ideas, information and data, and collaborate effectively in a complex world where laws and ethical guidelines often differ between nations and over time. PHOEBE worked to identify key issues and to help the groundwork for such harmonisation. A biobanking function at the "European-level" means identifying candidate biobanks and establishing optimal procedures for harmonisation between them. Harmonisation implies the use, where possible, of *complementary* protocols, this is not the same as the scientifically restrictive (and therefore unattractive) demand for *identical* protocols. In meeting these aims it is essential to pay attention to retrospective and prospective elements in order to cover major cohorts that already exist and new or planned initiatives. Harmonisation of those features that are common to many such studies will help to: (1) promote communication between major biobanking initiatives; (2) enhance the effective sharing and synthesis of information and data; and (3) avoid the expensive mistakes and inefficiencies that can arise when individual initiatives repeatedly "re-invent the wheel".

Harmonization of Europe's population-based biobank studies, in conjunction with its national health systems will place Europe in a unique position to capitalise on biomedical research opportunities today and long into the future of post-genomic science. If we can ensure that our biobanks are able to work together to address pivotal research questions that fall outside the scope of projects funded by single nations, or even of large cohorts running across several

nations, we can ensure that Europe remains at the cutting-edge of biomedical research internationally.

Building upon the intellectual foundations laid down at international biobanking meetings and in other EU funded projects (e.g. GenomEUtwin), PHOEBE was shaped around five key harmonization targets, each with a dedicated project workpackage (WP) and substantive focus:

WP1 – Epidemiology and Biostatistics
WP2 – Opportunities for Future Biobanking in Europe
WP3 – Databases and Biobank Information Management Systems
WP4 – Strategies for Genotyping in Large Scale Biobanks
WP5 – Ethical and Societal Issues

1.1.2 Specific Objectives

1. To contribute to and promote biobank harmonization across Europe from the specific perspectives of: epidemiology and biostatistics, retrospective and prospective opportunities, databank and biobank information management systems, strategies for genotyping and ethical and societal issues.
2. To identify and describe, in a standardized form, large pre-existing population-based biobanks and longitudinal cohort studies in Europe. Particular emphasis will be placed on studies that can contribute substantially to coordinated investigations of the genetic and environmental determinants of complex diseases.
3. To explore the statistical methodology underpinning the design, analysis and harmonization of population-based biobanks.
4. To identify new biobanking opportunities within Europe. This will include a particular focus on genetically isolated populations, and we will establish standard criteria for selection and collection of data and samples from these populations.
5. To review current best practice for Biobank Information Management Systems. Key issues of harmonisation in relation to the management of large and complex databases for biobanks will be explored with a focus on efficient technologies, high level programming and the development of flexible communication engines that support reliable, efficient and secure communication between biobanks.
6. To create an operational infrastructure for the evaluation of ongoing large-scale genotyping efforts in population cohorts. This will provide a natural forum for expert opinions regarding marker selection, genotyping methods, quality assessment steps, database structure and analysis of the produced genotypes.
7. To lay the groundwork for a harmonised approach to the assessment of a wide range of complex phenotypes and life-style exposures.
8. To establish the basis of a platform for ethical-legal and governance criteria consistent with the international norms and European practices that will enable data and sample sharing for research purposes.
9. To integrate collected European and Canadian expertise in relation to the statistical challenges that face us in study design and analysis, data synthesis across studies, and in creating general purpose platforms for developing and implementing mathematical models in genetic epidemiology and genetic statistics.

1.1.3 PHOEBE Partners

Phoebe is comprised of 18 partners representing 13 countries as listed in Table 1. Dr. Jennifer Harris (Jennifer.harris@fhi.no), Department of Genes and Environment, Division of Epidemiology at The Norwegian Institute of Public Health, Oslo Norway was the PHOEBE project coordinator.

Table 1. PHOEBE partners, respective countries and key personnel

PHOEBE Partners	Country	Key Personnel
1. Norwegian Institute of Public Health	Norway	Jennifer Harris, Coordinator Camilla Stoltenberg Elisabeth Shaw, Per Magnus
2. University of Bristol	United Kingdom	George Davey-Smith
3. University of Bonn	Germany	Max Bauer, Tim Becker
4. University of Trieste	Italy	Paolo Gasparini, Leader, WP 2
5. Universitat Pompeu Fabra	Spain	Jaume Bertranpetit
6. Karolinska Institutet	Sweden	Jan Eric Litton, Leader WP 3 Juni Palmgren
7. UK Biobank	United Kingdom	Stephen Walker/Andy Harris
8. National Public Health Institute	Finland	Leena Peltonen, Leader WP 4
9. McGill University	Canada	Thomas J. Hudson
10. Free University of Amsterdam	The Netherlands	Dorret Boomsma
11. INSERM U 558	France	Anne Cambon Thomsen, Leader WP 5
12. University of Montreal	Canada	Bartha Maria Knoppers Isabel Fortier
13. University of Leicester	United Kingdom	Paul Burton, Leader WP 1
14. Erasmus University Medical School	The Netherlands	Cornelia van Duijn
15. Estonian Genome Project	Estonia	Andres Metspalu, Kaiti Kattai
16. Charles University Prague	Czech Republic	Milan Macek Jr.
17. National and Kapodistrian University of Athens	Greece	Pagona Lagiou
18. Imperial College of Science, Technology and Medicine	United Kingdom	Paul Elliott

1.1.4 Work Performed and End Results

Through its diverse approaches and activities PHOEBE successfully fulfilled its mission to promote harmonization among epidemiological biobanks in Europe. Within the last year PHOEBE surpassed many of its original harmonization goals and, through the coordinated efforts of multiple projects, the science of biobanking matured substantially during PHOEBE's lifetime. An important consequence of these diverse harmonization initiatives has been the emergence of a new reservoir of knowledge, experience, and expertise that is crucial to share with the biobanking community and which paves the way for the next phase of harmonization objectives. PHOEBE has been committed to mobilizing this information within the biobanking community for the purpose of maximizing the scientific value, use and utility of our biomolecular resources. To help in this endeavour PHOEBE has been actively engaged in or leading key meetings, conferences, strategy building initiatives, biobanking projects and training. We have produced valuable reports and recommendations[1], guidelines, planned international conferences[2] to promote much needed dialogue within the community and between stakeholders, PHOEBE has played an instrumental role to enhance cross-talk and collaboration between the next wave of biobanking projects and thereby have 'passed the coordination torch' forward.

One of the largest international biobanking events in 2009 focused on cutting edge issues in harmonization due to the direct result of PHOEBE fulfilling a project deliverable. This conference, planned around the grand theme *'Harmonizing Biobank Research: Maximizing Value-Maximising Use'*, was held in Brussels on March 25-27, 2009. More than 250 people from over 35 countries attended the conference representing a diverse range of scientific and professional expertise in the various disciplines critical to biobanking. The conference provided a much-needed forum to understand the current state of play, provide a forum for information exchange, and engage in renewed thinking about the most pressing issues. PHOEBE co-organized the conference with The Public Population Project in Genomics (P^3G) and the BBMRI. All three of these initiatives worked in tandem during the course of PHOEBE to further biobank science and research.

Discussions at the conference constructively identified the next generation of challenges that have emerged in the wake of the progress already made. Specifically, the session dedicated to the topic of '*Building an International Biobanking Community*', reiterated concerns from the November 2008 meeting of 25 EU-funded biobanking projects which identified biobank sustainability and harmonization as top strategic priorities. PHOEBE has been following up on this mandate through the planned issuance of a White Paper.

Our goals related to the promotion biobank harmonization across Europe from the particular perspective of the specific PHOEBE workpackages were addressed through a wide array of activities conducted throughout the project, including through published manuscripts, the

[1] ftp://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks_en.pdf
[2] http://www.phoebe-eu.org/dav/2ecbab4a0f.pdf

creation of tools, information cataloguing, meetings, training, and the development of standards and recommendations. All information has been made available to the community and, where relevant, outputs have been integrated with other ongoing activities such that they will continue to be used, to be expanded upon and updated in order to remain useful to the biobanking field as it evolves.

1.1.4.1 PHOEBE harmonization from epidemiological and biostatistical perspectives

The PHOEBE epidemiology and biostatistics platform has been a driving force internationally addressing harmonization issues and advancing our ability to conduct international biobank-based science. This group has concentrated efforts on issues related to biobank design, phenotype harmonization, biobank cataloguing efforts, and statistical challenges. It has integrated expertise across Europe and beyond, including with P^3G in Canada to implement harmonization initiatives and the results and tools developed are now serving ongoing biobanking projects in many countries. The critical issues and proposed solutions have been elaborated upon in several manuscripts produced by PHOEBE scientists working on these issues.

PHOEBE's objective to lay the groundwork for a harmonized approach to the assessment of a wide range of complex phenotypes and life-style exposures is another area where the epidemiological team made great strides. Phenotype harmonization is one of the most urgent and difficult tasks facing biobanks who want to analyze comprehensive sets of data to address complex questions of disease etiology. Phenotype harmonization was a prominent area of focus throughout PHOEBE. Working in close collaboration with P3G, we developed a new and tool called *DataSHaPER* (Data Schema and Harmonization Platform for Epidemiological Research). The DataSHaPER maximizes the ability for different biobanks to collaborate. Many scientists have worked together and more than 25 biobanks worldwide have been involved. Nearly 200 measures have been harmonized thus far including many indexing for common life-style exposures. The DataSHaPER methodology has been described in a PHOEBE publication and the DataSHaPER can be easily accessed[3]. To avoid duplication and help develop common strategies PHOEBE scientists conducting the phenotype harmonization work communicated regularly with other similar initiatives (e.g. PhenX) and this has contributed to an internationally coordinated approach for phenotype harmonization. Through its work with the DataSHaPER PHOEBE greatly surpassed its original goal of laying the groundwork for a harmonized approach to the assessment of a wide range of complex phenotypes and life-style exposures.

One of the main harmonization goals met under the lead of the epidemiological platform included the identification and standardized description of large population-based biobanks and longitudinal cohort studies in Europe. The Catalogue of Studies[4] is a repository of such information and currently includes more than 112 biobanks, including more than 64 European biobanks with detailed meta-data available on 47 of these. This work has been conducted in full collaboration with the Public Population Project in Genomics (P^3G) and will continue to grow beyond the work of PHOEBE.

Several PHOEBE activities helped to fulfill our harmonization objectives focused on statistical methodology underpinning the design, analysis and harmonization of population-

[3] http://www.p3gobservatory.org/datashaper/presentation.htm
[4] http://www.p3gobservatory.org/studylist.htm

based biobanks. Early on in the project experts met to discuss the most profitable approaches to take within the project. They decided it was important to develop the GeneStat portal (www.genestat.org) as a publicly available knowledge base tool for statistical methods. Throughout the project the GENESTAT portal was expanded and information more widely disseminated via a published paper. PHOEBE biostatisticans are actively networked across Europe and beyond. They have collaborated to cross reference GENESTAT with the web-portal NORDICDB.

Advances in biobank data harmonisation are leading to increased attention on higher level computation and modeling. Information structures are becoming more complicated as the handling of biomedical research data requires integration of diverse types of data, harmonization, storage, data curation, access, tools, web services and high capacity networks. The PHOEBE biostatistics group has emphasized the need for an analysis pipeline to handle the growing complexity surrounding the phenotypic data, analytic strategies and the larger quantities of data being generated. The range of this pipeline would span from raw data via low level filtering to complex statistical analyses and educational aspects of future challenges. A session was organized around these issues and discussed at the PHOEBE final conference. These discussions helped to frame the next set of harmonization goals.

Additionally, several published manuscripts and chapters from the PHOEBE biostatistics group highlight statistical and design considerations underpinning the rationale for harmonization. Primary among these is a highly cited published manuscript that quantifies realistic sample size requirements for human genome epidemiology (Burton et al.,[5]).

1.1.4.2 PHOEBE harmonization from perspectives on opportunities for future biobanking in Europe

A unique aspect of PHOEBE was the emphasis on identifying new biobanking opportunities within Europe, with a particular focus on genetically isolated populations. The value of bridging data derived from genetically isolated populations with data from other types of study designs became increasingly clear during the course of the project as methodologies advanced. This progress reinforced the call for greater integration and harmonization both within and across biobanks of different populations in order to maximize their scientific utility and contribution. Our main harmonization goals were to establish standard criteria for selection and collection of data and samples from these populations. Work entailed designing a survey used to collect information from existing initiatives and promoting discussions at the most relevant international meetings where harmonization needs were discussed. This work has been instrumental to articulate aspects of biobanking issues unique genetic isolates from those that overlap with those from other types of populations. Decisions about study design in isolated populations will be population specific, yet greater harmonization—for example, interoperability between databases and phenotype harmonization that accounts for important differences between the groups--will facilitate comparisons between populations. PHOEBE scientists emphasized that the study of genetic isolates raises some unique ELSI and consenting issues. These studies often involved extensive genealogy information, small communities, and people who are related to each other. Thus, the relationship between participants and researchers are differently framed in these special populations and an individual's decision to participate may be much more revealing about extended family

[5] http://ije.oxfordjournals.org/cgi/content/full/dyn147v2

members than many population or clinical based studies. PHOEBE scientists with expertise in studies of genetic isolates and ELSI will work together to publish a manuscript that analyzes and maps ethical aspects to specific features of genetic studies in isolated populations in Europe.

1.1.4.3 PHOEBE harmonization regarding databases and biobank information management systems

Biobank interoperability hinges directly upon biobank information management systems. Biobanking has matured substantially in recent years, not least in terms of the sophisticated solutions employed to run operations and record research findings. A main objective of PHOEBE was to examine key issues of harmonization in relation to the management of large and complex databases. Particular emphasis was placed on the use of efficient technologies, high level programming and the development of flexible communication that supports reliable, efficient and secure communication between biobanks. This required a comprehensive review of existing and planned systems to arrive at a consensus on the requirements for a general information management system for biobanks. The report generated under PHEOBE, and in conjunction with other major biobank harmonization initiatives such as GenomEUtwin and BBMRI, serves as a knowledge source charting the experiences in IT-systems development and information management in large scale biobank organizations. Important findings include recognition of the many ways in which IT can help to ensure data quality, such as consideration of data modelling in general prior to data collection, automatic transmission of data from the measuring device to the computer, use of automated checks to validate manually-typed data values, requiring also a context for the data and monitoring sample transportation from collection site to laboratory. It also addresses format and variable standards, communications standards and transmission policies. Importantly, in order for integration of data sources between biobanks from different nations to be successful, it will require that the IT issues are addressed within the context of ELSI considerations. The compiled information will be pivotal for practical translation to ensure state-of-the art solutions for data curation and secure communication between biobanks. The most pressing of these issues were identified and discussed at the final PHOEBE conference with a focus on a) local, federated or central databases; b) local or central access oversight; c) controlled access; d) matching consents to end use purpose; e) identifiability; f) sharing individual and summary level data; and f) feedback to participants. These discussions highlighted that there must be strong communication between ELSI and IT in order to find rigorous solutions that will provide the flexibility to use the data securely and according to ethical practice.

1.1.4.4 PHOEBE harmonization regarding strategies for genotyping in large scale biobanks

PHOEBE harmonization efforts related to strategies for large-scale genotyping have created an operational infrastructure for the evaluation of ongoing large-scale genotyping efforts in population cohorts, as well as provide a forum for expert opinions regarding genotyping methods and quality assessment of these methods. Work surrounding these goals was undertaken in three interrelated sets of activities that included:

a) surveying and integrating information about existing strategies for genotyping,

b) researching and summarizing information related to standardization, quality control, costs, data storage and data handling, and
c) making information about genome-wide and targeted genome regions publicly available

During the course of their work in this area PHOEBE scientists continually encountered challenges related to the rapid developments in the field and the need to modify and update work plans and focus further on genome-wide platforms and technologies, data file merging and on issues related to integrating genotyping datasets. Ultimately, these activities will provide the international community with advice and standards that will promote harmonization in regards to selection of markers, genotyping quality control and cost, data collection and storage, and genotype database structures.

1.1.4.5 PHOEBE harmonization regarding ethical and societal issues

ELSI represents another major focus area of PHOEBE harmonization. Our objective was to establish a basis for ethical-legal and governance criteria consistent with international norms and European practices to enable data and sample sharing for research purposes. To ensure that these pieces of work were well integrated with other ELSI biobanking strategies we interfaced continually with leading efforts and collaborated extensively with several of these.

Examples of the methods used to reach our ELSI harmonization goals included:

a) elaborating theoretical frameworks of governance (which has been disseminated through a series of published documents),
b) developing governance tools (which are available online),
c) participation in the development and drafting of international guidelines related to biobanking,
d) organizing a workshop, training events and special sessions at international conferences, and,
e) network building

A number of diverse outputs resulted from these ELSI activities including the availability of the developed tools, web reports, publications, and consensus documents. Our specific consensus document, *Building a Model Framework for the Governance of Biobanks*[6], was generated in conjunction with P^3G. It examines the importance of public legitimisation, outlines why governance is important in the context of biobanks, reviews current governance mechanisms and lays the foundations for a model framework for the governance of biobanks. Additionally, a lexicon to facilitate a common understanding of ELSI and biobanking terms was completed in collaboration with P^3G. This is a living document, available online, which is continually updated. Another example of a valuable web-based tool is that developed in collaboration with an EU funded network of excellence (Ga2len, Coll. F Kauffmann) which provides access to information on legal requirements for exchanging samples across borders.

PHOEBE ELSI also collected and synthesized information collected from 25 EU-funded biobanking projects who participated in a meeting held under the auspices of DG Research of the European Commission on November 20-21, 2008 in Brussels (see footnote 1 above). A

[6] http://www.humgen.umontreal.ca/int/GE/en/2008-2.pdf

synthesis of the ELSI challenges and recommendations for ways forward was made based on information provided by the projects.

Of particular importance to the PHOEBE ELSI harmonization work was the need for horizon scanning to identify emergent issues as the field progresses and to broaden the scope of our activities where possible. Examples include the analysis of ELSI issues to topics such as children in long term biobanking and unique issues related to ethnicity and genetic isolates. Although the purview of PHOEBE is population-based biobanks, it became increasingly clear that traditional lines of distinction between population and clinical based biobanks will change as the science progresses and there will be a greater need for data exchange between these different sources. Consequently, the PHOEBE ELSI group wanted to encourage dialogue that could draw on the experiences of both population-based on clinical-based designs and elucidate specific ELSI issues. We developed a workshop entitled *"Translational medicine and public health policy: lessons from biobank ELSI"*, that was held in Geneva in 2007. Part of the motivation for this workshop stemmed from recognitions that socio-ethical and legal issues could vary depending on the nature of the disease under study and our current state of knowledge regarding the aetiology, and treatment and accompanying psychosocial factors. Therefore, we proposed a bidirectional exchange between those engaged in population biobanking and those targeting specific diseases to explore how lessons learned could be translated into useful knowledge between various types of biobanks or study focus.

Collectively, this broad array of ELSI work conducted under PHOEBE has produced valuable tools and information that play a prominent role in advancing ELSI harmonization.

1.1.4.6 Networking

Networking has been at the heart of PHOEBE successes, both for carrying out its goals under the formal project period, but perhaps more importantly for carrying forth its achievements into sustainable harmonization. From its inception PHOEBE recognized the importance of networking and has coordinated its WP activities accordingly within the relevant scientific communities. Furthermore, the PHOEBE project as a whole has worked closely with leading initiatives in biobanking to help bring coherence to biobanking issues, articulate a common vision and establish roadmaps for our strategy forward. This work progresses through close collaboration with ongoing projects and with projects in the planning phase.

Among our closest collaborators were the EU funded Genome-wide analyses of European twin and population cohorts to identify genes predisposing to common diseases (GenomEUtwin) (http://www.genomeutwin.org), The European Network for Genetic and Genomic Epidemiology (ENGAGE) (http:www.euengage.org), the Public Population Project in Genomics (P^3G) (http://www.p3g.org/) in Canada, the FP7 project Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) (http://www.bbmri.eu/) and the Public Health Genomics European Network (PHGEN) (http://www.phgen.nrw.de/typo3/index.php).

1.1.4.7 Beyond the formal objectives

As illustrated by the final PHOEBE conference, the collective work performed by PHOEBE impacted biobank harmonization far beyond the scope of the original aim and formal deliverables. Through our project endeavors we have identified, and in some cases begun to address, significant new developments that emerged in the biobanking arena during the course of PHOEBE. Primary among these are issues of biobank sustainability and targeted areas of harmonization. These were discussed in detail in our report (footnote 1 above) from the November, 2008 meeting of 25 EU funded biobanking projects. This meeting provided the opportunity to share achievements; identify obstacles, potential solutions, and areas for cross-project collaboration; and discuss critical issues, urgent needs, and practical next steps. PHOEBE and BBMRI were instrumental in co-coordinating this meeting with The Commission. Our report summarized priorities identified for the future; chief among these were issues of sustainability, phenotype harmonization and continued targeting of specific areas needed to achieve interoperabililty. We also emphasized that realizing these goals will necessitate sponsors to interface with each other to ensure a global response to the international need for a harmonized network of biobanks.

PHOEBE's efforts to bring together expertise across organizations, with complementary viewpoints are well illustrated by the structure of the sessions and participation at our final conference. Discussions found broad consensus that the most productive approach for moving forward as a community is to address the challenges ahead, with an eye toward avoiding duplication, for the benefit of all. It is crucial to continue to interact as science advances—to share insights, to continually raise the quality of biobanking science, and to speak as one voice when it counts. PHOEBE scientists are responding to this call by producing a white paper as a type of roadmap for the international biobanking community. Other highlights from the conference were published in a web report that has been widely distributed to the community (see footnote 2 above). The conference also identified the next set of critical themes which must be taken into account to ensure the success of our biobanking science in the world. Briefly, these include that:

a) all biobanks are facing similar strategic issues which need to be addressed using a consistent coordinated approach;

b) population- based biobanks will become more embedded in health care systems in many countries and will work together with the clinical-based biobanks;

c) communication between the diverse disciplines comprising the biobanking community is essential so that we can speak in a more unified voice with respect to biobanking science;

d) greater attention should be focused on building a truly global biobanking community to enable new technologies and knowledge to have clinical and pubic health impact;

e) international cooperation is essential so that finite resources are most efficiently harnessed and duplication is minimized;

f) the biobanking community should articulate a way forward through a common voice;

g) harmonisation of stakeholders is an essential aspect of harmonization. Harmonisation is needed not just between biobanks but across extant biobank member organizations, other organizing bodies (e.g., Organisation for Economic Co-operation and Development, WHO, United Nations Educational, Scientific and Cultural

Organization), government entities, funding organizations (e.g., Gates Foundation, European Commission [EC], NIH), industry, and the general research community;

h) we should develop novel ways to incentivize biobanking and recognize the contribution of this field to the overall science

1.2 Dissemination and Use

As illustrated in Table 1 below dissemination of PHOEBE results have occurred through a number of published outputs including journal articles, book chapters, consensus and policy statements and reports. Additionally, information is made available through web portals, participation at conferences, organization of conferences, meetings, seminars, symposiums, workshops and training events. These dissemination activities and their substantive outputs represent work that was completed across all 5 of the harmonization platforms at the core of PHOEBE. Under the principles of sharing and access we have made PHOEBE information widely and openly available. By interfacing with ongoing biobanking projects our efforts have been adapted into scientific studies and other initiatives related to guiding biobank development, the design of biobanks, analysis of information including phenotype harmonization, considerations for database information management and for establishing interoperability with other biobanks, and ethical and legal guidance.

One of our largest dissemination outlets was the final PHOEBE international conference held in Brussels on March 25-27, 2009 (see conference report and agenda below). This was conference open to the community and included more than 250 participants from 35 countries include participants from Europe, Canada, the USA Australia, Indonesia, Israel, Japan, Mexico, Nigeria, Singapore, and South Korea

Table 1. Overview of dissemination activities in PHOEBE

Dissemination Type	Number
Scientific Articles	38
Book chapters	12
Manuscripts	3
Policy Statement	1
Report	1
Web reports	2
Web portals	3
Conferences	45
Meetings	24
Seminars	4
Symposiums	8
Workshops	9
PHOEBE related courses	15