European Directory of DNA diagnostic Laboratories (EDDNAL)

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Final Report

Submitted to:

European Commission
Directorate-General Health & Consumer Protection
Directorate G – Public Health
Unit G4 – Communicable, Rare and Emerging Diseases

Programme of Community Action on Rare Diseases
(1999-2003)

Contents

Summary

This final report presents an account of the activities of the EDDNAL project for the year 2001-2002. Details are given concerning the development of the project as well as an assessment of usage of the EDDNAL web site as a proxy for impact.

EDDNAL is a non-profit registry, supported by grant from the EC, which is specifically intended for professional use. The information contained in EDDNAL is published as an online clinical resource (www.eddnal.com). It provides standardized information on diagnostic services for heritable syndromes and disorders offered by laboratories throughout fourteen EU countries as well as Switzerland, Norway, Poland. At present, the directory contains 337 laboratories, 906 genetic conditions and 756 contact persons.

An update, begun in 2000, has enabled the registry to collect more information on the diagnostic procedures performed by each laboratory, quality assessment scheme participation and logistical details concerning the organization of testing. The update has also acquired information on research being carried out within each laboratory.

In the past, the EDDNAL web site lacked certain functional parameters that would have enabled the publication of this information. Because the new updated laboratory information introduced more subtleties and details than the past web site could accommodate, a more sophisticated web application was required in order for the medical community to have access to this information. The EDDNAL administration negotiated a contract with an informatics company and the new site was officially launched in October 2002. The feedback from the scientific community has been entirely positive.

Throughout the past two years, the EDDNAL resource persons have been engaged in multiple other endeavours. The literature on gene discoveries and research is constantly reviewed with the aim of identifying and approaching laboratories which may provide diagnostic testing for inherited disorders but are as yet not included in the registry. In the past two years over 200 new laboratories have been invited to apply to be included in EDDNAL. The overall response has been positive. The EDDNAL Registry Manager has given multiple oral and poster presentations in diverse venues spanning both the European as well as North American continents.

Statistics on the use of the web site indicate a growing interest in and use of the information provided by the web site. In addition, these statistics show that the audience using the information in the EDDNAL registry, while primarily European, also come from North America, Australia, Oceania and Asia.

Introduction

To date, more than 12000 genes have been described and catalogued in the Online Mendelian Inheritance in Man (OMIM) directory[1], with over 7000 of these entries mapped to specific gene loci.[2] The rate of new gene discoveries, pioneered in large part by the Human Genome Project (HuGE), has far-reaching implications for health related research. It has been predicted that the information provided by the sequencing of the human genome will have profound effects on diagnostics, preventive medicine and therapy.[3] Indeed, these predicted effects can already be seen in the rapid increase in DNA based diagnostic testing for disorders ranging from uncommon specific genetic syndromes to common chronic diseases of public health concern. Furthermore, it has been suggested that virtually all human disease has a hereditary component[4], which suggests that even general practitioners require DNA based diagnostic resources.

Background

This rise in both the number of genetic diagnostic tests as well as the need for these diagnostic tools has necessitated the development of a comprehensive directory of European laboratories and a listing of the services they can offer. In 1995 European partners were identified in fourteen EU countries[5] as well as Switzerland and Norway with the aim of collecting standardised data for a Europe-wide directory. Efforts were made to identify, describe and list the diagnostic services offered by laboratories throughout these sixteen countries. This culminated in the creation of the on-line **European Directory of DNA diagnostic Laboratories** (**EDDNAL**): http://www.eddnal.com .

Current Status

The registry presently contains 337 laboratories, 906 genetic conditions and 756 contact persons. These numbers continue to grow as new laboratories are contacted and included within the registry.

[1] The Online Mendelian Inheritance in Man (OMIM) is a continuously updated catalogue of human genes and genetic disorders. OMIM focuses primarily on inherited, or heritable, genetic diseases. It is also considered to be a phenotypic companion to the human genome project. OMIM is based on the text Mendelian Inheritance in Man, authored and edited by Dr. Victor A. McKusick and a team of science writers and editors at Johns Hopkins University and elsewhere. http://ncbi.nlm.nih.gov:80/entrez/Omim

[2] Online Mendelian Inheritance in Man (OMIM). Center for Medical Genetics, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD), 2001.

[3] Collins FS, McKusick VA. Implications of the Human Genome Project for medical science. *JAMA.* 2001;285:540-544.

[4] Khoury MJ. Relationship Between Medical Genetics and Public Health : Changing the Paradigm of Disease Prevention and the Definition of a Genetic Disease. *American Journal of Medical Genetics*. 1997;71:289-291.

[5] Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain, Sweden and the United Kingdom

Introduction

European Partners

The EDDNAL registry enlists one National Coordinator (European Partner) from each country for which laboratories are listed in the database. The group of National Coordinators act as a Steering Committee for the activities of the EDDNAL registry. Each National Coordinator is the representative or expert (and in some situations, the sole contact person) for diagnostic services of medical genetics in his or her country. The National Coordinators recommend the best manner in which to proceed to collect information from laboratories in his or her country. They also approve or deny a laboratories application to become a part of the registry.

Final Report

This final report presents a summary of the multifarious activities that have been carried out from December 2000 through November 2002 under the rubric of the EDDNAL project. Specifically, details are presented concerning the progress and development of the project as well as an assessment of the impact of the project using statistics of web site usage as a proxy for impact.

Partners

National Coordinators

Name	*Country*	*Affiliation*
David E. BARTON	Ireland	National Centre for Medical Genetics, Dublin
Helge BOMAN	Norway	Haukeland Hospital, Bergen Department of Medical Genetics
Maria-Luis CARDOSO	Portugal	Instituto de Genetica Medica Jacinto de Magalhaes, Porto
Bruno DALLAPICCOLA	Italy	University La Sapienza, Roma Institute of Medical Genetics
Marc DELPECH	France	Universite Rene Descartes, Paris V
Rob ELLES	United Kingdom	Central Manchester Healthcare NHS Trust
Xavier ESTIVILL	Spain	Hospital Duran i Reynals, Barcelona
Christa FONATSCH	Austria	Universität Wien Institut für Medizinische Biologie
Emmanuel KANAVAKIS	Greece	Athens University First Department of Pediatrics
Clemens R. MÜLLER	Germany	University of Wuerzburg Department of Human Genetics
Magnus NORDENSKJOLD	Sweden	Karolinska Hospital, Stockholm Department of Molecular Medicine
Arto ORPANA	Finland	HUCH Laboratory Diagnostics, Helsinki Laboratory of Molecular Genetics
Daniel F. SCHORDERET	Switzerland	CHUV, Lausanne Division of Medical Genetics
Marianne SCHWARTZ	Denmark	Rigshospitalet, Copenhagen Department of Clinical Genetics
Hubert SMEETS	The Netherlands	Stichting Klinische Genetica Zuid-Oost Nederland, Maastricht
Lionel VAN MALDERGEM	Belgium	Institut de Pathologie et Génétique, Loverval Centre for Human Genetics

Partners

Organizations & Institutes

- IRSPG - Institute de Recherche Scientifique en Genetique et en Pathologie (1995 - 2003)
- Genzyme Belgium NV/SA (2002-2003) (www.genzyme.com)
- TKT (2001-2002) (http://www.tktx.com/)
- European Commission's Programme of Community Action on Rare diseases (1999-2002)(http://europa.eu.int/comm/health/ph/programmes/rare/index_en.htm)
- EMQN - European Molecular Genetics Quality Network (1997-2002) (http://www.emqn.org)

Development, Methods, Progress and Impact

Laboratory Information Questionnaire

In December 2000, a questionnaire was submitted to all laboratories and institutions listed within the EDDNAL database. This new form, considerably shorter than its predecessor, allows the EDDNAL administration to keep the information on the database up to date thereby facilitating its usefulness to physicians consulting the registry and expediting the diagnosis of genetically inherited syndromes and disorders. Specifically, the new form requests information on the testing methodology, number of positive results obtained, participation in quality assessment schemes, logistical details concerning shipment of samples as well as cost and reimbursement and, finally, research interests. Since, after having contacted each laboratory, the response rate was low we decided to re-design the presentation of the questionnaire. The new designs (in Excel spreadsheet and Adobe pdf.) have had great success.

A project to create a new database to house the newly collected information was completed in May 2001.

New Laboratories and Diagnostic Tests

The EDDNAL administration has commenced a search for new laboratories which provide DNA diagnostic testing and which are as yet not included in the database. This effort spans many sources and includes a continual review of the literature concerning the identification of new mutations causing genetic disorders. After sending messages to 196 laboratories, we have been in contact with 83 labs that have agreed to join the registry, and we have received completed applications from 39 new laboratories. The response has been wholly positive; even research laboratories that were contacted in error were pleased to learn of EDDNAL and to know where to direct future inquiries for genetic testing services.

In response to the sizeable amount of research laboratories looking for samples, we have recently considered the possibility of creating a separate section entitles – research only.

Most recently, with the EU's decision to extend its borders to include central Europe we have begun the search for National Coordinators in these countries. We have already confirmed a National Coordinator for Poland, Czech Republic and Lithuania. In addition we have begun gathering information on diagnostic laboratories in these countries in preparation for there inclusion in the database beginning January 1st 2004.

EDDNAL Annual Meetings

The 3rd Coordination Meeting with the European Partners took place at the 10th International Congress of Human Genetics in May 2001, in Vienna, Austria. During this meeting, a presentation was given describing research into the diversity among European diagnostic centres and the way in which the EDDNAL web site (www.eddnal.com) is able to provide information on diagnostic services provided in the different EU member states.

Development, Methods, Progress and Impact

EDDNAL Annual Meetings (continued)

For this presentation, the EDDNAL Registry Manager performed a review of the literature to ascertain the differences among European diagnostic laboratories of Europe as well as the problems specific to these countries. The EDDNAL representative then described how the EDDNAL registry provides information on the Access, Availability and Quality Ascertainment of DNA-based diagnostic testing throughout the European community. Following this presentation, a discussion was had concerning the future ways the on-line directory could better promote information exchange between European centres and improve awareness of the availability of services for rare genetic conditions

There was no annual meeting in 2002.

EDDNAL plans to organise its 4th annual meeting as a scientific conference – a satellite to the ESHG conference in May 2003.

Presentations

A presentation, similar in scope to the one given at the ICHG, was given by the Registry Manager for the EUROCAT (European Registry of Congenital Anomalies and Teratogens) Steering Committee meeting. At this meeting, possible collaboration between EUROCAT and EDDNAL was discussed.

A poster presentation describing the different facets of the EDDNAL project was given at the ICHG meeting in Vienna. Another poster was presented at the 51st Annual Meeting of the American Society of Human Genetics. Posters were also presented at the American Society of Human Genetics Conference in Baltimore (November 2002) and at the Belgian Human Genetics Conference (February 2003).

EDDNAL Website

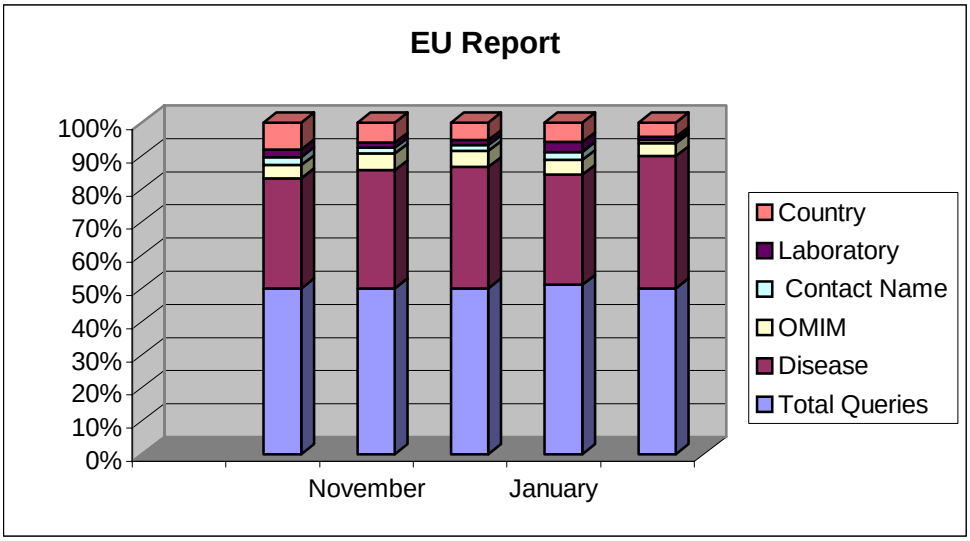
The EDDNAL administration has completed the new website on which is published all additional information that has been collected in the comprehensive update described above. In addition to its success, we are able to keep it update (to the day if necessary) as the updates are no longer the responsibility of an external company.

Results: Statistics

With the launching of the new website in October 2002 we are more able to keep track of the number of users on the site which has been increasing steadily since its launch. The obvious exception is the month of December when most geneticists have a two-week vacation.

Here are the statistics for the new website launched in October 2002:

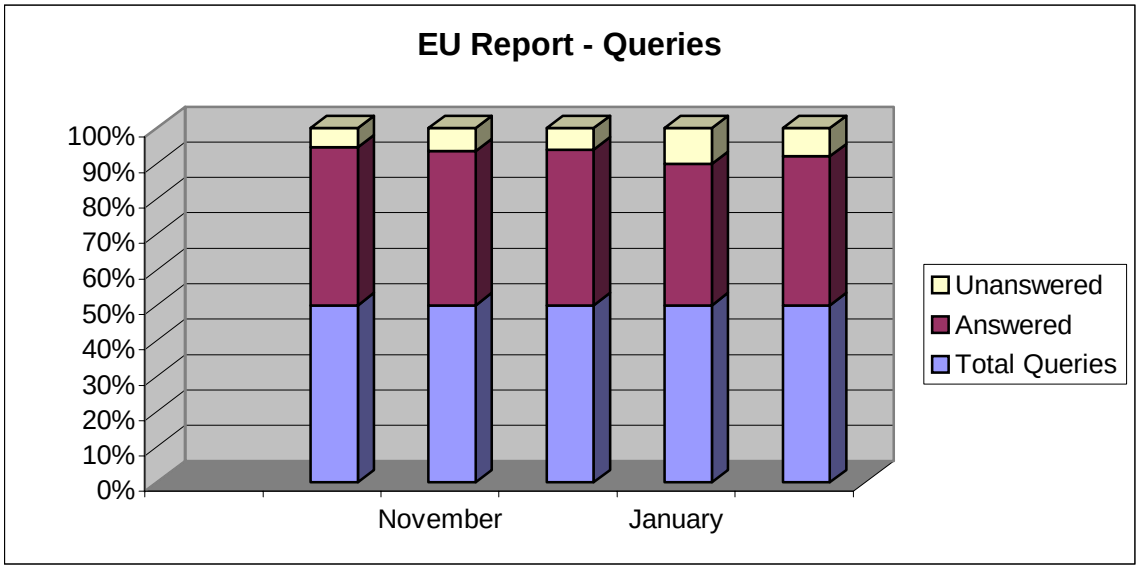
Month	Total Queries	Disease	OMIM	Contact Name	Laboratory	Country
October	3125	2076	245	152	145	507
November	3942	2814	386	146	111	485
December	3475	2547	334	116	113	365
January	4717	3068	413	217	278	541
February	4938	3939	372	100	92	435



Results: Statistics

The other useful information collected by the new website is the number of queries, the percentage answered and those unanswered. This allows us to know how many satisfied clients we have had and in addition we can attempt to gather information on the diseases we do not have laboratories for but which are being requested by the medical community. The results of this research are visible in the month of February where there is a relative (to the total) decrease in the percentage of unanswered queries.

Month	Total Queries	Answered	Unanswered
October	3125	2780	345
November	3942	3433	509
December	3475	3053	422
January	4517	3598	919
February	4938	4155	783



Goals & Conclusions

The future of the EDDNAL Project will entail the improvement and expansion of the services that it provides. EDDNAL endeavours to improve the completeness of the registry thereby simplifying the investigation procedure for professionals. EDDNAL also strives to insure that high quality and up to date information is available on a broad range of rare diseases. Third, EDDNAL hopes to promote laboratory participation in quality assessment schemes. Participation in such a scheme would enable the creation of a gold standard that should motivate all labs to rise to the standard of the European majority. Fourth, EDDNAL endeavours to maximize access to the information contained in its database.