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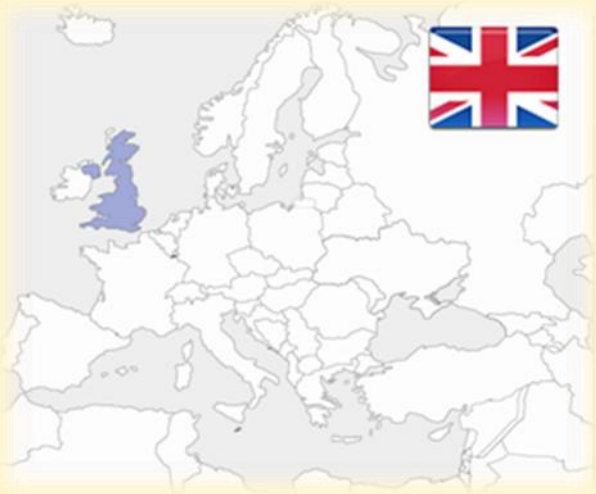
2012 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES



STATE OF THE ART OF RARE DISEASE ACTIVITIES IN THE UNITED KINGDOM

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More information on the European Union Committee of Experts on Rare Diseases can be found at www.eucerd.eu.

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ACRONYMS

General

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area (Iceland, Switzerland, Norway)
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization

Pilot European Reference Networks

Dyscerne - European network of centres of expertise for dysmorphology
ECORN-CF - European centres of reference network for cystic fibrosis
Paediatric Hodgkin Lymphoma Network - Europe-wide organisation of quality controlled treatment
NEUROPED - European network of reference for rare paediatric neurological diseases
EUROHISTIONET - A reference network for Langerhans cell histiocytosis and associated syndrome in EU)
TAG - Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses
PAAIR - Patients' Association and Alpha-1 International Registry Network
EPNET - European Porphyria Network - providing better healthcare for patients and their families
EN-RBD -European Network of Rare Bleeding Disorders
CARE-NMD -Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe project
ENERCA - European network for rare and congenital anaemia – Stage 3

GENERAL INTRODUCTION TO THE REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

The 2012 Report on the State of the Art of Rare Disease Activities in Europe was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2011. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the European Union Committee of Experts on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of either the European Commission, its Agencies or national health authorities.

The report is split into five parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2011
Part III: European Commission activities in the field of rare diseases
Part IV: European Medicines Agency activities and other European activities in the field of rare diseases
Part V: Activities in EU Member States and other European countries in the field of rare diseases

Each part contains a description of the methodology, sources and validation process of the entire report, and concludes with a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning the United Kingdom. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report[1].

[1] http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf

RARE DISEASE ACTIVITIES IN THE UNITED KINGDOM

Definition of a rare disease

There is no official definition of a rare disease in the UK. The National Specialised Commissioning Team (NSCT) commissions services, products or technologies for conditions affecting usually less than 500 patients across England, which currently covers around 60 conditions, diagnoses or procedures (mostly concerning genetic diseases, especially in children). The definition for specialist commissioning is the presence of conditions requiring a planning population of 1 million or more, as explained in the following section. Similar arrangements apply in the devolved administrations of Scotland, Wales and Northern Ireland.

National plan/strategies for rare diseases and related actions

Current organisation of health care for rare diseases in the UK

The basic concept in the National Health Service is not that of 'rare diseases' but rather that of 'specialised services'. There are three tiers for the planning and management of health services – local, specialist commissioning and national commissioning. 'Specialist commissioning' applies to any service with a planning population of 1 million or more, such as rare diseases. Services are selected into national commissioning by ministerial decision[2]. This involves an assessment of the population's needs and deciding what to prioritise taking into account a wide range of factors. A comprehensive list of services likely to need specialist commissioning has been developed (the Specialised Services National Definition Set).

The majority of services are commissioned by Primary Care Trusts (PCTs) in partnership with general practice. A large proportion of the money is spent on services for conditions affecting large numbers of people. Services for rarer or more unusual conditions, known as "specialised services" are subject to different commissioning arrangements. Specialised services are those with low patient numbers but which need a critical mass of patients to maintain quality and make treatment centres cost-effective; a catchment population of more than 1 million is needed. As these services are high-cost and low volume, under arrangements which were strengthened by the Carter Review in 2006, PCTs group together to commission such services through 10 specialised commissioning groups (SCGs). Each SCG covers a population of approximately 3-7 million people. The National Specialised Commissioning Group (NSCG), co-ordinated specialised commissioning.

In 2010 it was announced that a new advisory body will be created in England covering specialised services and treatments for extremely rare conditions typically affecting fewer than 500 patients. Following a consultation, the current National Commissioning Group was dissolved and a new body, the Advisory Group on National Specialised Services (AGNSS), was established. AGNSS makes recommendations directly to Ministers about which services should be designated for national commissioning. The Group will also consider a small number of new technologies for small patient populations which fall outside the National Institute for Health and Clinical Excellence's (NICE) remit, but which may be suitable for national specialised commissioning. Any decisions that AGNSS will make about services and technologies will be guided by a decision-making framework which draws in part on work done by the Specialised Healthcare Alliance[3] around ethical considerations. Membership of the group is wide-ranging and includes both commissioning and clinical representation, as well as an ethicist[4]. AGNSS met for the first time in September 2010.

Services for certain very rare conditions (generally less than 400 people nationally) were previously commissioned by the NCG, a standing committee of the NSCG. A list of specialised services[5] (see section on "National plan for rare diseases and related services") is available for use in determining whether services should be commissioned locally or by the specialist commissioning group, but there is no official list of rare diseases: this applies to England. Different but equivalent arrangements exist in Scotland, Wales and Northern Ireland. Health ministers in England agreed to national commissioning of services, effective 1 April 2011, for 6 more rare diseases: Stickler syndrome; Wolfram syndrome; Lymphangioleiomyomatosis; Insulin resistance

[2] List and criteria are available at www.ncg.nhs.uk

[3] http://www.shca.info/index.htm

[4] A full list of participants is provided here: http://www.specialisedservices.nhs.uk/info/agnss

[5] List and criteria of specialised services, developed by the Department of Health and now held by the National Specialised Services Team, are available at www.ncg.nhs.uk

syndromes (e.g. Donohue and Rabson Mendenhall syndromes); Severe and complex forms of osteogenesis imperfecta; and Pseudo-obstruction of gut in young children.

Different arrangements exist in Scotland, Wales and Northern Ireland. NHS Wales has recently undergone reorganisation and since April 2010, 7 Local Health Boards are responsible for planning health services for their population. For specialised services, the Welsh Health Specialised Services Committee (WHSCSC) is responsible for the joint planning of Specialised and Tertiary Services on behalf of Local Health Boards in Wales. In Scotland, the National Services Division commissions nationally designated specialist services funded by top sliced funding from the Scottish Government Health Directorates: a service may receive designation if the service need is very low and that there is a clinical need for such a service. In Northern Ireland, the Health and Social Care Board along with 5 local commissioning groups commission services.

Funds for care of patients with rare diseases are included in the current expenditure within the general NHS budget, although there is a separate budget for nationally commissioned service. Also each of the 10 specialist commissioning groups in England has its own budget, pooled from constituent PCTs: there are budgets for the equivalent structures in Scotland, Wales and Northern Ireland.

Steps towards a national plan/strategy for rare diseases

Although there are these measures in place, a national plan or strategy for rare diseases in the UK has not yet been adopted in the UK. The plan should be produced by the end of 2013.

Rare Disease UK (RDUK) has campaigned for the adoption of a plan for rare diseases and met with government officials and key people within the National Health Services in all four home nations to highlight the need for a strategy for rare diseases. RDUK also established 5 working groups comprising of expert stakeholders looking into various aspects of planning for rare diseases in the UK in order to aid the establishment of a plan. A UK National Conference on Rare Diseases, organised by RDUK and EURORDIS in the context of the Europlan conference, took place on 16 November 2010[6] in Manchester to examine proposals for a plan which were then launched on Rare Disease Day 2011. The proposals took the form of a report entitled 'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'[7], presented at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning, patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group.

The Specialised Healthcare Alliance (SHCA) held on 16 November 2010 the SHCA Conference on Delivering Quality in Specialised Care. The conference was opened by the Minister for Quality at the Department of Health. This conference helped inform the 2011 report *"Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions*[8]*"* (see section on "National patient alliances of patient organisations and patient representation": this report was part of the iterative process seeking to inform the UK's response to the EC Council Recommendation on an action in the field of rare diseases, as well as future arrangements for specialised commissioning.

A national plan, aided by the recommendations made by these groups, was developed during 2011. The public consultation was launched on 29 February 2012 to mark Rare Disease Day 2012[9]. The UK-wide consultation will be open until 25 May 2012. Responses to the consultation will inform the final plan, due to be produced by the end of 2013. The proposed plan recommends using specialist centres to make exact diagnosis; acknowledges that all doctors should have the right training to be aware of the possibility of a rare disease; and recommends that the care of patients with rare diseases be better coordinated.

Other related actions

The British Paediatric Surveillance Unit (BPSU) was established in 1986 to allow paediatricians to contribute to the epidemiological surveillance and further study of rare disorders affecting children. The BPSU publishes an each year a Scientific Annual Report[10]. This study typically includes 12 rare childhood disorders (or rare complications of common diseases) "of such low incidence or prevalence as to require cases to be ascertained

[6] http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_uk_europlan.pdf

[7] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf

[8] http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf

[9] http://www.dh.gov.uk/health/2012/02/consultation-rare-diseases/

[10] http://www.rcpch.ac.uk/what-we-do/bpsu/publications/annual-reports/annual-reports

nationally in order to generate sufficient numbers for study". Surveillance of conversion disorder has involved the newly established UK Child and Adolescent Surveillance System which investigates rare child psychiatric conditions. The report also includes a progress report of the international network of paediatric surveillance units (INoPSU). Following the establishment of the BPSU, other countries have developed similar methodologies, including Australia, Germany, Greece, Latvia, the Netherlands, New Zealand, Portugal, and Switzerland. Scotland and Belgium, though not yet members of the network, have similar such units, there is also interest in Argentina and Italy. International-level action over the past two years, according the report, includes the surveillance of 70 different rare conditions covering a child population of over 50 million and involving over 10,000 clinicians. Regular conferences are held the most recent being in 2010 in Dublin Ireland. A report of the conference and INoPSU activities are available from their annual report[11].

Deciphering Developmental Disorders (DDD)[12] was launched in 2011: this project aims to improve the diagnosis and care of children in the UK who fail to develop normally due to changes in their genetic makeup. The project seeks to capture the genetic make-up of up to 12 000 children with intellectual or physical delays or who have multiple malformations. A collaborative effort between the National Health Service Clinical Genetics Services across the UK and the Wellcome Trust Sanger Institute, the project will provide information for researchers and clinicians into rare chromosomal abnormalities and their possible role in disease. Another interesting facet to be explored by the project are the ethical and social aspects involved in the clinical use of new genomic technologies, including the perceptions and expectations of patients and families. The project is supported by the Health Innovation Challenge Fund, a parallel funding partnership between the Wellcome Trust and the Department of Health.

In 2011, the United Kingdom's first brain tumour tissue bank was created, housed in Southern General Hospital in Glasgow, Scotland. It will provide a large number of samples to researchers, with the goal of accelerating research toward treating this group of rare diseases. The new tissue bank, available to researchers from academia and industry, was made possible by funding from brain cancer charity Brainstrust[13].

Centres of expertise

The National Specialised Commissioning Team (NSCT) funds designated centres for the diagnosis and/or care of particular conditions. In line with the remit of the NSCT, designated centres provide services for conditions generally affecting less than 500 and no more than 1000 people nationally. Specialist centres themselves can apply for national commissioning of a particular service, subject to the agreed eligibility criteria.

Genetic services are commissioned regionally by the SCGs. Genetic testing and counselling is thus available regionally and for some conditions in specialist centres, often linked to an area of research. Genetic counselling is an officially recognised profession and training courses are available. These Genetics Centres help direct and sign-post patients and colleagues as regards centres of excellence and specialised services.

Health ministers in England have agreed to national commissioning of services, effective 1 April 2011, for patients with the following disorders: Stickler syndrome; Wolfram syndrome; Lymphangioleiomyomatosis; Insulin resistance syndromes (e.g. Donohue and Rabson Mendenhall syndromes); Severe and complex forms of osteogenesis imperfecta; and Pseudo-obstruction of gut in young children. National commissioning establishes national centres of expertise for a specific disease and streamlines funding to one centralised source rather than being scattered amongst different local budgets.

Arrangements are in place enabling patients in Scotland, Wales and Northern Ireland to access designated centres although funding is provided by the relevant body in each country. Regional specialist services also exist for genetic diseases but these are funded separately. There is an annual call for applications for national commissioning and designation. Research and epidemiology are not funded under this system.

There has been some criticism from patient groups that the lack of a co-ordinated approach to services for rare conditions engenders late, missed or incorrect diagnoses – sometimes with severe health consequences. A range of wait targets and measures are applied across the NHS: the target of particular importance to patients with rare diseases is the 'wait' target (the maximum wait from first contact with a doctor to initiation of definitive treatment). This implies a very strict approach to establishing a definitive diagnosis quickly as this wait is viewed from the patient's perspective.

[11] http://www.inopsu.com/publications/INoPSUAnnualReport2009.pdf
[12] http://www.sanger.ac.uk/about/press/2011/110322.html
[13] http://www.gla.ac.uk/news/headline_212335_en.html

Pilot European Reference Networks

British teams participate or have participated in the following European Reference Networks for rare diseases: Dyscerne (main partner), ECORN CF, EPI/EPNET, ENERCA, EUROHISTIONET, NEUROPED, Paediatric Hodgkin Lymphoma network, PAAIR, Care-NMD and EN-RBD.

Registries

In the UK registers are kept for individual conditions and some groups of conditions, including congenital anomalies.

The United Kingdom contributes to the following European registries: EUROCAT, EIMD, TREAT-NMD, AIR, EUROCARE-CF, EURO-WABB, EUHASS, EUROPAC, European Prader-Willi database and EUROWILSON.

Neonatal screening policy[14]

Under current policy in the United Kingdom, newborn screening is performed for five disorders using blood spot tests: phenylketonuria, congenital hypothyroidism, sickle-cell disorders (haemoglobinopathies), cystic fibrosis and medium chain acyl CoA dehydrogenase deficiency. There are some variations in the four countries of the UK.

Newborn screening is performed in England for phenylketonuria, congenital hypothyroidism, sickle cell disease, cystic fibrosis and medium-chain acyl-CoA dehydrogenase deficiency. Currently all babies in Scotland are offered screening for phenylketonuria, congenital hypothyroidism, cystic fibrosis, sickle cell disease and medium-chain acyl-CoA dehydrogenase deficiency. In Wales screening is offered for as part of routine care for hypothyroidism, cystic fibrosis, phenylketonuria and Duchenne Muscular Dystrophy (boys only). In Northern Ireland Universal screening of all infants at 5 days of age is offered for phenylketonuria, congenital hypothyroidism and cystic fibrosis; screening for homocystinuria and tyrosinaemia is also offered; and screening for medium chain acyl CoA dehydrogenase deficiency (MCADD) has been available from August 2009 and screening for sickle cell started in April 2010. An official list of screening policies is available http://www.screening.nhs.uk/policydb.php.

Genetic testing

In the UK, genetic testing for rare inherited conditions for patients being managed by the National Health Service are usually provided by laboratories that are part of a Regional Genetics Centre. Each Regional Genetics Centre comprises a clinical service and laboratories (molecular, cytogenetics and biochemical) that are usually co-located. There are 23 regional Genetics Centres that are situated in tertiary hospitals. There are also a number of specialised laboratories that provide some genetic testing. For example there is a network of laboratories that provide genetic testing for haemophilia and other individual laboratories testing for specific rare conditions such as retinoblastoma or porphyrias.

Commissioning policy in the UK identifies clinical genetics (clinical service and laboratory provision) as a specialised service. The specialised services are commissioned differently in each devolved country; England, Northern Ireland, Scotland and Wales. As noted above, In England specialised services are commissioned by Specialised Commissioning Groups or by the national commissioning team. In Scotland there is a consortium arrangement, in Wales the Welsh Health Specialised Services Committee is responsible for the joint planning of Specialised and Tertiary Services on behalf of Local Health Boards in Wales, in Northern Ireland the Regional Medical Services Consortium informs the Health and Social Services Boards who commission genetic services.

All the molecular and cytogenetic laboratories across the whole of the UK which are part of a Regional Genetics Centre are members of the UK Genetic Testing Network (UKGTN – www.ukgtn.nhs.uk). The focus for the UKGTN is to support equity of access to genetic testing services for patients being treated by the National Health Service for rare inherited conditions. The Network is a collaborative group of genetic testing laboratories, clinical geneticists, genetics commissioners and patient representatives. A small project team and three working groups carry out the work on behalf of the Clinical & Scientific Advisory Group and 53 member laboratories from regional genetics and specialist laboratories.

The core functions of the UKGTN include:

- Approval of molecular, cytogenetic and specialist laboratories for membership where quality standards are met;
- Audit/review of testing provision in order to highlight any areas where there may be inequity of access to genetic testing and to review laboratory compliance in meeting national standards;

[14] http://www.screening.nhs.uk/programmes

- Evaluation of new genetic tests for clinical utility and scientific validity to recommend new testing services for NHS funding through a process called the Gene Dossier process;
- Developing mechanisms to improve the commissioning of genetic services such as standard laboratory currencies;
- Maintaining a publicly available free online database of the member laboratories showing where national services are available and the providers of the tests listed in the NHS Directory of Genetic Testing. The database also provides access to approved gene dossiers and testing criteria;
- Advising NHS policy developers, the Department of Health, the National Specialised Commissioning Team and the National Institute for Health and Clinical Excellence (NICE) on new developments and provide a view on policies that impact on the provision of genetic testing services;
- Providing advice to genetics commissioners on new services and funding requirements.

It has long been recognised that the commissioning arrangements across England vary considerably for clinical genetics services and their associated laboratories. The UKGTN Commissioning working group explored the current arrangements for the Specialised Commissioning Groups in each region and recently published a report making recommendations and providing guiding principles. Although commissioning organisations are set to change following the White Paper on Liberating the NHS, the principles developed by the UKGTN can be applied in any setting.

The Government response to the House of Lords inquiry into genomic medicine (the inquiry took place in 2008 and the Government response was published in 2009) states that the Department of Health will "continue, via the UKGTN, to monitor commissioning structures within genetics and genomics". During the debate in the House of Lords in June 2010, on the report from the inquiry, the Parliamentary Under-Secretary of State, Earl Howe, endorsed the work that UKGTN is under taking with commissioners of genetic services. The Department of Health continues to support this work to develop a consistent model and guiding principles which will also inform commissioning of genetic testing in mainstream specialties.

The term "reference laboratories" is commonly used but it is often country specific and can also refer to different functions depending on the pathology discipline. In England there are two National Genetics Reference Laboratories based in Wessex and Manchester. These laboratories have been funded by the Department of Health since 2002 to support the UK genetic laboratory centres by bringing new technologies into service. The specific remit of the laboratories includes: technology development, assessment and validation; developing new quality management systems; developing reference and control reagents; developing information systems for genetics; and providing advice to government and other bodies.

The National Genetics Reference Laboratory in Manchester has developed particular expertise in health informatics and bioinformatics applied to genetic medicine. Its current work programme includes the support and development of databases and software tools used in genetic analyses, bioinformatics training for clinical scientists and developing best practice and support for clinical bioinformatics. It also participates in a number of UK and EU funded projects addressing health and bioinformatics issues in genetic medicine, including the GEN2PHEN[15] and EUCERD projects on clinical coding. UKGTN has also commissioned NGRL Manchester to develop a clinical genetics data set for use in the NHS and make recommendations to improve the laboratory information systems and their interoperability with NHS systems and other genetic centres

When laboratories request UKGTN to evaluate a new tests for inclusion on the NHS Directory of Genetic Tests an integral component of the Gene Dossier requires the submitting laboratories to develop 'testing criteria' (TC). The TC identifies the key features of the disorder, indicates the types of referrers who would be expected to order the test and aims to ensure that a particular genetic test is being used for the appropriate target population, i.e. those who are most likely to have the condition. TC can also have an educative role and are a helpful guidance tool. If a clinician is required to complete a TC form then they will get a succinct picture of what may well be a disease with which they are not familiar. TC are available from the UKGTN website by searching for testing services using the online database. Between 2004 and 2011 the UKGTN had evaluated 313 gene dossiers and made recommendation for 243 tests to be available for NHS service. During this time 255 testing criteria were developed. There are less testing criteria because this was concept was not introduced until 2006. A long term goal for the UKGTN is to draw up TC for all conditions available through the UKGTN including those that pre-date the development of TC in 2006. The Clinical Molecular Genetics Society also develops best practice guidelines which are available from their website. Individually laboratories may develop referral guidelines for local use.

Tests for patients in the NHS are funded through NHS commissioning mechanisms.

[15] www.gen2phen.org

It has been recognised that activity data collection from laboratories across the country is variable due to different methods of recording activity and therefore funding in each area is not comparable. The UKGTN has worked in collaboration with the Clinical Molecular Genetics Society (CMGS) to develop a reliable and easy to use workload measure for molecular genetic testing to be able to compare activity data across labs. The unit of activity developed is based on patient reports and is known as Molecular Units (MolUs). Each report is categorised into one of seven bands according to its complexity which is measured according to how many PCR amplicons or equivalent are involved in the test. Each band has a weight assigned to it and the number of reports in that band is multiplied by the weight to arrive at the number of MolUs of activity for a laboratory. The weights range from 1 for a DNA extraction report i.e. no testing within the lab to a weight of 40 for a band G report which involves testing and analysing over 100 amplicons. The weightings were established following testing by 6 pilot UKGTN laboratories of various sizes and with varied testing repertoires. Laboratory reports and the number of amplicons are relatively easy to count and allow for a transparent and flexible system that could also be used to allocate national tariffs. Laboratories are currently trialling this system for workload in 2010/2011. The Clinical Molecular Genetics Society and the UKGTN are collaborating with the Association for Clinical Cytogenetics to develop a similar system for cytogenetic testing. The CMGS issued an annual audit[16] of in 2011 genetic testing activity. Such information is valuable to understanding the rare disease demand for testing and pre- and post-natal activity in this area. The UK audit includes number of samples, number and type of disease, number and type of tests sent for analysis and staff/workload across laboratories. The 2009-2010 audit "...shows a continued growth in national activity for each of the postnatal, prenatal and predictive testing categories, an improvement in routine reporting times and encouraging data of the capturing and utility of activity…". Prenatal diagnosis reports were recorded for 120 different disorders, with 86% being for common aneuploidies. There were 12839 prenatal reports, of which 1744 were for disorders excluding aneuploidy. Non-invasive foetal sexing testing accounted for 19% of non-aneuploidy screening. Monogenic disorders include sickle cell anaemia (440), beta-thalassaemia (119), SMA type I (61), Duchenne muscular dystrophy (32), Huntington disease (25), craniosynostosis (9), and others. For postnatal activity, there was a 31% increase in single gene disorders for 2009-2010. This jump reflects the inclusion of data from a new large volume provider. There was a mean number of 789 reports for fragile X testing across 18 providers. There was a mean number of 706 cystic fibrosis reports across 20 providers.

In 2009 the National Genetics Reference Laboratories in the UK launched an innovative free online diagnostic technology forum destined for professionals in the field of genetic testing. Professionals internationally can share in-house assessments of diagnostic technologies ranging from diagnostic kits and sequencing platforms to analysis software. LabSight is a non-profit tool in response to a lack of reliable comparative reporting on new technologies. The forum will serve as an online resource for documentation, and will also list upcoming events and calls for collaborations. With rare disease research and diagnostics particularly vulnerable to limited budgets and resources, LabSight offers a money-saving tool helping professionals find the best technology for their diagnostic laboratories.

A new report[17] from the Foundation for Genomics and Population Health (commonly known as the PHG Foundation) encourages the mainstream medical specialities to become versed in the field of genetics, incorporating genetic knowledge and technology into their offer. The authors of the report propose "...a shift of the axis of main clinical responsibility for individual patients with inherited disease from clinical genetics to the relevant specialty - cardiology, ophthalmology, renal medicine, neurology or a host of other areas". Evoking a future in which, "…rather than genetics 'moving into mainstream medicine' … clinical areas develop and expand to integrate new clinical expertise relevant to inherited disease and a new set of genomic technologies into clinical pathways as relatively specialised areas within their own service", the report acknowledges that close cooperation with specialist clinical and laboratory genetics service would be necessary in order to promote and sustain such a shift.

Nowgen, a leading UK centre for genetics seeking to inform and improve genetic medicine via training, education, public engagement, research and innovation, issued its Review and Programme for 2011-2012[18] in 2011. Nowgen, working with Orphanet UK, will continue its commitment to facilitating access to high quality information on rare diseases and orphan medicinal products for professionals, patients and the public.

There are no restrictions on either clinicians or laboratories sending samples abroad for testing however laboratories receiving samples are normally expected to comply with recognised accreditation standards and take part in external quality assessment.

[16] http://www.cmgs.org/CMGS%20audit/2010%20audit/secure4Final_Audit09_10.pdf
[17] http://www.phgfoundation.org/file/7962/
[18] http://www.nowgen.org.uk/CubeCore/.uploads/documents/NowgenReviewandWorkProgramme20112012.pdf

Diagnostic tests are registered as available in the UK for 541 genes and an estimated 585 diseases in the Orphanet database[19]. The UKGTN has recommended tests for 536 diseases and 714 genes for NHS commissioning for service from April 2011.

National alliances of patient organisations and patient representation

The major alliances representing rare disease patient organisations in the UK are Rare Disease UK, the Specialised Health Care Alliance (SHCA) and the Genetic Alliance UK[20] (formerly the Genetic Interest Group). Rare Disease UK was established in November 2008 as a joint initiative between Genetic Alliance UK and others in response to the unmet health care needs of families who currently struggle to get access to integrated care and support from the NHS.

Rare Disease UK

Rare Disease UK is an alliance of patients, clinicians, industry, academics and researchers campaigning for a strategic plan for rare diseases in the UK. Rare Disease UK[21] (RDUK) has been lobbying for the *"implementation of a strategy for integrated service delivery for rare diseases to ensure quality care and the efficient use of limited NHS resources and scarce expertise"* in response to the Council Recommendation. Since its establishment, the RDUK has successfully *"developed links with key officials in all four governments and NHS of the UK; [gained the] support of a broad range of stakeholders including over 100 patient organisations, pharmaceutical companies, clinicians, academics and individuals; established five Working Groups comprising experts from a variety of fields to investigate various aspects of a strategy for rare diseases and make recommendations to the government; and provided a single voice to drive forward a strategy for rare diseases"*. In November 2008, Rare Disease UK launched in the UK to *"campaign for the adoption and implementation of national plans in each of the UK's home nations"* (England, Scotland, Wales and Northern Ireland). This past year, the five Working Groups of Rare Disease UK have been busy developing recommendations for a strategy for rare diseases. A consultation document[22] on the initial findings of the Working Groups was released for feedback in October 2010 from all relevant stakeholders located inside or outside of the UK.

RDUK launched a new report entitled 'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'[23] at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning, patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group. Following consultation and production of the strategy, RDUK will then be scrutinising the implementation of a strategy.

Specialised Healthcare Alliance (SHCA)

England's Specialised Healthcare Alliance (SHCA) was formed in 2003 specifically to lobby for rare disease patients and those with other complex illnesses that need specialised, frequently expensive, medical care. In 2010 the SHCA issued an overview[24] and critique of England's new arrangements for health service commissioning for small patient populations and has developed recommendations to enhance the approach to cost assessment of treatments for these patients. A discussion of the ethical framework that has been introduced to the assessment process for determining cost effectiveness is provided. The Coalition Government is consulting about a number of aspects of how the NHS in England will work, including the future of the proposed Innovation Pass that would allow funding of orphan products for a period of up to three years pending their appraisal.

In 2011 the SHCA published a new report. *"Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions[25]"* which takes stock of recent developments in specialised commissioning and *"identifies a series of key drivers in delivering improved care and value for people with rare and complex conditions"*. These include building on the Carter Review of Commissioning Arrangements for Specialised Services in 2005/06 (which *"…marked a watershed in the development of associated policy and has*

[19] Information extracted from the Orphanet database (September 2011).
[20] http://www.geneticalliance.org.uk/
[21] http://www.raredisease.org.uk/
[22] http://www.raredisease.org.uk/raredisease_strategy_consultation.htm
[23] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf
[24] http://www.shca.info/PDF%20files/The%20challenge%20of%20rarity%20-%20FINAL.pdf
[25] http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf

yielded real benefits for patients in the years that followed); the impetus of the patient organisations as a vehicle to "drive up standards"; improved patient-physician collaborations; the contribution of NICE quality standards; the development of multidisciplinary networks; outcome measures that maximise effectiveness and efficiency; and the development of patient registries with sharply focused datasets.

To produce this report, the SHCA organised a series of nine workshops focussing on quality and productivity in services including rare cancers, haemophilia, blood and marrow transplantation which fed into the report *"Leaving No One Behind"*

Stemming from the recommendation in this report concerning the central importance of patient registries in specialised care, the SHCA has now produced the *Registries Guide 2011*[26]. Intended for use by patient organisations - particularly those representing people with rare and complex conditions – the guide seeks to respond to two key questions: would it be useful and practicable for a particular patient organisation to set up a registry and what are the key issues that must be taken into account when setting up a registry. The guide also provides tips, case studies and useful links.

Genetic Alliance UK

Genetic Alliance UK, formerly the Genetic Interest Group, changed to its new name in 2010. The long-established non-profit group with over 130 member organisations believes the new name - Genetic Alliance UK[27] - as well as the updated slogan and logo more accurately reflect the work of the group.

Amongst the sources of funding available for patient organisations, the government makes funding available to patient organisations through a system known as a Section 64 grant. Many patient organisations have also obtained funding from the National Lottery which is obliged by law to give a percentage of its profits to charitable organisations: activities such as capacity building, networking, dissemination of information, educational events, exchange of best practices, capacity building to improve patients' integration in social environments and outreach to very isolated patients are all eligible for funding by these schemes. Grants are available to support patients' organisations: for example in 2008, the NCG accorded funding to two patient support groups in order to finance clinics in the UK for Alström Syndrome and Ataxia-telangiectasia. This is a novel structure where the clinic is partnered by patient groups, hospitals and the NHS.

Patient organisations are officially recognised thanks to a strong government policy for public and patient involvement (PPI). Hospitals and health services are required to consult their patients about changes to the service and there are continuous surveys a patient experience and patient satisfaction in NHS hospitals. Patient opinion is not binding. In most cases patients' representatives are eligible for reimbursement of expenses.

Sources of information on rare diseases and national help lines

Orphanet activity in the United Kingdom

Since 2004 there is a dedicated Orphanet team in the United Kingdom, hosted by the University of Manchester. Orphanet UK is in charge of collecting and validating data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in the United Kingdom and in Ireland for entry into the Orphanet database. The Orphanet UK team maintains a the Orphanet UK national website[28]. This team was officially designated by the Department of Health as the official Orphanet team in the United Kingdom in 2010.

Orphanet UK is represented at many major conferences and events such as workshops on rare diseases and the Rare Disease Day. Moreover, Orphanet together with Nowgen hosted the Europlan UK conference meeting on 16 November 2010 in Manchester. Orphanet UK has established collaborations with Dyscerne (A Network of Centres of Expertise for Dysmorpology), Rare Disease UK and Ataxia UK, a charity aiming to support everyone affected by ataxia and fund research into developing treatments. The team also works closely with the National Genetics Reference Laboratory (NGRL) Manchester and has established solid relations with other rare disease organisations such as the Genetic Alliance UK, the British Paediatric Surveillance Unit (BPSU) and the Myrovlitis Trust.

Official information centre for rare diseases

There is no official information centre for rare diseases in the UK other than Orphanet.

[26] http://www.shca.info/PDF%20files/Registries%20Guide%20-%20FINAL.pdf
[27] http://www.geneticalliance.org.uk/index.html
[28] http://www.orphanet.co.uk

Help line

There is no official helpline dedicated to rare diseases in the UK but there are national NHS helplines which differ slightly in each of the four countries. In England and Wales the helpline is known as NHSDirect, and in Scotland as NHS 24.

Other sources of information on rare diseases

Information, advice and support are generally provided by patient organisations dealing with particular rare diseases. Some information is provided by NHS websites: http://www.nhs.uk/, www.nsc.nhs.uk, www.specialisedservices.nhs.uk , and http://www.evidence.nhs.uk.

Contact-a-Family is a key resource for rare diseases. It runs a help line and an online service putting patients in contact with other patients with the same disease (rare or non-rare) and support groups. Other larger patient organisations, both large and small are instrumental in providing information and support. Many run help lines providing general and technical information, provide written information and psychological support: these are funded through various means including donations, fundraising, pharmaceutical companies and grants for the government and other organisations. Many hospitals, especially in the nationally commissioned services also run help lines: these are funded using general health services funds.

UK-based charity Unique[29] has been gathering information on specific chromosome disorders for almost 25 years and since 2003 has been producing family-friendly, medically-verified, disorder-specific information leaflets (learn more.) To date, Unique has published over 125 guides on individual chromosomal disorders, which are available free of charge, and frequently in other languages including Dutch, French, German and Spanish. The Unique newsletter reports that for many families, the leaflets are the first concrete source of information obtained for a specific disorder. Now another new guide, entitled After Diagnosis: What Happens Next? The Early Years, targets parents of pre-school children (0 to 4 years) with a rare chromosome disorder and/or global developmental delay. This guide responds to questions relevant to parents of a newly-diagnosed infant everywhere, and also lists resources available in the United Kingdom for affected children and their families.

Good practice guidelines

Nowgen[30], a centre of excellence in public engagement, education and professional training in biomedicine, part of the NIHR Manchester Biomedical Research Centre, in collaboration with Dyscerne[31] has published a portfolio of management guidelines for rare diseases (Angelman syndrome, Kabuki syndrome, Noonan syndrome, Williams syndrome, 22q11 Deletion Syndrome, Achondroplasia, Neurofibromatosis Type 1 & Neurofibromatosis Type 2) using validated methodologies[32].

A range of other guidelines for rare and very rare diseases are posted on the NCG website[33] or published in professional journals.

New guidance document[34] on the initial evaluation of paediatric patients with suspected sex development disorders was published in 2011. The free-access article appearing in *Clinical Endocrinology* provides guidance on the initial evaluation of an infant or adolescence with a suspected disorder of sexual development. The guidance also evokes the utility of networks and registries to support clinicians, and support groups and psychological services to support the patient and parents.

Training and education initiatives

A training session entitled 'Update in Neuromuscular Disorders' was held for the fourth year at the National Hospital for Neurology and Neurosurgery (13-16 June 2011). Nowgen's professional training team delivers a portfolio of training courses that are particularly relevant to healthcare professionals involved in the management and treatment of rare diseases. These include: Antenatal and Newborn Screening; Molecular Genetics for Genetic Counsellors; Molecular Genetics for Cytogeneticists and Bioinformatics for Clinical Geneticists. Many of these courses have included interactive sessions to inform delegates about Orphanet.

[29] http://www.rarechromo.org/html/home.asp and http://www.rarechromo.org/html/LeafletProtocol.asp
[30] www.nowgen.org.uk
[31] www.dyscerne.org
[32] www.dyscerne.org/dysc/Guidelines & http://www.mangen.co.uk/professionals/clinical-services/useful-documents.aspx).
[33] www.ncg.nhs.uk
[34] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132446/?tool=pubmed

National rare disease events in 2011

The UK based charity 'Jeans for Genes' holds an annual awareness day to raise funds for genetic disorders[35].

To mark Rare Disease Day 2011, RDUK coordinated a number of events across the UK. RDUK also launched a new report entitled 'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'[36] at the House of Commons on 28 February 2011, which was presented to Earl Howe, Minister at the Department of Health. The event brought together patient organisations, patients, carers, healthcare providers, clinicians, researchers, health workers, industry representatives and policy makers. Over one hundred and fifty delegates attended, representing more than one hundred organisations. The report outlines RDUK's recommendations for a strategy for rare diseases and is a product of a year and a half of work in collaboration with members and the broad rare disease community. Receptions were also organised at the Scottish Parliament (22 February 2011) Northern Ireland and Welsh Assemblies (16 March 2011) by RDUK and Genetic Alliance UK. At each of the events, attendees who participated in RDUK's contact campaign took the opportunity to meet with their local politician. Many other patient organisations mark the day with events.

Other events included the Annual Conference of Genetic Alliance UK (24 May 2011), 6th British Society Human Genetic (BSHG) Conference (5-7 September 2011).

Hosted rare disease events in 2011

Amongst the rare disease related events hosted by the UK and announced in *OrphaNews Europe* were: International Tuberous Sclerosis Complex Research Conference 2011 (21-24 September 2011, Belfast), Expanding Horizons in Friedreich Ataxia (6 October 2011, London), and the 5th International Workshop on AKU (Alkaptonuria) (18-19 November 2011, Liverpool).

Research activities and E-Rare partnership

National research activities

Rare diseases research has been supported in the UK up till now although no special funding mechanism is as of yet in place. Government funding is mostly available through the Research Councils (i.e. the Medical Research Council) and the National Institute for Health Research (NIHR). There are several major funding charities, particularly for cancer and heart diseases, and a number of rare diseases charities fund research (such as the Muscular Dystrophy Campaign, the Cystic Fibrosis Trust, the Dystrophic Epidermolysis Association etc). Many products for rare diseases have been put through trials in the UK by major pharmaceutical companies (i.e. enzyme replacement therapies, drugs for pulmonary hypertension, etc).

The Biomedical Research Centres, funded by the National Institute for Health Research (NIHR), also fund some research on rare diseases. The Manchester Biomedical Research Centre specialises in genetics and developmental medicine and is a leader in engaging and involving patients/publics in the research process. The patient involvement and public engagement programme for Manchester Biomedical Research Centre is led by Nowgen. Nowgen has undertaken a detailed mapping exercise with researchers and identified excellent practice. A comprehensive strategy for engagement and involvement has been developed by Nowgen and is being implemented through training courses and resources to support researchers. Examples of Nowgen's current work include: investigating young peoples' information needs when taking part in clinical research and developing a DVD in partnership with teenagers about gene therapy for Cystic Fibrosis. The London-based Biomedical Research Centre in London of the National Institute for Health Research (NIHR) has developed in 2010 a guide intended to aid researchers to involve patients, carers, families and patient groups in the various stages of research[37]. These include the development of grant applications, the design/management of research, the undertaking of research, the analysis of the research data, and the dissemination of research findings. The guide outlines ways in which patients and other users can be involved in each of these stages and how researchers can facilitate this involvement. In a press release, Dr David King, Director, NIHR Central Commissioning Facility is quoted as saying that *"Patient and Public Involvement (PPI) will increase in importance in the work of all NIHR Biomedical Research Centres and Units as it is increasingly recognised that PPI is a win/win for both patients and researchers. This new guide for research staff will greatly enhance PPI across the NIHR, especially in the area of experimental medicine."* Experimental medicine is an important area in the field of rare diseases.

[35] http://www.jeansforgenes.com/about

[36] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf

[37] http://www.guysandstthomas.nhs.uk/news/newsarchive/newsarticles/20100512user-involvement-guide.aspx

Participation in European research projects

British teams participate or have participated in European rare disease research projects including: AAVEYE, ANTEPRION, ANTIMAL, BIG HEART, BIOMALPAR, BNE, CARDIOGENET, CHD PLATFORM, CHEARTED, CRUMBS IN SIGHT, CILMALVAC, CLINIGENE, CONTICANET, CSI-LTB, EMSA-SG, EUROCRAN, EMVDA, EURADRENAL, ENRAH, EPOKS, EUMITOCOMBAT, EURAMY, EUREGENE, EUROBONET, EUROCARE CF, EUROGENTEST, EUROGLYCANET, EURO IRON1, EUROSCA, EUROTRAPS, EUCILIA, EURO-LAMINOPATHIES, EUNEFRON, EUROPADNET, EUROWILSON, ENCE-PLAN, EVI-GENORET, ESDN, GEN2PHEN, GENESKIN, INHERITANCE, HUMALMAB, LEISHDNAVAX, PWS, MITOTARGET, MPCM, MALARIA AGE EXPOSURE, MITOCIRCLE, MM-TB, MOLDIAG-PACA, MPCM, MYELINET, MYORES, NEOTIM, NEUPROCF, NEUROKCNQPATHIES, NEUROPRION, NEUROSIS, PSYCHCNVS, NEWTBDRUGS, PNSEURONET, PULMOTNESION, PWS, RATSTREAM, SPASTICMODELS, RD PLATFORM, STEM-HD, TAMAHUD, TREAT-NMD, VITAL and THERAPEUSKIN, Biology of cilia formation and intraflagellar transport project, and Relationship of BBS proteins in Wnt pathways project.

E-Rare

The UK is not currently a partner of the E-Rare project.

IRDiRC

The National Institute for Health Research is currently a committed member of the IRDiRC.

Orphan medicinal products[38]

The promotion of the development of orphan medicinal products in the UK takes place at a European, and not national, level: orphan medicinal products obtain Marketing Authorisation through the centralised procedure at the EMA. Orphan medicinal products obtain Marketing Authorisation through the centralised procedure at EMA. The body responsible for regulatory approval in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA): accessibility to medicinal products is generally determined by the National Institute for Clinical Excellence (NICE).

Orphan medicinal product committee

The Advisory Group for National Specialised Services (AGNSS) has recently developed a new framework for evaluating "ultra-orphan" drugs: ultra-orphan diseases affect less than 500 people in England. Ultra-orphan medicinal products are not subject to NICE appraisals, but to those of the AGNSS: applications are evaluated for clinical desirability on the information received from clinicians on a case-by-case basis[39].

Orphan medicinal product incentives

No specific incentives reported.

Orphan medicinal product market availability situation

No specific information has been provided concerning orphan medicinal products launched on the market in the United Kingdom.

Orphan medicinal product pricing policy

Control of branded manufacturer prices for all medicines is regulated by the Pharmaceutical Price Regulation Scheme which is essentially a profit cap adjusted to the company's capital in the UK. Value-priced pricing will come into effect from 2014 for newly launched branded medicines[40].

Orphan medicinal product reimbursement policy

The NHS provides all medicines almost free of charge to all patients: there is a small co-payment ('prescription charge') for out-of-hospital drugs. However the elderly, children and those on low income (and other groups) are exempt from this charge. There is no prescription charge in Scotland and Wales.

Licenced drugs are paid for by the NHS in the UK. Decisions are taken by relevant funding bodies at PCT level, not nationally, in the light of available funds. This has led to criticism that access to drugs can be a

[38] Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)

[39] *EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines,* C. Habl, F. Bachner (2011) p61

[40] *Orphan Drugs in Europe : Pricing, Reimbursement, Funding & Market Acces Issues,* Donald Macarthur (2011) pp.86-7

"postcode lottery" i.e. access varies widely depending on where an individual lives. The National Specialised Commissioning Team funds certain orphan medicinal products at national level.

Other initiatives to improve access to orphan medicinal products[41,42]

Orphan medicinal products, like other drugs, are distributed through hospital pharmacies and specialist centres. Home delivery is available for various products, for example enzyme replacement therapies.

Patients with rare diseases can receive unlicenced drugs; in such cases the doctor applies to the MHRA to import it on an individual named patient basis.

The United Kingdom's National Institute for Health and Clinical Excellence (NICE) has launched a consultation process for a new scheme that would permit patients with rare or uncommon disorders to access innovative treatments that have not yet been subject to appraisal by NICE. The NICE "Innovation Pass" will make selected innovative medicines available on the National Health Service for a time-limited period prior to receiving a NICE appraisal. Funding will be drawn from a new ring-fenced £25 million (€27.6 million) budget. The Innovative Pass allows patients earlier access to innovative medicinal products while simultaneously facilitating the gathering of further evidence to "support a subsequent NICE appraisal".

The National Institute for Health and Clinical Excellence (NICE) will start commissioning expert assessments for off-label medicine use starting spring 2012[43]. These assessments will not constitute formal guidance, but rather will provide "a summary of available evidence on selected unlicensed drugs to inform local decision-making". The National Health Service (NHS) in England receives some 1000 specific requests for off-label use annually. The announcement for the off-label product assessments has been met with approval from the rare disease community.

Orphan devices

No specific information reported.

Specialised social services

Respite care services are available in most parts of the UK and are provided by the NHS and charitable organisations. Patient groups also organise holiday camps for children and adolescents. Reimbursement varies: all NHS services are free but charities may ask for a small co-payment in some cases. The provision of recreational programmes is patchy but it is difficult to obtain full information: schemes are usually run by individual patient organisations or by local authority social service departments. A small co-payment is usually expected. Services to integrate patients in daily life are the responsibility of local authority social services departments which are government financed.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN THE UNITED KINGDOM

National plan/strategies for rare diseases and related actions

Although there are these measures in place, a national plan or strategy for rare diseases in the UK has not yet been adopted in the UK. The plan should be produced by the end of 2013.

Rare Disease UK (RDUK) and EURORDIS organised a UK National Conference on Rare Diseases, in the context of the Europlan conference on 16 November 2010[44] in Manchester to examine proposals for a plan which were then launched on Rare Disease Day 2011. The proposals took the form of a report entitled

[41] Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)

[42] Written using information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (p23).

[43] http://www.nice.org.uk/newsroom/news/BetterInformationOnUnlicensedDrugS.jsp

[44] http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_uk_europlan.pdf

'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'[45]**, presented** at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning, patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group.

The Specialised Healthcare Alliance (SHCA) held on 16 November 2010 the SHCA Conference on Delivering Quality in Specialised Care. The conference was opened by the Minister for Quality at the Department of Health. This conference helped inform the 2011 report *"Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions*[46]*"* (see section on "National patient alliances of patient organisations and patient representation": this report was part of the iterative process seeking to inform the UK's response to the EC Council Recommendation on an action in the field of rare diseases, as well as future arrangements for specialised commissioning.

A national plan, aided by the recommendations made by these groups, was developed during 2011. The public consultation was launched on 29 February 2012 to mark Rare Disease Day 2012[47]. The UK-wide consultation will be open until 25 May 2012. Responses to the consultation will inform the final plan, due to be produced by the end of 2013. The proposed plan recommends using specialist centres to make exact diagnosis; acknowledges that all doctors should have the right training to be aware of the possibility of a rare disease; and recommends that the care of patients with rare diseases be better coordinated.

Other related actions

Deciphering Developmental Disorders (DDD)[48] was launched in 2011: this project aims to improve the diagnosis and care of children in the UK who fail to develop normally due to changes in their genetic makeup. The project seeks to capture the genetic make-up of up to 12 000 children with intellectual or physical delays or who have multiple malformations. A collaborative effort between the National Health Service Clinical Genetics Services across the UK and the Wellcome Trust Sanger Institute, the project will provide information for researchers and clinicians into rare chromosomal abnormalities and their possible role in disease. Another interesting facet to be explored by the project are the ethical and social aspects involved in the clinical use of new genomic technologies, including the perceptions and expectations of patients and families. The project is supported by the Health Innovation Challenge Fund, a parallel funding partnership between the Wellcome Trust and the Department of Health.

In 2011, the United Kingdom's first brain tumour tissue bank was created, housed in Southern General Hospital in Glasgow, Scotland. It will provide a large number of samples to researchers, with the goal of accelerating research toward treating this group of rare diseases. The new tissue bank, available to researchers from academia and industry, was made possible by funding from brain cancer charity Brainstrust[49].

Centres of expertise

Health ministers in England have agreed to national commissioning of services, effective 1 April 2011, for patients with the following disorders: Stickler syndrome; Wolfram syndrome; Lymphangioleiomyomatosis; Insulin resistance syndromes (e.g. Donohue and Rabson Mendenhall syndromes); Severe and complex forms of osteogenesis imperfecta; and Pseudo-obstruction of gut in young children. National commissioning establishes national centres of expertise for a specific disease and streamlines funding to one centralised source rather than being scattered amongst different local budgets.

Genetic testing

The Clinical Molecular Genetics Society (CMGS) issued an annual audit[50] of in 2011 genetic testing activity. Such information is valuable to understanding the rare disease demand for testing and pre- and post-natal activity in this area. The UK audit includes number of samples, number and type of disease, number and type of tests sent for analysis and staff/workload across laboratories. The 2009-2010 audit "...shows a continued growth in national activity for each of the postnatal, prenatal and predictive testing categories, an improvement in

[45] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf
[46] http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf
[47] http://www.dh.gov.uk/health/2012/02/consultation-rare-diseases/
[48] http://www.sanger.ac.uk/about/press/2011/110322.html
[49] http://www.gla.ac.uk/news/headline_212335_en.html
[50] http://www.cmgs.org/CMGS%20audit/2010%20audit/secure4Final_Audit09_10.pdf

routine reporting times and encouraging data of the capturing and utility of activity…". Prenatal diagnosis reports were recorded for 120 different disorders, with 86% being for common aneuploidies. There were 12839 prenatal reports, of which 1744 were for disorders excluding aneuploidy. Non-invasive foetal sexing testing accounted for 19% of non-aneuploidy screening. Monogenic disorders include sickle cell anaemia (440), beta-thalassaemia (119), SMA type I (61), Duchenne muscular dystrophy (32), Huntington disease (25), craniosynostosis (9), and others. For postnatal activity, there was a 31% increase in single gene disorders for 2009-2010. This jump reflects the inclusion of data from a new large volume provider. There was a mean number of 789 reports for fragile X testing across 18 providers. There was a mean number of 706 cystic fibrosis reports across 20 providers.

A new report[51] from the Foundation for Genomics and Population Health (commonly known as the PHG Foundation) encourages the mainstream medical specialities to become versed in the field of genetics, incorporating genetic knowledge and technology into their offer. The authors of the report propose "...a shift of the axis of main clinical responsibility for individual patients with inherited disease from clinical genetics to the relevant specialty - cardiology, ophthalmology, renal medicine, neurology or a host of other areas". Evoking a future in which, "…rather than genetics 'moving into mainstream medicine' … clinical areas develop and expand to integrate new clinical expertise relevant to inherited disease and a new set of genomic technologies into clinical pathways as relatively specialised areas within their own service", the report acknowledges that close cooperation with specialist clinical and laboratory genetics service would be necessary in order to promote and sustain such a shift.

Nowgen, a leading UK centre for genetics seeking to inform and improve genetic medicine via training, education, public engagement, research and innovation, issued its Review and Programme for 2011-2012[52] in 2011. Nowgen, working with Orphanet UK, will continue its commitment to facilitating access to high quality information on rare diseases and orphan medicinal products for professionals, patients and the public.

The UKGTN has recommended tests for 536 diseases and 714 genes for NHS commissioning for service from April 2011.

National alliances of patient organisations and patient representation

Rare Disease UK

RDUK launched a new report entitled *'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'*[53] at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning,patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group. Following consultation and production of the strategy, RDUK will then be scrutinising the implementation of a strategy.

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To produce this report, the SHCA organised a series of nine workshops focussing on quality and productivity in services including rare cancers, haemophilia, blood and marrow transplantation which fed into the report *"Leaving No One Behind"*

[51] http://www.phgfoundation.org/file/7962/
[52] http://www.nowgen.org.uk/CubeCore/.uploads/documents/NowgenReviewandWorkProgramme20112012.pdf
[53] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf
[54] http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf

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National rare disease events in 2011

To mark Rare Disease Day 2011, RDUK coordinated a number of events across the UK. RDUK also launched a new report entitled ***'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'***[57] at the House of Commons on 28 February 2011, which was presented to Earl Howe, Minister at the Department of Health. The event brought together patient organisations, patients, carers, healthcare providers, clinicians, researchers, health workers, industry representatives and policy makers. Over one hundred and fifty delegates attended, representing more than one hundred organisations. The report outlines RDUK's recommendations for a strategy for rare diseases and is a product of a year and a half of work in collaboration with members and the broad rare disease community. Receptions were also organised at the Scottish Parliament (22 February 2011) Northern Ireland and Welsh Assemblies (16 March 2011) by RDUK and Genetic Alliance UK. At each of the events, attendees who participated in RDUK's contact campaign took the opportunity to meet with their local politician. Many other patient organisations mark the day with events.

Other events included the Annual Conference of Genetic Alliance UK (24 May 2011), 6th British Society Human Genetic (BSHG) Conference (5-7 September 2011).

Research activities and E-Rare partnership

IRDiRC

The National Institute for Health Research is currently a committed member of the IRDiRC.

Orphan medicinal products

Other initiatives to improve access to orphan medicinal products[58,59]

The National Institute for Health and Clinical Excellence (NICE) will start commissioning expert assessments for off-label medicine use starting spring 2012[60]. These assessments will not constitute formal guidance, but rather will provide "a summary of available evidence on selected unlicenced drugs to inform local decision-making". The National Health Service (NHS) in England receives some 1000 specific requests for off-label use annually. The announcement for the off-label product assessments has been met with approval from the rare disease community.

[55] http://www.shca.info/PDF%20files/Registries%20Guide%20-%20FINAL.pdf
[56] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132446/?tool=pubmed
[57] www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf
[58] Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)
[59] Written using information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (p23).
[60] http://www.nice.org.uk/newsroom/news/BetterInformationOnUnlicensedDrugS.jsp

LIST OF CONTRIBUTIONS[61]

Contributions in 2010
Dian Donnai and Idoia Gomez-Paramio *(Orphanet UK and Ireland, University of Manchester)*
Edmund Jessop *(NHS Specialist Commissioning Group)*
Stephen Nutt *(Rare Disease UK & The Genetic Interest Group)*
Anil Mehta *(University of Aberdeen)*
Christine Lavery *(MPS Society)*

Contributions in 2011
Dian Donnai and Idoia Gomez-Paramio *(Orphanet UK and Ireland, University of Manchester)*
Stephen Nutt *(Rare Disease UK)*
Edmund Jessop *(NHS Specialist Commissioning Group)*
Angela Davis *(Nowgen)*
Kate Dack *(Nowgen)*
Jane Deller and Jacquie Westwood *(UKGTN)*
Andrew Devereau *(NGRL Manchester)*

Contributions in 2012
Edmund Jessop *(NHS Specialist Commissioning Group)*
Jane Deller *(UKGTN)*
John Murray *(Specialised Healthcare Alliance – SHCA)*

Validated by: Edmund Jessop *(EUCERD Representative UK, NHS Specialist Commissioning Group)*

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[61] The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.
[62] All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report: http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf

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  http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf