2013 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE

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

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  
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
GENERAL INTRODUCTION

This document 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 present 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 2012. 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 the European Commission, its Agencies or national health authorities.

The report is split into six parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2012
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
Part VI: Activities at National level in each EU Member State and other European countries in the field of rare diseases

Each part contains the following 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.
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
In the past, the basic concept in the National Health Service is not that of ‘rare diseases’ but rather that of ‘specialised services’. However, this changed as of 1 December 2012, in preparation for the new framework for healthcare delivery in England. Whilst all aspects of specialised service provision remain under the control of the NHS, for the first time, rare diseases policy (including the development of the UK Plan for Rare Diseases) is now the responsibility of the genetics and genomics team in the Health Science and Bioethics Division of the Department of Health England.

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.

Since 2010, the Advisory Group on National Specialised Services (AGNSS) has operated as the advisory body for England covering specialised services and treatments for extremely rare conditions typically affecting fewer than 500 patients.

In 2012, proposals were developed to disband the Advisory Group on National Specialised Services (AGNSS). This will take effect as of April 2013. The services currently commissioned on a national basis will continue to be commissioned by a new NHS Commissioning Board. The Clinical Reference Groups during the transition of specialised services to the new NHS Commissioning Board will continue to be the source of clinical advice as the NHS Commissioning Board moves forward in its direct commissioning role. The Clinical Advisory Group (CAG) for Prescribed Services took evidence from these Clinical Reference Groups and has released a report outlining which services should be directly commissioned by the new NHS Commissioning Board (many of these are services for rare diseases). A public consultation on specialised services to be commissioned nationally by the NHS Commissioning Board was launched in December 2012, with the results to be published in early 2013.

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
The Department of Health launched a consultation on a UK Plan for Rare Diseases on 29 February 2012 (Rare Disease Day). The consultation ran for 12 weeks and showed strong support for a UK Plan for Rare Diseases. Over 350 consultation responses were received from a range of sources including patients, carers, academics, clinicians, researchers and patient support groups. A summary of the consultation responses was published on 16 November 2012.

Throughout 2012, healthcare services in England were making preparations in readiness to transfer to a new delivery and governance system. As part of the changes, patient services for those with rare disease continued to be part of specialised services, led by the NHS Commissioning Board. However, for the first time, there is now a nominated lead for rare diseases policy within the Department of Health (DH). The DH rare diseases policy lead will have responsibility to deliver the UK Plan for Rare Diseases in line with EU recommendations.

A new report entitled Forgotten Conditions: Misdiagnosed and Unsupported, How Patients are Being Let Down, issued from a roundtable of stakeholders from government, academia, and medicine held in June 2012, finds that low prevalence disorders are little understood and frequently misdiagnosed in the United Kingdom. The report also evokes the “postcode lottery” rare disease patients face, in which access to service and treatment depends upon the part of the UK in which one resides, with patients in Wales and Scotland enjoying greater access for certain conditions than those in England. The report offers several recommendations to remedy the current state of affairs, including: developing shared care pathways for best practice clinical guidance and expertise; education for medical students that broadens the scope of rare disease diagnostics; harnessing new technology to improve diagnostics; encouraging and supporting self-diagnosis and self-care for patients; and ensuring that the National Commissioning Board takes rarer conditions into account when developing guidance for Clinical Commissioning Groups.

Other related actions
On 25 January 2012, the Human Genomics Strategy Group, which was set up in 2010 as part of the Government’s response to the House of Lords Science and Technology Select Committee’s report on Genomic Medicine with a remit to develop strategic options for genomics in the NHS and to oversee broader developments in relation to genetics in NHS services, produced its report: Building on our inheritance: genomic technology in healthcare. This presented a vision for the development and adoption of genomic technology in healthcare and made recommendations on its implementation. The report and its recommendations were welcomed by the UK Government.

Following on from the report, on 10 December 2012 the Prime Minister announced that the UK will sequence 100,000 whole genomes of NHS patients at diagnostic quality over the next three to five years, earmarking £100 million:

- to train a new generation of British genetic scientists to lead on the development of new drugs, treatments and cures, building the UK as the world leader in the field.;
- to pump-prime DNA sequencing for cancer and rare inherited diseases; and,
- to build the NHS data infrastructure to ensure that this new technology leads to better care for patients.

The Department of Health has earmarked up to £100 million for the genomics initiative, which will support development of skills and data infrastructure within the NHS and will pump prime the sequencing work. Rare diseases is one of the three priority areas of the initiative, along with cancer and infectious disease.

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

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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.

The Department of Health issued a report in September 2012 specifying which specialised services for
rare diseases should be commissioned at the national level from April 2013. 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.

An article appearing in the Orphanet Journal of Rare Diseases applies the Systematic Component of
Variation (SCV) in order to look at access to nationally commissioned services in England, particularly for highly
specialised healthcare, generally affecting fewer than 500 people in England or involving services where “fewer
than 500 highly specialised procedures are undertaken each year”. Centralising specialised services in a few
centres ensures a volume high enough to maintain excellence, although there is an obligation to ascertain that
patients geographically far from such centres are not disadvantaged. The authors applied the Systematic
Component of Variation, taking “access” (measured as “service use”) in order to study access to services
commissioned by the National Specialised Commissioning Team (NPCT) in England. The results of this study
suggest that “…equity of access can usually be achieved at about five years after establishing a service, and this
is not dependent, within the geography of England, on the number of centres designated”.

The UK Genetic Testing Network (UKGTN – see page 7 under “Genetic Testing”) has been reviewing
genetic testing rates for rare conditions, by geographical regions, based on information from the UKGTN
member laboratories. It finds variation in genetic testing rates over the past four years although it is suggested
that this is likely due to data quality. This is improving and should yield results for 2011/12 that will be
published.

A report of the Joint Committee on Medical Genetics released in 2012 identifies the challenges
inherent in integrating genomic medicine into the wide range of existing clinical areas. Amongst the points
raised in the report, is the need for genetics sub-specialist training in existing clinical areas such as paediatrics
and antenatal care. The report encourages the development of such training to complement and collaborate
with existing genetics infrastructures. To combat inequity in the availability of access to specialist centres for
heritable disorders, the authors recommend “the formal inclusion in the new commissioning structures of
resourced, multidisciplinary expert groups, which may be specialty or disease specific depending on the context,
able to give advice (via Public Health England or otherwise) on specifications for quality assured pathways to
assist commissioners”.

Registries

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

In England, a government-backed initiative will allow researchers unprecedented access to
anonymised patient health records. The Clinical Practice Research Datalink (CPRD) is a new observational data
and interventional research service of the National Health Service (NHS), jointly funded by the NHS National
Institute for Health Research (NIHR) and the Medicines and Healthcare products Regulatory Agency (MHRA).
The CPRD is “… designed to maximise the way anonymised NHS clinical data can be linked to enable many types
of observational research and deliver research outputs that are beneficial to improving and safeguarding public
health”. Data confidentiality is a top priority for the new service and several mechanisms are in place to protect
patient privacy. Access to patient data could help rare disease researchers advance knowledge and understanding of rare conditions.

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2 http://www.ojrd.com/content/7/1/85/abstract
3 http://www.phgfoundation.org/reports/12093/
The United Kingdom contributes to the following European registries: EUROCAT, EIMD, TREAT-NMD, AIR, EUROCare-CF, EURO-WABB, EUHASS, EUROPAC, SCNIR, European Prader-Willi database and EUROWILSON.

Neonatal screening policy

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 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.

The National Health Service revised its screening programme standards in 2011 for sickle cell disease and thalassaemia: the revised screening standards provide new material relating to objectives and performance indicators and will take effect from April 2012.

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 country of the UK. 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.ukgttn.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.

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;
- 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;

http://www.screening.nhs.uk/programmes
- 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 arrangements for the Specialised Commissioning Groups in each region and published a report in March 2011 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 and to establish the Human Genomic Strategy Group. The Board and three working groups met during 2010 and 2011 and a report was published in January 2012. The report referenced UKGTN in supporting commissioning, including ongoing collaboration with NICE, genetic test evaluation, monitoring quality of member laboratories and supporting the medical genetics Clinical Reference Group.

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 were funded by the Department of Health from 2002 to 2012 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\(^2\) 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 Disorders/Genes for Commissioning 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 2012 the UKGTN had evaluated 371 gene dossiers and made recommendation for 293 tests to be available for NHS service. During this time 312 testing criteria were developed. There are more testing criteria than Gene Dossiers approved because some TC have been developed for tests already provided by laboratories prior to the introduction of TC. 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.

All NHS services are required to return data to commissioners on service activity in order to inform contracts and future developments. Historically genetics laboratories used a system of “workload units” with one unit being equivalent to one minute of working time. There was little standardisation and laboratories applied them inconsistently. Consequently the UKGTN, in collaboration with professional organisations, developed a system that would be easy to use and consistently applied. The system is called Genetic Units (GenUs) and can be applied to laboratories that use both molecular and cytogenetic techniques. It is based on a system of 8 weighted bands. The molecular element is based on amplicons and the cytogenetic element is

\(^{2}\text{www.gen2phen.org}\)
based on the cytogenetic methodologies but the system shares weightings. One of the major benefits of this robust system is that it can be expanded and adapted to cover technological developments. Additional bands with new weights can be added or a disorder can be moved from one band to another if technology makes testing more efficient and less labour intensive. It has been agreed through the Medical Genetics Clinical Reference Group that the GenU system is adopted for all activity relating to clinical genetics. It will become the standard measurement for all contracted activity related to all service specifications that include molecular pathology activity.

The CMGS issued an annual audit\(^\text{10}\) in 2013 of genetic testing activity in 2011-12. 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.

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\(^\text{11}\) 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.

Diagnostic tests are registered as available in the UK for 644 genes and an estimated 747 diseases in the Orphanet database\(^\text{12}\). Between 2004 and September 2012 the UKGTN has recommended tests for 604 disorders and 810 genes for NHS commissioning in addition to 11 panel tests using Next Generation Sequencing (with some of these panels testing over 100 conditions).

**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\(^\text{13}\) (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\(^\text{14}\) (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\(^\text{15}\) 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.

**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\(^\text{16}\) and critique of England’s new arrangements for health service

\(^{10}\) [http://www.cmgs.org/CMGS%20audit/2012%20audit/CMGSAudit11_12_FINAL.pdf](http://www.cmgs.org/CMGS%20audit/2012%20audit/CMGSAudit11_12_FINAL.pdf)


\(^{12}\) Information extracted from the Orphanet database (December 2012).

\(^{13}\) [http://www.geneticalliance.org.uk/](http://www.geneticalliance.org.uk/)

\(^{14}\) [http://www.raredisease.org.uk/](http://www.raredisease.org.uk/)

\(^{15}\) [http://www.raredisease.org.uk/raredisease_strategy_consultation.htm](http://www.raredisease.org.uk/raredisease_strategy_consultation.htm)

\(^{16}\) [http://www.shca.info/PDF%20files/The%20challenge%20of%20rarity%20-%20FINAL.pdf](http://www.shca.info/PDF%20files/The%20challenge%20of%20rarity%20-%20FINAL.pdf)
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 has decided to transfer responsibility for the assessment of ultra-orphan technologies to NICE with effect from April 2013. Meanwhile, partly in response to lobbying by the Alliance, a Specialised Services Commissioning Innovation Fund has been announced to help support the evaluation and adoption of new technologies for smaller patient populations.

In 2011 the SHCA published a new report, “Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions” 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 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. 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.

The Alliance arranged further workshops in 2012 looking at some of the key issues raised Leaving no one behind, notably around the role which shared decision-making with patients could play in assisting earlier diagnosis of rare conditions and the integration of specialised services with local aspects of care. For the rest, the Alliance has been largely focused on seeking to ensure that the major changes in specialised commissioning in England are tailored to the best interests of all those needing specialised care.

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 - as well as the updated slogan and logo more accurately reflect the work of the group.

A project supported by Genetic Alliance UK, and facilitated by the Welsh Institute for Health and Social Care, examines the benefit/risk ratio of new medicinal products for rare and serious diseases. The report published in 2012 exposes the findings determined by a Citizen’s Jury composed of twelve rare and/or serious genetic disease patients or family members, who explored certain key questions: How do patients with rare and/or serious conditions perceive the risks and benefits of new medicines? To what extent should regulators be more permissive in their marketing authorisation decisions? How should patients be involved in the assessment of risks and benefits, and regulatory decision making? After exploring hypothetical case studies and hearing from expert and advocate witnesses on the existing regulatory system and its various strengths and weaknesses, followed by a period of reflection and debate, the jury was able to establish four key recommendations: Regulators should include psychosocial factors in their decision making; Regulators should be more permissive for people with rare and/or serious conditions; Patients should be more involved from setting the research agenda, to post-marketing authorisation decisions; and Patients should be supported in their decision making.

The Northern Ireland Rare Disease Partnership (NIRDP) was formally launched on Rare Disease Day 2012 with support from patients, families, health professionals and government representatives. A non-profit organisation, the NIRDP seeks to bring together rare disease patients and organisations with clinicians and other health professionals, researchers and producers of specialist medicines and equipment, health policy...
Report on the State of the Art of the Rare Disease Activities in the United Kingdom

makers and academics to find “...practical ways of improving the quality of life, treatment and care for those with rare diseases in Northern Ireland”. The new association will work closely with the Patient Client Council, with other Health and Social Care Agencies in Northern Ireland, with RDUK, IPOSSI, and GRDO in the Republic of Ireland.

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.

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.

Sources of information on rare diseases and national help lines

*Orphanet activity in the United Kingdom*

Since 2004 there is a dedicated Orphanet team for the United Kingdom (Orphanet UK) hosted at the University of Manchester. This team was officially designated by the Department of Health as the official Orphanet team in the United Kingdom in 2010.

Orphanet UK is in charge of collecting and validating data on rare disease related services (expert centres, medical laboratories, patient organisations, clinical trials, patient registries, mutation databases/biobanks and ongoing research), in the UK and in Ireland for entry into the Orphanet database. The Orphanet UK team maintains the Orphanet UK national website that aims to be an interactive communication tool between the team and the rare disease community. The team represents Orphanet at many major national conferences and events such as workshops on rare diseases and the Rare Disease Day and it also participates regularly at the ESHG (European Society of Human Genetics) conference. 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 Dysmorphism), 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.

*Help line*

There is no official helpline specifically 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](http://www.nhs.uk), [www.nsc.nhs.uk](http://www.nsc.nhs.uk), [www.specialisedservices.nhs.uk](http://www.specialisedservices.nhs.uk), and [http://www.evidence.nhs.uk](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.

[21](http://www.orphanet.co.uk)
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**\(^{22}\) 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**\(^{23}\), 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**\(^{24}\) 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\(^{25}\).

A range of other guidelines for rare and very rare diseases are posted on the NSCT website\(^{26}\) or published in professional journals.

A guidance document\(^{27}\) 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**

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.

**National rare disease events in 2012**

The UK based charity ‘Jeans for Genes’ holds an annual awareness day to raise funds for genetic disorders\(^{28}\). Rare Disease UK and their member organisations planned a number of events to mark Rare Disease Day 2012 across the United Kingdom. This included a contact campaigns aimed at politicians in each of the UK parliaments/assemblies, as well as a specific Rare Disease Day event at Royal Holloway University and a Northern Ireland Rare Disease Partnership event at Stormont Estate where the group launched a report looking into experiences of obtaining a diagnosis of a rare disease in Northern Ireland.

An event entitled, "Rare Diseases in the UK - Vision 2020" was held in Cambridge on 4 July 2012, bringing together to discuss the application of exome sequencing technologies.

**Hosted rare disease events in 2012**

Amongst the rare disease related events hosted by the UK and announced in *OrphaNews Europe* were: 3rd Annual Orphan Drug Summit (London, 25-26 July 2012), 8th International Prader-Willi Syndrome Conference (Cambridge, 17-21 July 2013), 4th International DSD (Disorders of Sex Development) Symposium (Glasgow, 7-9 June 2013), Translating Genomics Conference (Cambridge, 4 December 2012), Genomic Disorders 2012 (Cambridge, 21-24 March 2012), 13th International Conference on Neuronal Ceroid Lipofuscinosis and 1st

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\(^{23}\) [www.nowgen.org.uk](http://www.nowgen.org.uk)

\(^{24}\) [www.dyscerne.org](http://www.dyscerne.org)


\(^{26}\) [www.ncg.nhs.uk](http://www.ncg.nhs.uk)

\(^{27}\) [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132446/?tool=pubmed](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132446/?tool=pubmed)

\(^{28}\) [http://www.jeansforgenes.com/about](http://www.jeansforgenes.com/about)
Research activities and E-Rare partnership

**National research activities**

Rare diseases research has been supported in the UK. Government funding is mostly available through the Research Councils (e.g. the Medical Research Council) and the National Institute for Health Research (NIHR). Many of the NIHR-funded Biomedical Research Centres (BRCs) and Biomedical Research Units (BRUs) undertake translational health research into rare diseases, and in April 2012 a new round of BRCs and BRUs commenced with £800 million investment over 5 years. In addition, as announced in the *Strategy for UK Life Sciences*, the Department of Health is creating a new NIHR BioResource, to provide a national cohort of healthy volunteers, patients and their relatives who wish to participate in experimental medicine research, and are willing to provide clinical information and samples that will enable them to be recalled for specific studies. These studies will have the potential to rapidly advance the understanding of disease mechanisms, identify potential drug targets, and improve insight into the therapeutic potential and limitations of existing and emerging therapies. The BioResource is on track to be launched in early 2014, however it is already supporting translational research into rare diseases, which is one of its 4 themes of focus. On the basis of the research into rare diseases being undertaken in the NIHR, the Department of Health has confirmed NIHR’s membership of the International Rare Disease Research Consortium (IRDiRC) this consortium.

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 British Heart Foundation and the Fight for Life). There are many charities that support research into rare conditions, including the National Organization for Rare Disorders (NORD), which funds and advocates for research into rare diseases. In 2012, a new funding mechanism was created by global charitable foundation the Wellcome Trust. The Pathfinder Awards support academic-industry partnerships dedicated to early-stage applied research in the field of rare and neglected diseases. Open to international participation, the Pathfinder Awards seek to kick-start pilot research initiatives showing potential for developing innovative medicinal products for rare or neglected diseases. The first two awards were granted in 2012, both for rare diseases.

In 2012, the Medical Research Council awarded the University of Edinburgh’s MRC Human Genetics Unit and the MRC Institute of Genetics and Molecular Medicine £60 million (£74.2 million) in funding over a five-year period to study illnesses and inherited disorders, including cystic fibrosis, retinitis pigmentosa, anophthalmia, and other rare conditions.

**Participation in European research projects**

British teams participate or have participated in European rare disease research projects including: AAVEYE, ALPHAMAN, ACADEMIC GMP, ANTEPRION, ANTIMAL, BIG HEART, BIOMALPAR, BNE, BALANCE, CARDIOGENET, CHD PLATFORM, CHEARDED, CRUMBS IN SIGHT, CILMALVAC, CLINI Li, CONTICANET, CELL PID, CSI-LTB, DARTRIX, DSDLIFE, DEMCHILD, EMSA-SG, EUROCRA, EMVDA, EURADRENAL, ENRAH, EPOKS, EUMITOCOMBAT, EURAMY, EUREGENE, EUROBONET, EUROcare CF, EUROGENTEST 1&2, EUROGLYCANET, EURO IRON1, EUROMotor, ENCCA, ENSAT, ESPORI, ERORSAC, EURERONICs, EUROSCA, EUROTRAPS, EUCILIA, EURO-LAMINOPATHIES, EUUNEFRO, EUROPADNET, EUROWILSON, ENCE-PLAN, EVI-GENORET, ESIO, FIGHTHLH, GEN2PHEN, GRIP, GAPVAC, GENEGRF, GENESKiN, INHERITANCE, IMMOMEC, INTREALL, INTERPREGGEn, HUMALMAB, LEISHDNAVAX, PWS, MITOTARGET, MPCM, Malaria AGE EXPOSURE, MABSOT, MITOCIRCLE, MM-TB, MOLDIGA-PACA, MPCM, MYELINET, MYORES, NEUROCNICS, NEOTIM, NEUROPCF, NEUROKQNNPATHIES, NEUROPRION, NEOUSIS, PSYCHCNVS, NEWTDRUGS, OVER-MYR, PADDINGTON, PNSUORCN, PULMOTNESION, PWS, RATSTREAM, STRONG, SPASTICMODELS, RDCONNECT, RAREBESTPRACTICES, RD PLATFORM, STEM-HD, TAMAHUD, TISSUGEN, TIRCON, TAIN, TREAT-NMD, VITAI 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 a committed member of the IRDiRC.

Orphan medicinal products
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) 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. However, Health Ministers in England announced in 2012 that from April 2013 NICE will take on the role of appraising drugs for ultra-rare conditions, defined as those affecting fewer than 500 patients in England (equating to a prevalence of 1 in 100,000 or fewer).

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.

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

Other initiatives to improve access to orphan medicinal products
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

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29 Written using information from KCE reports 112B: Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 62-66)
20 EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines, C. Habl, F. Bachner (2011) p61
32 Written using information from KCE reports 112B: Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 62-66)
33 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).
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) started to commissioning expert assessments for off-label medicine use from spring 2012. These assessments do not constitute formal guidance, but rather 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.

On 18 February 2012 an evidence session was held in the Scottish Parliament a result of the petition sent by Rare Disease UK for the government to address two issues in relation to access to orphan medicinal products in Scotland, namely that the Scottish Medicines Consortium (SMC) appraisal process is not suitable for orphan medicines, and that the Individual Patient Treatment Request (IPTR) process discriminates against patients affected by rare diseases, due to the difficulty in proving exceptionality. Whilst the session was looking at issues of access broadly, access to orphan medicines was also discussed.

Other therapies for rare diseases
No specific information reported.

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 2012 IN THE UNITED KINGDOM

National plan/strategies for rare diseases and related actions
Current organisation of health care for rare diseases in the UK
In the past, the basic concept in the National Health Service is not that of ‘rare diseases’ but rather that of ‘specialised services’. However, this changed as of 1 December 2012, in preparation for the new framework for healthcare delivery in England. Whilst all aspects of specialised service provision remain under the control of the NHS, for the first time, rare diseases policy (including the development of the UK Plan for Rare Diseases) is now the responsibility of the genetics and genomics team in the Health Science and Bioethics Division of the Department of Health England.

In 2012, proposals were developed to disband the Advisory Group on National Specialised Services (AGNSS). This will take effect as of April 2013. The services currently commissioned on a national basis will continue to be commissioned by a new NHS Commissioning Board. The Clinical Reference Groups during the transition of specialised services to the new NHS Commissioning Board will continue to be the source of clinical advice as the NHS Commissioning Board moves forward in its direct commissioning role. The Clinical Advisory

Group (CAG) for Prescribed Services took evidence from these Clinical Reference Groups and has released a report\textsuperscript{35} outlining which services should be directly commissioned by the new NHS Commissioning Board (many of these are services for rare diseases). A public consultation\textsuperscript{36} on specialised services to be commissioned nationally by the NHS Commissioning Board was launched in December 2012, with the results to be published in early 2013.

**Steps towards a national plan/strategy for rare diseases**

The Department of Health launched a consultation on a UK Plan for Rare Diseases on 29 February 2012 (Rare Disease Day). The consultation ran for 12 weeks and showed strong support for a UK Plan for Rare Diseases. Over 350 consultation responses were received from a range of sources including patients, carers, academics, clinicians, researchers and patient support groups. A summary of the consultation responses was published on 16 November 2012\textsuperscript{37}.

Throughout 2012, healthcare services in England were making preparations in readiness to transfer to a new delivery and governance system. As part of the changes, patient services for those with rare disease continued to be part of specialised services, led by the NHS Commissioning Board. However, for the first time, there is now a nominated lead for rare diseases policy within the Department of Health (DH). The DH rare diseases policy lead will have responsibility to deliver the UK Plan for Rare Diseases in line with EU recommendations.

A new report entitled *Forgotten Conditions: Misdiagnosed and Unsupported, How Patients are Being Let Down*\textsuperscript{38} issuing from a roundtable of stakeholders from government, academia, and medicine held in June 2012, finds that low prevalence disorders are little understood and frequently misdiagnosed in the United Kingdom. The report also evokes the “postcode lottery” rare disease patients face, in which access to service and treatment depends upon the part of the UK in which one resides, with patients in Wales and Scotland enjoying greater access for certain conditions than those in England. The report offers several recommendations to remedy the current state of affairs, including: developing shared care pathways for best practice clinical guidance and expertise; education for medical students that broadens the scope of rare disease diagnostics; harnessing new technology to improve diagnostics; encouraging and supporting self-diagnosis and self-care for patients; and ensuring that the National Commissioning Board takes rarer conditions into account when developing guidance for Clinical Commissioning Groups.

**Other related actions**

On 25 January 2012, the Human Genomics Strategy Group, which was set up in 2010 as part of the Government’s response to the House of Lords Science and Technology Select Committee’s report on Genomic Medicine with a remit to develop strategic options for genomics in the NHS and to oversee broader developments in relation to genetics in NHS services, produced its report: *Building on our inheritance: genomic technology in healthcare*. This presented a vision for the development and adoption of genomic technology in healthcare and made recommends on its implementation. The report and its recommendations were welcomed by the UK Government.

Following on from the report, on 10 December 2012 the Prime Minister announced that the UK will sequence 100,000 whole genomes of NHS patients at diagnostic quality over the next three to five years, earmarking £100 million:

- to train a new generation of British genetic scientists to lead on the development of new drugs, treatments and cures, building the UK as the world leader in the field;
- to pump-prime DNA sequencing for cancer and rare inherited diseases; and,
- to build the NHS data infrastructure to ensure that this new technology leads to better care for patients

The Department of Health has earmarked up to £100 million for the genomics initiative, which will support development of skills and data infrastructure within the NHS and will pump prime the sequencing work. Rare diseases is one of the three priority areas of the initiative, along with cancer and infectious disease.

\textsuperscript{35} \url{http://www.dh.gov.uk/health/2012/09/cagreport/}
\textsuperscript{36} \url{http://www.commissioningboard.nhs.uk/ourwork/d-com/spec-serv/consult/}
\textsuperscript{37} \url{http://www.dh.gov.uk/health/2012/11/response-rare-disease/}
\textsuperscript{38} \url{http://www.2020health.org/2020health/Publication/Wellbeing-and-Public-Health/forgotten-conditions.html}
Centres of expertise
The Department of Health issued a report\(^{39}\) in September 2012 specifying which specialised services for rare diseases should be commissioned at the national level from April 2013. 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.

An article\(^{40}\) appearing in the Orphanet Journal of Rare Diseases applies the Systematic Component of Variation (SCV) in order to look at access to nationally commissioned services in England, particularly for highly specialised healthcare, generally affecting fewer than 500 people in England or involving services where “fewer than 500 highly specialised procedures are undertaken each year”. Centralising specialised services in a few centres ensures a volume high enough to maintain excellence, although there is an obligation to ascertain that patients geographically far from such centres are not disadvantaged. The authors applied the Systematic Component of Variation, taking “access” (measured as “service use”) in order to study access to services commissioned by the National Specialised Commissioning Team (NPCT) in England. The results of this study suggest that “…equity of access can usually be achieved at about five years after establishing a service, and this is not dependent, within the geography of England, on the number of centres designated”.

The UK Genetic Testing Network (UKGTN – see page 7 under “Genetic Testing”) has been reviewing genetic testing rates for rare conditions, by geographical regions, based on information from the UKGTN member laboratories. It finds variation in genetic testing rates over the past four years although it is suggested that this is likely due to data quality. This is improving and should yield results for 2011/12 that will be published.

A report\(^{41}\) of the Joint Committee on Medical Genetics released in 2012 identifies the challenges inherent in integrating genomic medicine into the wide range of existing clinical areas. Amongst the points raised in the report, is the need for genetics sub-specialist training in existing clinical areas such as paediatrics and antenatal care. The report encourages the development of such training to complement and collaborate with existing genetics infrastructures. To combat inequity in the availability of access to specialist centres for heritable disorders, the authors recommend “the formal inclusion in the new commissioning structures of resourced, multidisciplinary expert groups, which may be specialty or disease specific depending on the context, able to give advice (via Public Health England or otherwise) on specifications for quality assured pathways to assist commissioners”.

Registries
In England, a government-backed initiative will allow researchers unprecedented access to anonymised patient health records. The Clinical Practice Research Datalink (CPRD) is a new observational data and interventional research service of the National Health Service (NHS), jointly funded by the NHS National Institute for Health Research (NIHR) and the Medicines and Healthcare products Regulatory Agency (MHRA). The CPRD is “…designed to maximise the way anonymised NHS clinical data can be linked to enable many types of observational research and deliver research outputs that are beneficial to improving and safeguarding public health”. Data confidentiality is a top priority for the new service and several mechanisms are in place to protect patient privacy. Access to patient data could help rare disease researchers advance knowledge and understanding of rare conditions.

Neonatal screening policy\(^{42}\)
The National Health Service revised its screening programme standards in 2011 for sickle cell disease and thalassaemia: the revised screening standards provide new material relating to objectives and performance indicators and will take effect from April 2012.

Genetic testing
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 and to establish the Human Genomic Strategy Group. The Board and three working groups met during 2010 and 2011 and a report was published in January 2012. The report referenced UKGTN in supporting commissioning, including ongoing

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40 http://www.ojrd.com/content/7/1/85/abstract
41 http://www.phgfoundation.org/reports/12093/
42 http://www.screening.nhs.uk/programmes
collaboration with NICE, genetic test evaluation, monitoring quality of member laboratories and supporting the medical genetics Clinical Reference Group.

Between 2004 and 2012 the UKGTN had evaluated 371 gene dossiers and made recommendation for 293 tests to be available for NHS service. During this time 312 testing criteria were developed. There are more testing criteria than Gene Dossiers approved because some TC have been developed for tests already provided by laboratories prior to the introduction of TC. 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.

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 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.

National alliances of patient organisations and patient representation

Specialised Healthcare Alliance (SHCA)
The Specialised Healthcare Alliance (SHCA) arranged further workshops in 2012 looking at some of the key issues raised Leaving no one behind, notably around the role which shared decision-making with patients could play in assisting earlier diagnosis of rare conditions and the integration of specialised services with local aspects of care. For the rest, the Alliance has been largely focused on seeking to ensure that the major changes in specialised commissioning in England are tailored to the best interests of all those needing specialised care

Genetic Alliance UK
A project supported by Genetic Alliance UK, and facilitated by the Welsh Institute for Health and Social Care, examines the benefit/risk ratio of new medicinal products for rare and serious diseases. The report published in 2012 exposes the findings determined by a Citizen’s Jury composed of twelve rare and/or serious genetic disease patients or family members, who explored certain key questions: How do patients with rare and/or serious conditions perceive the risks and benefits of new medicines? To what extent should regulators be more permissive in their marketing authorisation decisions? How should patients be involved in the assessment of risks and benefits, and regulatory decision making? After exploring hypothetical case studies and hearing from expert and advocate witnesses on the existing regulatory system and its various strengths and weaknesses, followed by a period of reflection and debate, the jury was able to establish four key recommendations: Regulators should include psychosocial factors in their decision making; Regulators should be more permissive for people with rare and/or serious conditions; Patients should be more involved from setting the research agenda, to post-marketing authorisation decisions; and Patients should be supported in their decision making.

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45 http://www.jeansforgenes.com/about
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**Hosted rare disease events in 2012**


**Research activities and E-Rare partnership**

**National research activities**

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**Orphan medicinal products**

**Orphan medicinal product committee**

The Advisory Group for National Specialised Services (AGNSS) 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. However, Health Ministers in England announced in 2012 that from April 2013 NICE will take on the role of appraising drugs for ultra-rare conditions, defined as those affecting fewer than 500 patients in England (equating to a prevalence of 1 in 100 000 or fewer).

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

EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines, C. Habl, F. Bachner (2011) p61
Orphan medicinal product pricing policy
Value-priced pricing will come into effect from 2014 for newly launched branded medicines.\footnote{Orphan Drugs in Europe: Pricing, Reimbursement, Funding & Market Acces Issues, Donald Macarthur (2011) pp.86-7}

Other initiatives to improve access to orphan medicinal products\footnote{Written using information from KCE reports 112B: Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 62-66)}\footnote{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).}

The National Institute for Health and Clinical Excellence (NICE) started to commissioning expert assessments for off-label medicine use from spring 2012.\footnote{http://www.nice.org.uk/newsroom/news/BetterInformationOnUnlicensedDrugS.jsp} These assessments do not constitute formal guidance, but rather 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.

On 18 February 2012 an evidence session was held in the Scottish Parliament a result of the petition sent by Rare Disease UK for the government to address two issues in relation to access to orphan medicinal products in Scotland, namely that the Scottish Medicines Consortium (SMC) appraisal process is not suitable for orphan medicines, and that the Individual Patient Treatment Request (IPTR) process discriminates against patients affected by rare diseases, due to the difficulty in proving exceptionality. Whilst the session was looking at issues of access broadly, access to orphan medicines was also discussed.
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  www.ncg.nhs.uk
- Advisory Group for National Specialised Services (AGNSS)
  http://www.specialisedservices.nhs.uk/info/agnss
- UK Genetic Testing Network
  http://www.ukgttn.nhs.uk/gtn/Home
- Screening Programmes in the UK
  http://www.screening.nhs.uk/programmes
- Orphanet UK national website
  http://www.orphanet.co.uk
- Genetic Alliance
  http://www.geneticalliance.org.uk/
- Rare Disease UK
  http://www.raredisease.org.uk/
- Contact A Family

52 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.
53 All websites and documents were last accessed in May 2013.
● Consultation – UK Plan for Rare Diseases
  http://www.dh.gov.uk/health/2012/02/consultation-rare-diseases/

● Europlan UK National Conference Final Report

● Rare Disease UK Report: Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy

● Specialised Healthcare Alliance Report: The Challenge of rarity
  http://www.shca.info/PDF%20files/The%20challenge%20of%20rarity%20-%20FINAL.pdf

● Specialised Healthcare Alliance Report: Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions

● Health 2020 Forgotten Conditions: Misdiagnosed and Unsupported, How Patients are Being Let Down