

**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
FRANCE**

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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 Porphyrin 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 France. 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 report¹.

¹ <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArRDActivities.pdf>

RARE DISEASE ACTIVITIES IN FRANCE

Definition of a rare disease

Stakeholders in France accept the European Regulation on Orphan Medicinal Products definition of a prevalence of no more than 5 in 10 000 people.

National plan/strategy for rare diseases and related actions

First French National Plan for Rare Diseases 2004-2008

France was the first EU country to set up a comprehensive rare disease plan in 2004-2008 with allocated funding. This first plan included 10 objectives:

- Increase knowledge of the epidemiology of rare diseases;
- Recognise the specificity of rare diseases;
- Develop information on rare diseases for patients, health professionals and the general public;
- Train health professionals to better identify rare diseases;
- Organise screening and access to diagnostic tests;
- Improve access to treatment and quality of healthcare provision for patients;
- Continue efforts in favour of orphan medicinal products;
- Respond to the specific needs of accompaniment of patients suffering from rare diseases and develop support for patients' organisations;
- Promote research and innovation on rare diseases, in particular on treatments;
- Develop national and European partnerships in the domain of rare diseases.

The first national plan provided for the official recognition, funding and evaluation of 131 centres of expertise (called "*Centre de référence maladies rares*" in France - "Reference Centres"); this national network was completed in 2008 by the recognition of a second level network of 500 centres working in close connection with the Reference Centres (called "*Centre de compétences maladies rares*" which are the equivalent of regional centres of expertise). New rare disease research networks and research projects were supported by a national call for proposals. Information on rare diseases, orphan medicinal products and related fields was developed by Orphanet (established in 1997, but whose budget was increased significantly thanks to the plan). A helpline for patients (called "*Maladies Rares Info Services*" – MRIS², the French rare disease information service helpline) was developed. Several new information products for health professionals were developed such as emergency guidelines and clinical practice guidelines (called "*protocole national de diagnostic et de soins*" – PNDS – "*national diagnosis and treatment protocol for a rare disease*"); all these guidelines are published on the Orphanet website. Emergency cards to be used by the patients in case of need were also produced.

Funding for this plan was provided within the general health system budget with ad hoc funding on the basis of rare disease projects (over €100 million for the five year period).

Evaluation of the First Plan

The first French National Plan for Rare Diseases underwent intense scrutiny when its five-year term ended in 2008. The main goal of the evaluation of the plan was to provide data to serve for the elaboration of a second plan, initially expected in 2010. An Evaluation Committee consisting of health, economic and sociology experts, under the authority of the French Council for Public Health, measured the initial objectives of the plan against the corresponding actions undertaken during the five years of the plan. The official evaluation report was rendered to the French Minister of Health in May 2009. The document provided an analysis of the accomplishments, advances, and shortcomings of each of the ten objectives of the plan. A series of propositions and recommendations for the elaboration of the second plan was also provided.

Throughout the evaluation, the Evaluation Committee underscored the satisfaction of the different stakeholders towards the overall results of the plan. The objectives judged most pertinent – access to information (Orphanet and MRIS), healthcare organisation (Reference Centres), research funding, orphan product accessibility, and partnerships with European institutions – have benefited from corresponding actions that have satisfactorily fulfilled the planned goals. The need to strengthen these successful actions was underlined in the evaluation. However, some objectives – specifically those concerning epidemiology, professional training for rare diseases, and screening and diagnostic programmes – were considered

² <http://www.maladiesraresinfo.org>

insufficiently developed. The strategies to meet these goals need to be reformulated taking stock of the difficulties encountered and defining actions to overcome obstacles.

The tenth objective of the plan, “Develop national and European partnerships in the field of rare diseases” received an overall favourable evaluation with propositions formulated to enhance and encourage European collaboration. Furthermore, the Evaluation Committee proposed the development of measures to bring non-European industrialised and developing countries into the fold. Indeed, throughout the evaluation of the plan, the necessity for European- and international-level coordination and resource-sharing was emphasised.

The Evaluation Committee’s report³ was completed by a self-assessment report⁴ drawn up by the Steering Committee of the plan within the Ministry of Health. These two reports and the testimonies of rare disease health professional, industry and patient organisation stakeholders who contributed to the first plan were presented and discussed at the final meeting of the Follow-up Committee of the plan.

On 30 September 2010, the French Alliance Maladies Rares, in collaboration with EURORDIS, organised a national conference on rare diseases⁵ in the context of the Europlan project. The theme of the conference was “The French plan in the European landscape”. This conference focused on lessons drawn from the first plan for the benefit of other European countries.

Second French National Plan for Rare Diseases 2011-2014

The second French National Plan for Rare Diseases⁶ was elaborated by the Ministry of Health during 2009-2010 from the results of the evaluation of the first plan and from the conclusions of seven working groups, which had gathered during 34 meetings 184 representatives of health professionals, rare disease experts, researchers, patients’ organisations and administration. The second plan was launched on 28 February 2011 on the occasion of Rare Disease Day, with a budget of €180 million. The ten objectives of the first plan have been consolidated into three main objectives:

- Improve the quality of care for rare disease patients;
- Develop research on rare diseases;
- Amplify European and international cooperation in the field of rare diseases.

These three objectives encompass actions such as:

- Quality assessment and networking of the French Reference Centres;
- Improvement of access to biological and genetic diagnosis;
- Development of neonatal screening of rare diseases;
- Proper use and facilitated access to drugs, orphan medicinal products and any other medical product necessary to patients;
- Information and training of health professionals;
- Information for patients;
- Strengthening of research.

The second plan includes 15 measures and 47 specific actions. The key measures of the plan are:

- Creation of a Foundation for Scientific Cooperation on Rare Diseases (called the “*Fondation Maladies Rares*”⁷);
- Creation of a National Rare Disease Database (called “*Banque Nationale de Données Maladies Rares*” or BNDMR) to allow mapping of patients’ needs and healthcare delivered, and facilitate their recruitment for clinical trials;
- Improvement of the monitoring of various activities relating to rare disease patients, which includes the adoption of the Orphanet nomenclature;
- Organisation of access to next-generation sequencing (NGS) technology for genetic diagnosis. Most of the French academic laboratories will be equipped at the end of the second year of the plan with NGS facilities to optimise molecular diagnosis for a large set of rare diseases. Various levels of NGS will be developed during the plan for maximal diagnosis coverage;
- Restructuring of rare disease Reference and Competence Centres into a limited number (around twenty) of coherent “clinical networks” (called “*filières maladies rares*”), gathering all rare disease relevant stakeholders and centered on a homogeneous group of diseases. These networks aim to

³ http://www.hcsp.fr/docspdf/avisrapports/hcspr20090317_maladiesRares.pdf

⁴ http://www.sante.gouv.fr/IMG/pdf/Evaluation_interne_Plan_National_Maladies_Rares_2005-2008.pdf

⁵ http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_france_europlan.pdf

⁶ http://www.sante.gouv.fr/IMG/pdf/Plan_national_maladies_rares.pdf

⁷ The “Fondation Maladies Rares” was created in February 2012: <http://fondation-maladiesrares.org>

allow a better and easier orientation of patients towards appropriate diagnosis, treatment, social care and follow-up. These future French clinical networks should be connected to the future European networks for rare diseases.

The additional actions foreseen in the plan to improve the quality of care are:

- Setting up of a permanent working group for the monitoring of rare disease Reference Centres and future reference networks;
- Measures to ensure access and reimbursement of new drugs or drugs necessary to patients but prescribed out of their marketing authorisation;
- Enhancement of clinical practice guideline development;
- Training of medical doctors and paramedical professionals;
- Coordination of health care and social care.

The implementation of the second plan is the mission of a dedicated Steering Committee (called the “*Comité de suivi et de prospective*”) which held its first meeting on 19 May 2011. Five thematic working groups reporting to the Steering Committee were established to help implementing the plan. These include a permanent group dedicated to the monitoring of Reference Centres and their future networks. The Steering Committee is in charge of the follow up of the plan and making sure that the implementation of the plan is on schedule, of the effective involvement of relevant bodies and institutes in the implementation, and of surveying new methods of diagnosis, prevention, treatment and care for patients with rare diseases.

In addition to this, the evaluation of this second plan will soon be considered, and before the end of 2013 a third plan will be discussed to extend this work.

Second French National Plan for Cancers (including rare cancers) 2009-2013

A second national plan for cancers⁸ was announced on 2 November 2009 for the period 2009-2013. This plan follows a first plan⁹ covering the period 2003-2007, and includes rare cancers. The six main measures of the plan are: research, observation, prevention, screening, care, and living with and after cancer. The plan specifically aims to develop specialised care for patients with rare cancers, including the labelling of “reference centres for rare cancers”.

The National Cancer Institute (*Institut National du Cancer – INCa*) has published a report entitled “The Situation of Cancer in France in 2011”. This report gives an overview of the measures in place for cancers, including rare cancers, and gives key facts and figures concerning the situation of patients in France. The report was published at the same time as a new web portal on cancer data on the INCa site¹⁰. The INCa also released at the end of 2011 its first report on the activity of expertise for rare cancers of adult patients, including updates on their organisation, collaborations, translational research and clinical trials, survey of cases in national databases, and elaboration of recommendations for rare cancers amongst other actions¹¹.

French National Plan for Rare Disabilities 2009-2013

A plan aimed at rare disabilities (of which rare diseases can be a cause) was adopted on 27 October 2009 for the period 2009-2013¹². The National Solidarity Fund for Autonomy (*Caisse Nationale de Solidarité pour l’Autonomie – CNSA*) is in charge of implementing this plan. According to this plan (“National Scheme for Rare Disabilities”), the definition of a “rare disability” is the coexistence of prevalence of no more than 1 in 10 000 people, rare combination of severe deficiencies or diseases (vision or hearing disability, dysphasia, severe epilepsy etc.), complex care and rarity of competent professionals. The main objectives of the plan are:

- The centralisation and dissemination of information on rare disabilities in collaboration with Orphanet;
- The consolidation, development and evolution of specialised expertise at national level;
- The reinforcement and organisation of the identification of rare disabilities and multidisciplinary functional evaluation across France;
- The creation of interregional relays;
- The development of the offer of services at home and in establishments for patients with rare disabilities.

⁸ http://www.plan-cancer.gouv.fr/images/stories/fichiers/plancancer20092013_english.pdf

⁹ <http://www.plan-cancer.gouv.fr/images/stories/fichiers/plancancer20032007.pdf>

¹⁰ <http://lesdonnees.e-cancer.fr/>

¹¹ <http://www.e-cancer.fr/toutes-les-actualites/360/6714-synthese-de-lactivite-2010-des-centres-experts-cliniques-pour-cancers-rares-de-ladulte>

¹² http://www.cnsa.fr/IMG/pdf/CNSA_Schema-national-Handicap-rare-2.pdf; http://www.cnsa.fr/article.php3?id_article=726

Measures of the plan include the creation of 300 additional places in care centres, regional relays, and national “resource centres”. Three national “resource centres” were created for patients with a visual or hearing deficiency associated with other deficiencies or diseases. A national “resource centre” for patients with rare disabilities and severe epilepsy will be created soon in 2012. A national “resource centre” for patients with rare disabilities and behaviour disorders is in project. Cooperation between national “resource centres” for rare disabilities and “reference centres” for rare diseases is planned.

Other French national initiatives related to rare diseases

On 16 May 2008, the French Ministry of Health announced the second National Plan for Autism for the period 2008-2010. This plan aimed at improving the diagnosis and the treatment of patients with autism, children and adults, their access to social and educational services, and the information of health professionals about this rare disease. In 2011, the evaluation of this plan began in the perspective of a next third plan.

In June 2008, a national plan concerning visual handicap (of which rare diseases can be a cause) for the period 2008-2011 was published. This plan aimed at improving treatment, social care, mobility and social integration of people with visual handicap¹³.

In February 2010, a national plan concerning deafness and hearing-impairment (of which rare diseases can be a cause) for the period 2010-2012 was published¹⁴, with 52 measures including: improvement of the prevention and screening of hearing disorders; better support of deaf and hearing-impaired people through their life; and to make social life more accessible to them.

A system of digital, personal medical record (called the “Dossier Médical Personnel” – DMP) was relaunched in 2009 in France and began to be operational in 2010¹⁵ with further deployment in 2011. This initiative will hopefully ensure a more efficient medical follow-up for patients, among them rare disease patients. The DMP will facilitate communication of information between the different specialists, GPs and centres of expertise involved in the follow-up of rare disease patients.

The French National Authority for Health (*Haute Autorité de Santé* – HAS) and the French Biomedicine Agency (*Agence de la Biomédecine*) signed a collaboration on 14 December 2010¹⁶ to work together during 3 years on project to improve healthcare in four fields in which the *Agence* is principally involved: organ donation, transplants, medically assisted reproduction and human genetics.

On 25 January 2011 the Minister of Research funded the RADICO (“Rare Diseases Cohorts”) project for a duration of 10 years and for a total of €10 million. The RADICO project finality is to create and follow selected cohorts of rare disease patients in the perspective for instance of therapeutic research or better understanding of the condition.

In 2011, the web portal “Epidemiology – France”¹⁷ was launched, aiming to provide a directory of databases to advance research and expertise in the field of health in France. The initiative is supported by the INSERM (French National Institute for Healthcare and Medical Research), the National Competitiveness, Industry and Services Directorate of the French Ministry of the Economy and the LEEM (French Pharmaceutical Companies Union). It brings together information on around 300 databases and includes a search by the theme “Rare Diseases”, which includes mostly nationally designated registries.

Centres of expertise

The first National Plan for Rare Diseases (2004-2008) introduced a structured organisation of healthcare for rare disease patients. A designation process was created to name centres of scientific and clinical excellence in the field of rare diseases. By the end of the plan, 131 “Reference Centres” were named by the French Minister of Health and received a specific financial support for their missions. These centres have 6 main missions:

- To facilitate diagnosis and define the course of treatment;
- To define and publish national clinical practice guidelines for rare diseases (pnds) in collaboration with the *haute autorité de santé* (has);
- To coordinate research and participate in epidemiological surveillance in collaboration with the french institute for public health surveillance (*institut de veille sanitaire* – invs);

¹³ http://www.solidarite.gouv.fr/IMG/pdf/Dossier_de_presse_2JUN08.pdf; www.cnsa.fr/IMG/doc/Plan_handicap_visuel_1_-2.doc

¹⁴ http://www.travail-emploi-sante.gouv.fr/IMG/pdf/Plan_en_faveur_des_personnes_sourdes_ou_malentendantes_-_10_02_2010.pdf

¹⁵ http://esante.gouv.fr/sites/default/files/CP_OuvertureServiceDMP_141210.pdf. In March, 2012, 100 000 DMP were created.

¹⁶ http://www.has-sante.fr/portail/jcms/c_1007980/la-haute-autorite-de-sante-et-lagence-de-la-biomedecine-sengagent-pour-ameliorer-la-qualite-des-soins

¹⁷ <http://epidemiologie-france.fr/>

- To participate in training and information programmes for health professionals, patients and their families, in collaboration with the french national institute of prevention and health education (*institut national de prévention et d'éducation pour la santé – inpes*);
- To coordinate networks of health visitors and social workers;
- To be the contact point for patient organisations and social workers. Each centre has a double role: it is an expert centre for 1 or more diseases for which it is labelled, and it is a resource centre for patients referred to it.

The reference centres are evaluated over time, first through self-evaluation after 3 years as a designated centre, then with an external evaluation at 5 years. The external evaluation is organised by the HAS published its 2010 activity report in 2011, with one section dedicated to its activity in the evaluation of reference centres¹⁸. During the first plan, a National Consultative Designation Committee (*Comité National Consultatif de Labellisation*) analysed the results of the external evaluation and gave advice to the Ministry of Health. This Committee has not been continued. The new designation process is still in progress. It will probably be based on the permanent working group set up during the second plan to monitor Reference Centres and their future clinical networks.

A second type of centres was designated in 2008: named “*Centres de compétences*” (Regional Centres), these qualified centres were identified by each Reference Centre and designated by Regional Hospital Agencies (*Agences Régionales d'Hospitalisation – ARH*). The aim of these regional centres is to assume responsibility for diagnosis, treatment and follow-up of the patient close to their home, and to participate in the activities of the reference centres. The regional centres have not received specific financial support for their activities, and they are not included in the evaluation process of the reference centers. These qualified regional centres take in charge patients from their region: 500 of these centres have been named corresponding to 1 centre per region in each of the large categories of reference centres.

Rare cancers had been excluded from the first national plan for rare diseases (2004-2008) as a national plan for cancer including measures for rare cancers was already in place. The National Cancer Institute (*Institut National du Cancer - INCA*¹⁹) published a report²⁰ on the advances made in the structuring of the health care offer for rare cancers, which was one of the key measures of the Second National Cancer Plan (2009 -2013): this includes the creation of a system of national “reference centres” and regional “competence centres” for rare cancers. As of 2009, 15 “rare cancer centres” have been designated and four reference networks have been set up. These designated centres receive financial support.

Three resource centres for rare disabilities have been designated in 2011.

In 2011 the Hospitals of Angers and Nantes in association with the French Alliance for Rare Diseases created a platform to support patients with rare disease in the Pays de la Loire region. This unique platform composed of a team including neurologists, a dermatologist, a psychologist, an occupational therapist, a social worker and a coordination assistant, will help patients to find their way in the health and social care system.

An experimental programme is underway in Montpellier to provide support to patients with rare disease and training sessions to professionals of health and social sector. This action is set up with the partnership of the French Alliance for Rare Diseases and centres of expertise settled in the area.

Pilot European Reference Networks

France participates, or has participated, in the following European Reference Networks for rare diseases: Dyscerne, EPNET/EPI (main partner), EUROHISTIONET (main partner), NEUROPED, Paediatric Hodgkin Lymphoma Network, EN-RBD, and TAG (main partner).

Registries

The National Rare Disease Registry Committee was created in October 2006 as part of objective 1 “Improve Knowledge of Epidemiology of Rare Diseases” of the first National Plan for Rare Diseases. The Committee is aimed at:

- proposing a policy for registries based on healthcare and epidemiological research needs;
- giving an opinion on whether to create new registries or maintain existing registries, and on the suitability of the envisaged means for managing registries;
- helping to diffuse and valorise information produced by qualified registries.

¹⁸ http://www.has-sante.fr/portail/jcms/c_1070314/rapport-annuel-d-activite-2010

¹⁹ <http://www.e-cancer.fr/soins/prises-en-charge-specifiques/cancers-rares>

²⁰ <http://www.e-cancer.fr/toutes-les-actualites/360/6714-synthese-de-lactivite-2010-des-centres-experts-cliniques-pour-cancers-rares-de-ladulte>

Members of the Committee include official members (French Institute For Public Health Surveillance, French National Institute of Health and Medical Research, Ministry of Health etc.) and professionals with expertise in the field of rare diseases or public health, and representatives of patient organisations. They are nominated for a 3- year term. In December 2008, 6 registries were qualified by the National Rare Disease Registry Committee for the period 2009-2011. Three new national registries were qualified in 2010 for the period 2011-2013 for the following rare diseases: esophageal atresia, arterial pulmonary hypertension and hereditary immune system disorders. In December 2010 a new representatives of professionals were nominated to the National Rare Disease Registry Committee. A new call for proposals was launched in 2011 as each year. A new set of seven national registries were qualified for the period 2012-2015 for the following rare diseases: thalassemia, Gaucher disease, congenital neutropenia, Pompe disease, cystic fibrosis, histiocytosis, and biliary atresia.

The Second National Plan for Rare Diseases foresees the creation of a National Rare Disease Database (BNDMR) containing a minimal data set to be filled in concerning rare disease patients in order to collect a minimum amount of common information.

The French Institute for Public Health Surveillance (*Institut de Veille Sanitaire*) has already analysed some data collected via a range of available sources (The National Database of Medical Mortalities - CépiDC, The National Database of Inpatient Registrations – PMSI etc.) in order to build epidemiological indicators for a few rare diseases. This work has been cited in the Second National Plan for Rare Diseases and the first results are available online²².

France contributes to European registries including EUROCAT, EUROHISTIONET, EPI-EPNET, EURECHINOREG, the European central hypoventilation syndrome registry, EIMD, EUROWABB, EUROTRAPS, CHS, EURO CARE CF, ECFS, INFEVERS and TREAT-NMD.

Neonatal screening policy

A neonatal screening programme exists in France for all newborns for the following four diseases: cystic fibrosis, phenylketonuria, congenital adrenal hyperplasia, congenital hypothyroidism, and for sickle cell anaemia only for newborns at risk of developing the disease.

In 2010, an assessment of the opportunity to extend neonatal screening to one or more inborn metabolic errors of metabolism by tandem mass spectrometry in the general French population began. The first results were published in 2011 by the HAS. The HAS recommends the extension of the screening programme to medium chain acyl-CoA dehydrogenase deficiency. The decision to put this recommendation into practice has not yet been taken. That requires reorganising first the whole neonatal screening programme because tandem mass spectrometry cannot replace all the existing screening techniques, and cannot be used in all the laboratories which currently participate in the programme. Furthermore the HAS is still working on the possibility of extending the programme to other inborn metabolic errors and on the generalisation of sickle cell anaemia screening to all newborns in France.

Neonatal screening for deafness (of which rare diseases can be a cause), on which the HAS had given recommendations in 2007, will be launched in a near future.

Genetic testing

The French Biomedicine Agency (*Agence de la Biomédecine*), a public organisation operating under the supervision of the Minister of Health, was created under the Bioethics Law of August 2004. Its overriding function is to “*guarantee equity, ethics, and transparency for the activities under its responsibility and for anticipated developments*”. The Biomedicine Agency published its 2010 annual report²³ in 2011. For the second consecutive year, the Agency includes data on postnatal genetic testing carried out in France culled via a partnership with Orphanet. The annual report reveals that 361 169 tests were performed in France in 2010, including 11 564 pharmacogenetic tests (3.2%) – an area of increasing activity. The data come from 236 laboratories, representing 98% of the total laboratories included in the survey. Of these, 75 have at least one cytogenetic activity (including molecular testing) and 188 have at least one molecular genetic activity. In the domain of molecular genetics (including pharmacogenomics), diagnostic tests were undertaken for 950 diseases (of a total offer of 1 084 diseases for which testing is possible in France). Of the 950 diseases tested, 665 tests are available in only one laboratory in the country. The tests involved nearly 1 100 different genes.

²¹ <http://www.legifrance.gouv.fr/affichTexte.do?dateTexte=&categorieLien=id&cidTexte=JORFTEXT000023386975&fastPos=1&fastReqId=1558215089&oldAction=rechExpMesuresNominatives>

²² <http://www.invs.sante.fr/surveillance/index.htm> (Section “Maladies Rares”)

²³ http://www.agence-biomedecine.fr/uploads/document/RA_BIOMED_2010_Internet.pdf

Two indications (hemochromatosis and non rare thrombophilia) represented over 40% of the total analyses conducted in 2010.

There were also 70 997 karyotype analyses performed in 2010 and 13 928 in situ hybridisation (FISH). The percentage of abnormalities (balanced and unbalanced) diagnosed by postnatal cytogenetic karyotype in 2010 was 8.4% for intellectual deficit and malformation syndromes, 3% for reproductive disorders, 13% for chromosome breakage syndromes, and 13.9% for family studies.

In the arena of prenatal diagnosis (PND), of the 35 783 cases examined in 2009, 6 993 certificates were issued for a medical termination of pregnancy (MTP). Of these, 578 pregnancies were pursued although a MTP had been issued. Among MTP cases, 43.1% were for malformations or malformation syndromes, 39.2% for chromosomal abnormalities, 5.4% for genetic abnormalities, 3.2% for maternal conditions, and 1.4% involved infections.

Ultrasound is the most practiced prenatal examination tool in France. Unregulated by law, its practice does not fall within the competence of the Biomedicine Agency. Biologically, PND involves sampling either the foetus and/or its annexes (amniotic fluid, chorionic villi, foetal blood), or the mother's blood. Among the 74 629 foetuses studied by cytogenetic analysis, 3 849 were affected. Among 2 728 foetuses studied by molecular genetics, 534 anomalies were detected. Biochemistry and foetal serum markers resulted in 27 diagnoses of hereditary diseases: 50 in endocrinology (abnormal genital or genotype-phenotype discordance, abnormal thyroid or 21-hydroxylase deficiency); 251 involved neural tube defects and 550 detected trisomy 21 (determined by serum markers on 660 629 women tested). The only non-invasive prenatal genetic diagnosis involves the analysis of foetal DNA circulating in the maternal blood, which yielded 5 921 diagnoses in 2009. The number of foetal Rh determination using this technique is increasing: from 384 cases in 2005 to 5 359 in 2009. Finally, the number of medically assisted procreation procedures employing pre-implantation genetic diagnosis in 2009 led to the birth of 59 children in France (versus 71 in 2008).

The French Bioethics Law of August 2004 stipulated the prohibition of embryonic research, but allowed the possibility of research under certain conditions for a maximum of five years following the publication of the decree. The moratorium period expired in February 2011. Between September 2004 and February 2011, 173 permits to conduct such research were issued, of which 71 were for research protocols, 24 involved the conservation of embryonic stem cells and 46 the importation of embryonic stem cell lines. The revised Bioethics Law of July 2011 maintains the possibility of French scientists to conduct research under certain conditions.

The 2010 report of the Biomedicine Agency demonstrates that France continues to be a model for other countries in terms of the range of its genetic test offered, its healthcare coverage in this area, and its remarkable transparency of data.

Diagnostic tests are registered as available in France for 1 129 genes and an estimated 1 092 diseases in the Orphanet database²⁴.

The final text of the Bioethics Law²⁵ was adopted on 23 June 2011 and published in July 2011. The text includes indications on how to inform family members in the case of genetic disease, as well as the delivery of tests proposed to pregnant women. The legislation on research using embryos will remain unchanged.

National alliances of patient organisations and patient representation

The *Alliance Maladies Rares* (French Alliance for Rare Diseases) is the national umbrella organisation dealing with rare diseases. It plays a major role in organising working groups, communicating on rare diseases, offering support to organisations of patients and families, and contributing to the development of the French National Plans for Rare Diseases and their evaluation. This alliance played a major role in the elaboration of the first and second National Plan and in the evaluation of the reference centres. The French Rare Disease Alliance celebrated its 10 anniversary in 2010 and marked the occasion with a reunion of its members on 15 February 2010 in Paris: the Alliance's new website was launched as were the forthcoming information documents created by the Alliance. In 2011 the Alliance launched a practical guide to rare diseases to make it available in centres of expertise for rare diseases and for members of the Alliance. The guide is destined to patients and their families, and provides information on the organisation of expert care and the services in place for patients and their families. The guide also gives information on the organisations of patients with rare diseases in France. The Alliance also launched an awareness raising campaign aimed at children via the newspaper for

²⁴ Information extracted from the Orphanet database (September 2011).

²⁵ <http://www.service-public.fr/actualites/001820.html>;

<http://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000024323102&dateTexte=&oldAction=rechJO&categorieLien=id>

children called *Le Petit Quotidien*; information packs for teachers were also made available to help classes understand what is a rare disease and life for children with such a condition.

The *Alliance Maladies Rares* and other patient organisations have received some public funding during the first and second plans for various support activities and awareness campaigns.

Sources of information on rare diseases and national help lines

Orphanet activities in France

In terms of public information measures, support for the French Rare Disease Platform (*Plateforme Maladies Rares*, established in 2001 in Paris), and more particularly for the Orphanet web portal on rare diseases, has been reinforced under the two National Plans, and has been designated by the Ministry of Health in the upcoming Orphanet Joint Action financed by the European Commission.

Orphanet was established in 1997 and is the reference for all rare disease information in France. The team, hosted by the INSERM in Paris, is in charge of collecting data on services for rare diseases (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) for France, and of coordinating the activity of Orphanet's external teams across Europe as well as maintaining the encyclopaedia and inventory of rare diseases. The team also maintains the Orphanet France²⁶ national website. A new more user-friendly version of Orphanet portal was launched in 2008 with additional features. Recent new Orphanet features include the encyclopaedia for patients in French, emergency guidelines, a search by sign facility and a national entry point for France in French. Since 2003, Orphanet also edits a twice-monthly newsletter concerning political and scientific news in the field of rare diseases and orphan medicinal products entitled *OrphaNews France*.

In December 2009, Orphanet signed a partnership with the CNSA (French Agency in charge of the autonomy of the elderly and disabled people '*Caisse Nationale de Solidarité pour l'Autonomie*') and is in charge of leading a project in the framework of the National Scheme for Rare Disabilities to develop the information available concerning such situations, and to make rare diseases and rare disabilities visible in the disability coding systems. Orphanet will introduce specific chapters on disability in the General Public encyclopedia concerning rare diseases leading to disability, whether this disability is 'rare' or not. Orphanet will also provide methodological support to resource centres for rare disabilities (three such centres exist today in France) in order to help them produce good practice guidelines for paramedical and social care of patients with rare disabilities. In addition to this, the disabilities associated with rare diseases will be indexed with the WHO's ICF (International Classification of Functioning, Disability and Health), in order to allow rare diseases to be found when searched by any kind of disability. This 3-year cooperation is an opportunity to develop information on some crucial aspects of rare diseases that have not been addressed specifically before in Orphanet. This information will be useful to patients, families and professionals dealing with disabilities.

Official information centre for rare diseases

Orphanet is the official source of information on rare diseases in France.

Help line

The help line *Maladies Rares Info Services* provides support and information on rare diseases. It is the first health information service in France to have a quality certification (ISO 9001). This service launched in 2011 a series of internet chat sessions on the first Monday of each month: each session has a theme and internet users can ask the team questions the hour-long sessions. *Maladies Rares Info Services* also implemented a "rare diseases barometer". The purpose of this barometer is to collect objective data on the issues to which patients are confronted. Data are collected by means of qualitative and quantitative surveys targeting users of the information and support service.

The AFM (*Association française contre les myopathies*) provides a help line for information on neuromuscular diseases.

Other sources of information on rare diseases

The French Agency for the Sanitary Security of Health Products (*Agence Française de Sécurité Sanitaire des Produits de Santé – AFSSAPS*²⁷) has published on its website since 2009 a registry of clinical trials on medicinal

²⁶ <http://www.orphanet-france.fr/national/FR-FR/index/page-d-accueil/?lng=FR>

²⁷ The AFSSAPS was given a new name and new missions on 1st May 2012, following the law reinforcing the monitoring of safety of drugs and other healthcare products, published in December 2011. : *Agence Nationale de Sécurité des*

products conducted in France including those on rare diseases, an updated list of compassionate use authorisations (cohorts) with respective summary of product characteristics and leaflet, updated list of medicinal products available within nominative temporary use authorisations (ATU) with specific information if applicable and other general information on hospital preparations.

Since June 2006, the French General Directorate for Health (*Direction Générale de la Santé* - DGS) in the French Ministry of Health has produced health care and information cards for the rare disease patients, in close collaboration with health professionals and patient organisations, within the scope of the first French National Plan for Rare Diseases. These cards are distributed by health professionals treating the patients concerned. They provide information for health professionals about the patient and gives the patient brief information on his/her disease. Within the second plan, a new model of card for patients will be produced.

In 2009, the French Minister for Health relaunched the Personal Medical Record (DMP) project. The actual deployment will start in 2012, after building of infrastructures and services in 2010-2011. This facultative digital record, which will concern rare disease patients (as it is primarily aimed at patients with a chronic illness), should improve the quality of coordination of treatment for both patients and health professionals, and help information exchange.

In 2010, the site www.droitsdesmalades.fr, which informs all citizens about their healthcare rights, was launched. In addition, the patient organisation Sparadrap²⁸ has published an informative guide concerning children's rights when they are admitted into healthcare facilities, including issues such as consent to participate in research and financial aid.

Good practice guidelines

Since the beginning of the first national plan, the Reference Centres produced 45 national good practice guidelines (PNDS) for diagnosis, treatment and follow-up of patients with rare disease. These guidelines are published on Orphanet, HAS²⁹ and Reference Centre websites.

The HAS published clinical practice guidelines³⁰ for the follow-up of children with deafness under the age of six and their family.

Concerning rare tumours, two national good practice clinical guidelines were published respectively in 2009 and 2010 concerning surgical practices in digestive neoplasia, including peritoneal pseudomyxoma, and gestational trophoblastic disease.

Training and education initiatives

All health professionals, medical doctors, midwives, nurses and paramedics follow two hours of training during their undergraduate medical studies on the topic of rare diseases. Every year, 3rd year medical students at the Necker-Cochin faculty of medicine in Paris are offered an optional 30 hour training course on rare diseases during which experts in the field and representatives of rare disease patient organisations are present.

The Paris-based Institute of Myology organises an annual a Summer School in Paris: this offers the possibility to train in myology via a condensed 10-day course.

National rare disease events 2011

Each year in December, an annual *Téléthon* is organised by the AFM (*Association française contre les myopathies*) over 30 hours: around €100 million are raised annually during this campaign. The funds raised go towards rare disease research, information services (including the French Rare Disease Platform), awareness campaigns, patient care and patient organisations. Each year, to coincide with the *Téléthon* organised by the AFM, the *Alliance Maladies Rares*, in association with the *Groupama Fondation pour la santé* and the AFM, organises a Rare Disease March (*Marches des Maladies Rares*) involving patients and patient organisations. The *Téléthon*³¹ and Rare Disease March³² aim to raise awareness about rare diseases in addition to the Rare Disease Day which is celebrated each February.

A number of events were organised to mark 2011's Rare Disease Day. Firstly, the 28 February 2011 marked the official publication of the second French National Plan for Rare Diseases which will cover the period

Médicaments et des Produits de Santé (French National for Medicine and Medical Product Safety Agency)

<http://www.ansm.sante.fr/>.

²⁸ <http://www.sparadrap.org/SPARADRAP>

²⁹ http://www.has-sante.fr/portail/jcms/c_5237/affections-de-longue-duree?cid=c_5237

³⁰ [http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-03/surdite de lenfant - 0 a 6 ans - recommandations.pdf](http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-03/surdite_de_lenfant_-_0_a_6_ans_-_recommandations.pdf)

³¹ <http://www.afm-telethon.fr/le-telethon/le-telethon-2011>

³² <http://www.alliance-maladies-rares.org/article/marche-des-maladies-rares-2011-98>

2011-2014. The plan was launched by the Secretary of State for Health, Nora Berra, and the Minister of Higher Education and Research, Valérie Pécresse.

The French Alliance for Rare Diseases and Orphanet joined forces with the high speed train (TGV) network from 26-27 February 2011 to raise awareness of rare diseases: TGV passengers were encouraged to participate in a quiz about rare diseases and to learn more of the issues surrounding these conditions in the buffet coaches of trains between Paris and six major French towns.

On 28 April 2011, *France Television* confirmed their support of the *Téléthon* for another 3 years. The 2011 edition, the 25th anniversary, was aired, for the first time, on all five national channels of the French network to assure 30 uninterrupted hours of coverage.

Every year in June, Orphanet and the *Alliance Maladies Rares* organise jointly a one day meeting for all patient organisations to discuss themes of interest in the field of information and dissemination of good practices. On 30 June 2011 the 12th Forum³³ was held at the *Groupama Foundation* around the theme "Sharing of health data for better healthcare". Topics discussed include the personal medical record (DMP), and the centralisation of data collected by reference centres.

Eurobiomed organised the conference Rare2011 on 2-4 November 2011 in Montpellier in collaboration with local and national partners both from the public and the private sector. This second conference (the first one was organised in 2009) started with two days dedicated to rare diseases at national level, and finished with one day focused on the European context, organised by the EUCERD. Over 300 participants were present from 19 countries. In particular the measures foreseen by the second French National Plan for Rare Diseases were presented in addition to a number of topics concerning research and development, and access to orphan medicinal products, as well as a discussion on how stakeholders should best work together in the field of rare diseases.

Hosted rare disease events in 2011

Amongst the events in the field of rare diseases hosted in France in 2011 and announced in *OrphaNews Europe* were: CliniGene Network of Excellence: Gene Transfer and Therapy: State of the Art and eCHIPS - European Conference on Human iPS (7-9 April 2011, Paris), 4th International Friedreich's Ataxia Scientific Conference (5-7 May 2011, Strasbourg), 4th International Congress of Myology (9-13 May 2011, Lille), 3rd International Symposium on Pheochromocytoma and Paraganglioma (14-17 September 2011, Paris), EurokeratoConus II: 2nd European Congress on Keratoconus (23-24 September 2011, Bordeaux), Tuberosus Sclerosis Complex Scientific Day (14 October 2011, Paris), Rare 2011: The Eurobiomed Meetings on Rare Diseases (2-4 November 2011, Montpellier), Genodermatoses in the Mediterranean - Together Against Genodermatoses (13- 15 October 2011, Paris), European Wilson Disease Congress (14-15 November 2011, Paris), Sixth European Workshop on Immune-Mediated Inflammatory Diseases (23-25 November 2011, Nice).

France also hosted the European Advanced Postgraduate Course in Classical and Molecular Cytogenetics, co-organised by the European Cytogeneticists Association and two French Universities, as well as the 32nd Annual Course of Pediatric Dermatology on 26-29 April in Arcachon.

Research activities and E-Rare partnership

National research activities

Public funding is available for rare disease research projects from:

- the National Agency for Research (*Agence Nationale de la Recherche – ANR*) for basic research;
- the General Directorate for Provision of Healthcare (*Direction Générale de l'Offre de Soins – DGOS*) in the French Ministry of Health for clinical research via funding of the PHRC Programme (*Programme Hospitalier de Recherche Clinique – Hospital Clinical Research Programme*) sponsored by National Health Insurance of the French Social Security System;
- the INSERM for translational clinical research.

In addition, some charities and private foundations provide funding for research, such as the AFM. The AFM launched only one out of the two usual annual calls for proposals in 2011.

The articulation between these funding sources should be improved under the second plan to make it easier to apply for funding for rare diseases. The future *Fondation Maladies Rares*, foreseen in the second plan, will participate to research activities for rare diseases.

The *GIS Maladies Rares* (Institute for Rare Diseases) was created in 2002 to coordinate and support research into rare diseases and to initiate and implement research on rare diseases at national and European levels. At national level, the *GIS Maladies Rares* has been instrumental in implementing in the early 2000

³³ <http://www.orpha.net/orphacom/cahiers/docs/FR/XIIforum.pdf>

research programmes (through yearly calls for research projects) on rare diseases (in particular networks), which have been later on entrusted to the French National Agency for Research (ANR) in the context of the first French National Plan for Rare Diseases (2004-2008). Several targeted strategic actions are carried out by the *GIS Maladies Rares*³⁴ to facilitate (and fund) access to technology platforms (i.e. genetically modified animal models, high throughput sequencing, drug-screening etc.) for the French community of researchers on rare diseases.

In 2009, different public bodies joined together to create the “*Plateforme Mutation*” that aims to identify unknown mutations in rare diseases by means of high throughput sequencing technology.

In 2010, the Ministry for Higher Education and Research gave the outlines of the Health and Biotechnology programme of the national “grand emprunt” (loan): this scheme aims to invest €8 billion into research, including national and European technological platforms, genotyping, screening and production of stem cells, industrial production of cellular therapies, creation of laboratories for the production of biomedicines, running of clinical trials, acquisition of phenotyping material etc. All of these areas would be beneficial to the field of rare diseases.

In 2010, the AFM allocated a budget of €73 million to research the field of neuromuscular diseases and rare diseases.

In June 2010, Généthon announced³⁵ the opening of a production unit for vectors for genetic therapies (Généthon Bioprod) in 2011. The production of industrial-sized batches is a step towards clinical trials of genetic therapies for rare diseases.

OrphanDev launched its first newsletter in October 2010: the aim of this network is to increase the number of clinical trials for rare diseases in France and to improve their quality. The network has been formed within the *Centre de Gestion des Essais des Produits de Santé* – CeGEPS (Centre for the Management of Health Product Trials).

According to a report published every two years by the LEEM (French Pharmaceutical Companies Union) on international clinical research, the number of clinical trials carried out in France is diminishing in comparison to other countries. This trend could be explained by factors such as cost, quality and speed, but also factors linked to patients such as the ability to find patients who have never been treated for a certain disease. However, the report notes that a large proportion of trials in phase 1 and 2 are carried out in France, and that France is the best performing country in a number of fields including rare diseases³⁶.

Other funding opportunities for rare disease research in 2011 included grants and calls launched by the following organisations/institutes: Fédération Nationale d’Aide aux Insuffisants Rénaux, Fondation Groupama, la Fondation de France, Association pour la Recherche sur la Sclérose latérale, Fondation de recherche ELA, National Niemann-Pick Disease Foundation (NNPDF), Universal Biotech, ARTHRITIS Fondation Courtin, Connaître les Syndromes Cérébelleux (CSC), Association Strümpell-Lorrain (ASL-HSP) et Association Française Ataxie de Friedreich (AFAF), Institut de Recherche en Santé Publique (IReSP), Fondation Line Pomaret Delalande, Association Neurofibromatoses et Recklinghausen, Fondation Jérôme Lejeune, ECD Global Alliance, Vaincre la Mucoviscidose, Agence de la biomédecine, NA Advocacy, Genespoir, Association pour l’étude de la pathologie pédiatrique, Retina France etc.

Participation in European projects

France participates, or has participated, in European rare disease research projects including: ARISE, ANTEPRION, ANTIMAL, AUTOROME, BIOMALPAR, BIO-NMD, BRAINCAV, BNE, CARDIOGENET, CAV-4-MPS, CUREFXS, CLINIGENE, CONTICANET, CONTICABASE, CHEARTED, CRUMBS IN SIGHT, CUREHLH, CRANIRARE, ELAST-AGE, EDEN, EPOKS, EMINA, ERMION, EVI-GENORET, EPINOSTICS, EUROBFNS, EuroGeBeta, ENRAH, ENS@T-ACC EUNEFRON, EMSA-SG, EUMITOCOMBAT, EURAMY, EUREGENE, EURO CARE-CF, EURO GENTEST, EURO GLYCANET, EUROPEAN LEUKEMIA NET, EUROWILSON, EUROAS, EURO IRON1, EURO-LAMINOPATHIES, EURORETT, EURO-CDG, EURO-SCAR, EUROSCA, EURSPA, EUROTRAPS, ENCE-PLAN, EUSTAR, EPOKS, EURO-PADNET, EURIOFNET, FAD, GETHERTHAL, GENESKIN, GENOMIT, GENOSTEM, HMA-IRON, HSCR, HEMO-IPS, HAEIII, HUE-MAN, IPF-AE, INHERITANCE, IMMUNOPRION, KINDLERNET, LEISHMED, LYMPHANGIOGENOMICS, MANASP, MILD-TB, MITOCIRCLE, MM-TB, MTMPATHIES, MTMPATHIES2, MPCM, MITOTARGET, MYASTAID, MYORES, MYELINET, NEUROBID, NEOTIM, NEUPROCF, NMD-CHIP, NOVSEC-TB, NM4TB, NEUROSIS, NEUROPRION, NOVELPID, NEMMYOP, NEUTRONET, NSEuroNet, OSTEOPETR, PODONET, PEMPHIGUS, RARE-G, RATSTREAM, RAPOSDI, RISCA, SKIN-DEV, SKINTHERAPY, STEM-HD, SIOPEN-R-NET, RHORCOD, RDPLATFORM, TB

³⁴ The *GIS Maladies Rares* will join the *Fondation Maladies Rares (FMR)* when the FMR will be set up.

³⁵ <http://www.genethon.fr/index.php?id=368>

³⁶ <http://www.leem-media.com/leem/content/download/6775/43352/file/13-01-2011-leem-enquete-attractivite-2010-rapport.pdf>

CHINA, TRANSPOSMART, THERAPEUSKIN, TUB-GENCODEV, WHIPPLE'S DISEASE, WHIM-Thernet and WHIMPath.

E-Rare

The *GIS Maladies Rares* is the coordinating partner of the E-Rare for Research Programmes on Rare Diseases, and organised the first joint transnational call in 2007³⁷ for research on rare diseases, with the participation of 6 countries and a total of 13 funded consortia (French research teams participated in each of these funded projects/consortia). France took part in the 2nd E-Rare Joint Transnational Call in 2009 and France is represented in 11 of the 16 consortia selected for funding, with funding totalling around €2 million. France also took part in the 3rd transnational call launched at the start of 2011 in the context of E-Rare2: French research teams have been funded to participate in 13 of the projects selected for funding.

IRDIRC

The AFM (*Association Française contre les myopathies*) and French National Agency for Research (*Agence Nationale de la Recherche*), are committed members of the IRDiRC.

Orphan medicinal products^{38,39}

Four institutions are involved in the field of orphan medicinal products on the French market: the French Agency for the Sanitary Security of Health Products (AFSSAPS, which will become the ANSM⁴⁰ in 2012), the French National Authority for Health (HAS), the French Economic Committee for Health Products (*Comité Economique des Produits de Santé – CEPS*), and the Ministry of Health.

The LEEM (French Pharmaceutical Companies Union) is a constituted professional organisation that represents the pharmaceutical industry in France, i.e. the companies whose missions are research, development, manufacturing and marketing of medicinal products. Rare diseases became priority action in the LEEM's strategy in 2002: a rare disease working group made up of key stakeholders in the public and private sectors meets regularly to discuss: innovative therapies for rare diseases (and how to bring these therapies to patients), the provision of health care for rare disease patients, the communication of information on rare diseases and treatment, ways to create the correct conditions for optimal and innovative clinical treatment and ways to support the national plan for rare diseases. The LEEM organises a workshop dedicated to orphan medicinal products every year. Since 2001 the LEEM evaluates the advances made in clinical research in France, including clinical research in the field of rare diseases.

The LEEM presented their 10th annual overview of therapeutic advances with an edition covering 2010⁴¹. Thirty-five contributions to the improvement of medical services were noted, especially in the fields of cancer, infection and rare diseases. Five new products were presented in the field of rare diseases: Ilaris, Fibrogammin, Eirfapse, Revolade and Myozyme. Torisel, Gliolan and Afinitor were also cited.

Orphan medicinal product committee

There is no orphan medicinal product committee currently in France, apart from the multistakeholder group at the LEEM (see above).

Orphan medicinal product incentives

Initiatives are in place to stimulate orphan medicinal product development: research support is provided through national funding programmes: *GIS Maladies Rares*, the Hospital Clinical Research Programme (*Programme Hospitalier de Recherche Clinique - PHRC*). During orphan medicinal product development, free scientific advice is available from the AFSSAPS; and budgetary incentives (from 2001) are available in the form of a tax exemption from the National Health Insurance and the AFSSAPS. Other incentives measures, such as free early advice and fast track process of the assessment for reimbursement by the Transparency Committee are being performed by the HAS.

Free scientific advice is available for medicines from the AFSSAPS as well as CT authorisation and compassionate use authorisation (cohort ATU) from the AFSSAPS. The HAS is performing early meetings at the

³⁷ http://www.e-rare.eu/images/stories/e-rare_final_list_of_funded_projects.pdf

³⁸ This section has been written using the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp45-49)*

³⁹ This section has been written using the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. 2005 Revision (pp12-14)*

⁴⁰ www.ansm.sante.fr

⁴¹ <http://www.leem.org/sites/default/files/Bilan%20des%20avanc%C3%A9es%20th%C3%A9rapeutique%202010.pdf>

national level, the European level (within the EUNETHTA network of Health technology agencies) on request of pharmaceutical industry or on its own request. These scientific meetings aim to let the marketing authorisation (MA) owner know the expectations of the HTA bodies on the data expected concerning especially the relative effectiveness assessment in usual care.

Sponsors of orphan medicinal products are exempted from taxes to be paid by enterprises promoting pharmaceutical specialities or wholesale distributors under health and social legislation. These taxes are: the tax on the promotion of pharmaceuticals, based on the promotion costs of laboratories; the tax paid by the laboratories for the AFSSAPS; the safeguard clause for medicinal products; the tax on direct sales; the tax on the distribution of medicines. These are some of the initiatives aimed at stimulating research by the pharmaceutical industry into rare diseases in addition to the provisions of the European Regulation on Orphan Medicinal Products.

A report published by the French Economic Committee for Health Products (*Comité Economique des Produits de Santé – CEPS*) on 31 July 2010, cited a study of the evolution of sales of orphan medicinal products and called for a revision of the subventions and benefits accorded to orphan medicinal products which made a turnover equal to, or above, €20 million.

In October 2010, a proposed law to finance the French Social Security system included specific provisions for tax exemptions for orphan medicinal products: the Minister for Health accepted to raise the threshold for tax exonerations to orphan medicinal products, which was initially foreseen to be fixed at €20 million of sales. This threshold will now be raised to orphan medicinal products making a turnover equal to, or above, €30-40 million.

The public authorities have also evoked in 2010 abrogating the framework agreements which exempt orphan medicinal products from certain regulations, and for orphan medicinal products costing more than €50 000 per year and per patient that the revenue and international pricing be capped. An obligation to treat all patients concerned was also proposed.

A law adopted by Parliament on 22 March 2011 will allow non-profit organisations to become pharmaceutical establishments and will give the status of medicine to gene-therapy products. As a direct result, the Généthon Bioprod non-profit laboratory, inaugurated in November 2010, will be able to produce products for gene-therapy for clinical trials.

Orphan medicinal product pricing policy

Before any pricing, all drugs including orphan medicinal products are assessed by the Transparency Committee of the HAS for reimbursement purpose. This committee provides the Ministry of Health and National Health Insurance an opinion about the actual benefit that defines the pertinence of reimbursement and the level of copayment, and specifies the clinical added value of the drug that assesses the relative effectiveness and is the basis for price definition. For innovative drugs (new therapeutic modality, efficacy and tolerance presumably good, and covering an unmet medical need), often including orphan medicinal products, the Transparency Committee performs a fast track assessment before MA and delivers its opinion rapidly after MA is granted. This fast track reduces the usual timelines, which is of 90 days after MA, to 15 days.

After that step, an Industry-government agreement via the French Economic Committee for Health Products (*CEPS*) is defined, which sets the rules for the pricing of reimbursed medicines in France.

Orphan medicinal product market availability situation

According to the registry of the French Agency for the Sanitary Security of Health Products (AFSSAPS) website, the availability of orphan medicinal products in France can be represented as follows:

- Orphan medicinal products with valid market authorisation and with mention of commercialisation: Aldurazyme, Arzerra, Atriance, Busilvex, Carbaglu, Cayston, Cystadane, Diacomit, Elaprased, Evoltra, Exjade, Fabrazyme, Firazyf, Firdapse, Flinsit, Gliolan, Glivec, Increlex, Inovelon, Kuvan, Litak, Lysodren, Mozobil, Myozyme, Naglazyme, Nexavar, Nplate, Orfadin, Pedeia, Photobarr, Prialt, Replagal, Revatio, Revlimid, Revolade, Rilonacept, Regeneron, Savene, Siklos, Soliris, Somavert, Sprycel, Tassigna, Thalidomide Celgene, Torisel, Tracleer, Trisenox, Ventavis, Vidaza, Volibris, Vpriv, Wilzin, Xagrid, Yondelis, Zavesca.
- Orphan medicinal products with valid market authorisation without mention of commercialisation: Ceplene, Esbriet, Mepact, Peyona, Plenadren, Tobi Podhaler, Votubia, Vyndaqel.

Orphan medicinal product reimbursement policy

Orphan medicines can be dispensed in out-patient or in-patient settings through one of the two corresponding lists: list for medicines reimbursed by National Health Insurance and available in community pharmacies, and

list for hospital pharmacies. Within the hospital list, the drugs are generally funded through *GHS* (*Groupes H*, a diagnostic-related group system established by the *T2A* (*tarification à l'activité*) policy. However, some expensive drugs used in hospitals are fully reimbursed to the hospitals by the National Health Insurance. These drugs are listed in a specific list (called "*liste hors GHS*") established by the French Ministry of Health. Some of the drugs available in hospital pharmacies can be made available to outpatients (retrocession list) and paid for by the National Health Insurance. Orphan medicinal products intended for ambulatory use and that have a very low target populations are generally made available through this retrocession process⁴².

Within the 62 orphan medicinal products that have been granted MA in Europe, all but one have been granted a positive advice for reimbursement in France.

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*⁴³, "*particular prescribing conditions are in place for: drugs for hospital use, drugs with hospital prescription, drugs with initial hospital prescription, drugs with prescription only by specialists, drugs with a particular follow up during the treatment.*" From 1 January 2010, the Ministry of Health and the French National Health Insurance made it obligatory for the first prescription for an orphan medicinal product to be validated by a Reference Centre designated for the patient's rare disease when available, or by the Competence Centre directly linked to the Reference Centre.

In 2006, the law for the financing in 2007 of French Social Security system planned a derogative pathway for exceptional coverage of off-label use of pharmaceutical products and of non-covered medical devices or services by the National Health Insurance⁴⁴. Pharmaceutical products (orphan or non-orphan medicinal products) used off-label, medical devices or services intended for rare diseases are in particular concerned. The coverage is allowed for a limited renewable period by the French Ministry of Health after the HAS has given a positive advice or a recommendation; concerning drugs, the HAS has to ask for the advice of the AFSSAPS before giving its own recommendation. This process will be modified in 2012 further the law reinforcing the monitoring of safety of drugs and other healthcare products, published in December 2011.

Other initiatives to improve access to orphan medicinal products

Compassionate use for individual patients takes the form of either cohort use (cohort Temporary Authorisation for Use) or named patient supply (nominative Temporary Authorisation for Use) prior MA granted both by the AFSSAPS. Patients can also be treated with drugs before these drugs have received MA through clinical trials or hospital preparations. Reimbursement measures are in place for compassionate use.

Innovative drugs are eligible for an *ATU* (Temporary Authorisation for Use) from the AFSSAPS if there is a public health need. The drug must fulfil the following criteria: the drug must treat a serious or rare disease; no therapeutic alternative to the drug should be available; the drug must have a positive risk/benefit and the patient cannot be treated within a clinical trial. The aspect of the drug (quality, security and efficacy) and the medical environment (disease and alternatives) are evaluated before receiving the *ATU*. Protocols for therapeutic use and information collecting are mandatory for cohort *ATU* and optional for nominative *ATU*.

The AFSSAPS gave in its 2009 activity report⁴⁵, published in 2010, an overview of the *ATU* and of the *Plans d'Investigations Pédiatriques* (Paediatric Investigation Plans - PIP): these two areas concern the field of rare diseases and orphan medicinal products. In 2009, for the 9 orphan medicinal products with a new European MA, 6 were already available within the *ATU* system.

Temporary Treatment Protocols (*Protocoles temporaires de traitement*) can also be used to extend the indication for a drug or device with reimbursement permitted. Temporary Treatment Protocols are limited to expensive drugs used only in hospitals and registered on a special list.

The new law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011, maintains the possibility of an *ATU*, in particular in the case of rare diseases. The drug must fulfil the following criteria: the treatment cannot be postponed; there is no alternative therapeutic to the drug; the efficacy and security of the drug are strongly presumed from the results of clinical trials (cohort *ATU*) or from scientific published data and knowledge (nominative *ATU*); the patient cannot be treated within a clinical trial. The *ATU* is given for a limited period, but renewable. A therapeutic protocol and data collection concerning safety and efficacy are mandatory for both cohort and nominative *ATU*.

⁴² *EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines*, C. Hahl, F. Bachner (2011) pp. 49-50.

⁴³ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*. 2005 Revision (p14)

⁴⁴ Article L162-17-2-1 of the Social Security Legal Code.

⁴⁵ http://www.afssaps.fr/var/afssaps_site/storage/original/application/a40deaca3add3f9e767493ab831897e0.pdf

The AFSSAPS also established a national public register of clinical trials on medicines conducted in France, which is regularly updated.

Orphan devices

No specific information reported.

Specialised social services

Respite care services are available for patients whose care is demanding on behalf of their relatives: this is only partially reimbursed for some rare diseases. Therapeutic recreational programmes are available mostly within hospital organisations and patient organisations or local institutions, and are mostly fully reimbursed. Social assistance centres (*Centres communaux d'action social - CCAS*), social assistants within hospital structures and services provided by patient organisations all aim to assist the integration of patients with rare disease into daily life. These services are financed either by government budgets or patient organisations. The AFM has a number of administrative, medical and social coordinators who assist families with their specialised needs.

On 9 February 2010 an interministerial observatory was created to evaluate the accessibility of public buildings, housing, work places, transport and footpaths/roads to all persons.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN FRANCE

National plan/strategy for rare diseases and related actions

The second French National Plan for Rare Diseases⁴⁶ was elaborated by the Ministry of Health during 2009-2010 from the results of the evaluation of the first plan and from the conclusions of seven working groups, which had gathered during 34 meetings 184 representatives of health professionals, rare disease experts, researchers, patient organisations and administration. The second plan was launched on 28 February 2011 on the occasion of Rare Disease Day with a budget of €180 million. The ten objectives of the first plan have been consolidated into three main objectives:

- Improve the quality of care for rare disease patients;
- Develop research on rare diseases;
- Amplify European and international cooperation in the field of rare diseases.

These three objectives encompass actions such as:

- Quality assessment and networking of the French Reference Centres;
- Improvement of access to biological and genetic diagnosis;
- Development of neonatal screening of rare diseases;
- Proper use and facilitated access to drugs, orphan medicinal products and any other medical product necessary to patients;
- Information and training of health professionals;
- Information of patients;
- Strengthening of research.

The second plan includes 15 measures and 47 specific actions. The key measures of the plan are:

- Creation of a Foundation for Scientific Cooperation on Rare Diseases (called the "*Fondation Maladies Rares*"⁴⁷);
- Creation of a National Rare Disease Database (called the "*Banque Nationale de Données Maladies Rares*" or BNDMR) to allow mapping of patients' needs and healthcare delivered, and facilitate their recruitment for clinical trials;

⁴⁶ http://www.sante.gouv.fr/IMG/pdf/Plan_national_maladies_rares.pdf

⁴⁷ The "Fondation Maladies Rares" was created in February 2012: <http://fondation-maladiesrares.org>

- Improvement of the monitoring of various activities relating to rare disease patients, which includes the adoption of the Orphanet nomenclature;
- Organisation of access to next-generation sequencing (NGS) technology for genetic diagnosis. Most of the French academic laboratories will be equipped at the end of the second year of the plan with NGS facilities to optimize molecular diagnosis for a large set of rare diseases. Various levels of NGS will be developed during the plan for maximal diagnosis coverage;
- Restructuring of rare disease Reference and Competence Centres into a limited number (around twenty) of coherent “clinical networks” (called “*filières maladies rares*”), gathering all rare disease relevant stakeholders and centered on a homogeneous group of diseases. These networks aim to allow a better and easier orientation of patients towards appropriate diagnosis, treatment, social care and follow-up. These future French networks should be connected to the future European networks for rare diseases.

The additional actions foreseen in the plan to improve the quality of care are:

- Setting up of a permanent working group for the monitoring of rare disease Reference Centres and future reference networks;
- Measures to ensure access and reimbursement of new drugs or drugs necessary to patients but prescribed out of their marketing authorization;
- Enhancement of clinical practice guideline development;
- Training of medical doctors and paramedical professionals;
- Coordination of health care and social care.

The implementation of the second plan is the mission of a dedicated Steering Committee (called the “*Comité de suivi et de prospective*”) which held its first meeting on 19 May 2011. Five thematic working groups reporting to the Steering Committee were established to help implementing the plan. These include a permanent group dedicated to the monitoring of Reference Centres and their future networks. The Steering Committee is in charge of the follow up of the plan and making sure that the implementation of the plan is on schedule, of the effective involvement of relevant bodies and institutes in the implementation, and of surveying new methods of diagnosis, prevention, treatment and care for patients with rare diseases.

In addition to this, the evaluation of this second plan will soon be considered, and before the end of 2013 a third plan will be discussed to extend this work.

Second French National Plan for Cancers (including rare cancers) 2009-2013

A second national plan for cancers⁴⁸ was announced on 2 November 2009 for the period 2009-2013. The National Cancer Institute (*Institut National du Cancer – INCa*) has published a report entitled “The Situation of Cancer in France in 2011”. This report gives an overview of the measures in place for cancers, including rare cancers, and gives key facts and figures concerning the situation of patients in France. The report was published at the same time as a new web portal on cancer data on the INCa site⁴⁹. The INCa also released at the end of 2011 its first report on the activity of expertise for rare cancers of adult patients, including updates on their organisation, collaborations, translational research and clinical trials, survey of cases in national databases, and elaboration of recommendations for rare cancers amongst other actions⁵⁰.

Other French national initiatives related to rare diseases

A plan aimed at rare disabilities (of which rare diseases can be a cause) was adopted on 27 October 2009 for the period 2009-2013⁵¹. The National Solidarity Fund for Autonomy (*Caisse Nationale de Solidarité pour l’Autonomie – CNSA*) is in charge of implementing this plan. Measures of the plan include the creation of 300 additional places in care centres, regional relays, and national “resource centres”. Three national “resource centres” were created in 2011 for patients with a visual or hearing deficiency associated with other deficiencies or diseases. Cooperation between “resource centres” for rare disabilities and “reference centres” for rare diseases is planned.

On 16 May 2008, the French Ministry of Health announced the second national plan for autism for the period 2008-2010. In 2011, the evaluation of this plan began in the perspective of a next third plan.

On 25 January 2011 the Minister of Research funded the RADICO (“Rare Diseases Cohorts”) project for a duration of 10 years and a total of €10 million. The RADICO project finality is to create and follow selected

⁴⁸ http://www.plan-cancer.gouv.fr/images/stories/fichiers/plancancer20092013_english.pdf

⁴⁹ <http://lesdonnees.e-cancer.fr/>

⁵⁰ <http://www.e-cancer.fr/toutes-les-actualites/360/6714-synthese-de-lactivite-2010-des-centres-experts-cliniques-pour-cancers-rares-de-ladulte>

⁵¹ http://www.cnsa.fr/IMG/pdf/CNSA_Schema-national-Handicap-rare-2.pdf; http://www.cnsa.fr/article.php3?id_article=726

cohorts of rare disease patients in the perspective for instance of therapeutic research or better understanding of the condition.

In 2011, the web portal "Epidemiology – France"⁵² was launched, aiming to provide a directory of databases to advance research and expertise in the field of health in France. The initiative is supported by the INSERM (French National Institute for Healthcare and Medical Research), the National Competitiveness, Industry and Services Directorate of the French Ministry of the Economy and the LEEM (French Pharmaceutical Companies Union). It brings together information on around 300 databases and includes a search by the theme "Rare Diseases" which includes mostly nationally designated registries.

Centres of expertise

The reflection on restructuring of the existing rare disease Reference Centres into a limited number of "clinical networks" began in 2011 within the framework of the second National Plan. It will continue in 2012.

In 2011 the Hospitals of Angers and Nantes in association with the French Alliance for Rare Diseases created a platform to support patients with rare disease in the *Pays de la Loire* region. This unique platform will help patients to find their way in the health and social care system.

An experimental programme is underway in Montpellier to provide support to patients with rare disease and training sessions to professionals of health and social sector. This action is set up with the partnership of the French Alliance for Rare Diseases and centres of expertise settled in the area.

Registries

The second National Plan foresees the creation of a National Rare Disease Database (BNDMR) containing a minimal data set to be filled in concerning rare disease patients in order to collect a minimum amount of common information. The reflection on the minimum data set began in 2011.

A new call for proposals for national rare diseases registries was launched in 2011 as each year. A new set of seven national registries were qualified for the period 2012-2015 for the following rare diseases: thalassemia, Gaucher disease, congenital neutropenia, Pompe disease, cystic fibrosis, histiocytosis, and biliary atresia.

Neonatal screening policy

In 2010, an assessment of the opportunity to extend neonatal screening to one or more inborn metabolic errors of metabolism by tandem mass spectrometry in the general French population began. The first results were published in 2011 by the HAS. The HAS recommends the extension of the screening programme to medium chain acyl-CoA dehydrogenase deficiency. The decision to put this recommendation into practice has not yet been taken. That requires reorganising first the whole neonatal screening programme because tandem mass spectrometry cannot replace all the existing screening techniques and cannot be used in all the laboratories which currently participate in the programme. Furthermore the HAS is still working on the possibility of extending the programme to other inborn metabolic errors and on the generalisation of sickle cell anaemia screening to all newborns in France.

Neonatal screening for deafness (of which rare diseases can be a cause), on which the HAS had given recommendations in 2007, will be launched in a near future.

Genetic testing

The French Biomedicine Agency published its 2010 annual report⁵³ in 2011. For the second consecutive year, the Agency includes data on postnatal genetic testing carried out in France culled via a partnership with Orphanet. The 2010 report of the Biomedicine Agency demonstrates that France continues to be a model for other countries in terms of the range of its genetic test offered, its healthcare coverage in this area, and its remarkable transparency of data.

The final text of the Bioethics Law⁵⁴ was adopted on 23 June 2011 and published in July 2011. The text includes indications on how to inform family members in the case of genetic disease, as well as the delivery of tests proposed to pregnant women. The legislation on research using embryos will remain unchanged.

⁵² <http://epidemiologie-france.fr/>

⁵³ http://www.agence-biomedecine.fr/uploads/document/RA_BIOMED_2010_Internet.pdf

⁵⁴ <http://www.service-public.fr/actualites/001820.html>;

<http://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000024323102&dateTexte=&oldAction=rechJO&categorieLien=id>

National alliances of patient organisations and patient representation

In 2011 the *Alliance Maladies Rares* (French Alliance for Rare Diseases) launched a practical guide to rare diseases to make it available in centres of expertise for rare diseases and for members of the Alliance. The guide is destined to patients and their families, and provides information on the organisation of expert care and the services in place for patients and their families. The guide also gives information on the organisations of patients with rare diseases in France. The Alliance also launched an awareness raising campaign aimed at children via the newspaper for children called *Le Petit Quotidien*. Information packs for teachers were also made available to help classes understand what is a rare disease and life for children with such a condition.

Sources of information on rare diseases and national help lines

Help line

The help line *Maladies Rares Info Services* launched in 2011 a series of internet chat sessions on the first Monday of each month: each session has a theme and internet users can ask the team questions the hour-long sessions. *Maladies Rares Info Services* also implemented a “rare diseases barometer”. The purpose of this barometer is to collect objective data on the issues to which patients are confronted. Data are collected by means of qualitative and quantitative surveys targeting users of the information and support service.

National rare disease events 2011

Each year in December, an annual *Téléthon* is organised by the AFM (*Association française contre les myopathies*) over 30 hours: around €100 million are raised annually during this campaign. The funds raised go towards rare disease research, information services (including the French Rare Disease Platform), awareness campaigns, patient care and patient organisations. Each year, to coincide with the *Téléthon* organised by the AFM, the *Alliance Maladies Rares*, in association with the *Groupama Fondation pour la santé* and the AFM, organises a Rare Disease March (*Marches des Maladies Rares*) involving patients and patient organisations. The *Téléthon*⁵⁵ and Rare Disease March⁵⁶ aim to raise awareness about rare diseases in addition to the Rare Disease Day which is celebrated each February.

A number of events were organised to mark 2011's Rare Disease Day. Firstly, the 28 February 2011 marked the official publication of the second French National Plan for Rare Diseases which will cover the period 2011-2014. The plan was launched by the Secretary of State for Health, Nora Berra, and the Minister of Higher Education and Research, Valérie Pécresse.

The French Alliance for Rare Diseases and Orphanet joined forces with the high speed train (TGV) network from 26-27 February 2011 to raise awareness of rare diseases: TGV passengers were encouraged to participate in a quiz about rare diseases and to learn more of the issues surrounding these conditions in the buffet coaches of trains between Paris and six major French towns.

On 28 April 2011, *France Television* confirmed their support of the *Téléthon* for another 3 years. The 2011 edition, the 25th anniversary, was aired, for the first time, on all five national channels of the French network to assure 30 uninterrupted hours of coverage.

Every year in June, Orphanet and the *Alliance Maladies Rares* organise jointly a one day meeting for all patient organisations to discuss themes of interest in the field of information and dissemination of good practices. On 30 June 2011 the 12th Forum⁵⁷ was held at the *Groupama Fondation* around the theme “Sharing of health data for better healthcare”. Topics discussed include the personal medical record (DMP), and the centralisation of data collected by reference centres.

Eurobiomed organised the conference Rare2011 on 2-4 November 2011 in Montpellier in collaboration with local and national partners both from the public and the private sector. This second conference (the first one was organised in 2009) started with two days dedicated to rare diseases at national level, and finished with one day focused on the European context, organised by the EUCERD. Over 300 participants were present from 19 countries. In particular the measures foreseen by the Second National Plan for Rare Diseases were presented in addition to a number of topics concerning research and development, and access to orphan medicinal products, as well as a discussion on how stakeholders should best work together in the field of rare diseases.

⁵⁵ <http://www.afm-telethon.fr/le-telethon/le-telethon-2011>

⁵⁶ <http://www.alliance-maladies-raises.org/article/marche-des-maladies-raises-2011-98>

⁵⁷ <http://www.orpha.net/orphacom/cahiers/docs/FR/XIIforum.pdf>

Research activities and E-Rare partnership

National research activities

Apart from national funding programmes covering rare diseases, funding opportunities for rare disease research in 2011 included grants and calls launched by the following organisations/institutes: Fédération Nationale d'Aide aux Insuffisants Rénaux, Fondation Groupama, la Fondation de France, Association pour la Recherche sur la Sclérose latérale, Fondation de recherche ELA, National Niemann-Pick Disease Foundation (NNPDF), Universal Biotech, ARTHRITIS Fondation Courtin, Connaître les Syndromes Cérébelleux (CSC), Association Strümpell-Lorrain (ASL-HSP) et Association Française Ataxie de Friedreich (AFAF), Institut de Recherche en Santé Publique (IReSP), Fondation Line Pomaret Delalande, Association Neurofibromatoses et Recklinghausen, Fondation Jérôme Lejeune, ECD Global Alliance, Vaincre la Mucoviscidose, Agence de la biomédecine, NA Advocacy, Genespoir, Association pour l'étude de la pathologie pédiatrique, Retina France etc.

E-Rare

France took part in the 3rd transnational call launched at the start of 2011 in the context of E-Rare2: French teams have been funded to participate in 13 of the selected projects.

IRDiRC

The AFM (*Association Française contre les myopathies*) and French National Research Agency (*Agence Nationale de Recherche*), are committed members of the IRDiRC.

Orphan medicinal products

Orphan medicinal product incentives

A law adopted by Parliament on 22 March 2011 will allow non-profit organisations to become pharmaceutical establishments and will give the status of medicine to gene-therapy products. As a direct result, the Généthon Bioprod non-profit laboratory, inaugurated in November 2010, will be able to produce products for gene-therapy for clinical trials.

Orphan medicinal product reimbursement policy

This process for off-label use and reimbursement of medicinal products will be modified in 2012 further the law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011.

Other initiatives to improve access to orphan medicinal products

The new law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011, maintains the possibility of an ATU (temporary use authorisation), in particular in the case of rare diseases. The drug must fulfill the following criteria: the treatment cannot be postponed; there is no alternative therapeutic to the drug; the efficacy and security of the treatment are strongly presumed by the results of clinical trials (cohort ATU) or from scientific published data and knowledge (nominative ATU); the patient cannot be treated within a clinical trial. The ATU is given for a limited period, but renewable. A therapeutic protocol and data collection concerning safety and efficacy are mandatory for both cohort and nominative ATU.

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⁵⁸ 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.

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⁵⁹ 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>