



Bundesministerium  
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# European Conference on Rare Diseases ECRD

Overview of  
national research policies and  
collaboration between member states

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# contents of the presentation

## rationalis

## national activities

Countries participating in the ERA-Net on rare diseases:  
Belgium, France, Germany, Israel, Italy, Netherlands, Spain,  
Turkey,

## international activities

E-RARE consortium of research funders

## summary

## Rationals: analysis

### Basic science on rare diseases seems to be reasonably established

- in systems which have strong bottom-up mechanisms for funding research, basic sciences on rare diseases seems to be relatively strong e.g.: good basis in human genetics: for more than 1500 diseases genetic variants identified

### Clinical sciences are less well established

- clinical description of diseases may be too unprecise for clinical studies
- diagnostic procedures are evolving (esp. genetic testing)
- treatment options for rare diseases are underdeveloped



## Rationals: difficulties

- (1) Rare diseases are defined by prevalence ( $< 5/10,000$ ). Except for rarity and associated structural problems, there are **few common denominators**.
- (2) research is hampered by lack of resources and infrastructures at several levels:
  - a) Few **scientists** work on one specific disease.
  - b) There are few **patients** scattered over a large geographic area, causing difficulties to gather the necessary **cohorts**.
  - c) Existing **databases** and **material** collections are usually local, **small**, and not accessible or standardised.
  - d) Diseases often have complex clinical phenotypes and require **interdisciplinary approaches** to treatment and interdisciplinary cooperation for research.
- (3) In general, there are deficits in knowledge, and the state of knowledge is **heterogeneous**.



## Conclusion and Consequence

### Conclusion:

1. Due to heterogeneity in type of disease and state of knowledge **bottom-up approach** of funding is most promising.
2. **Translation** of knowledge from basic science to patients must be improved (bench to bedside to bench to bedside)
3. translational research needs **interdisciplinarity** and therefore networking between (basic) researchers and physicians
4. efficient use of limited resources needs networking (e.g. access to technological platforms and facilities, sharing of databases)

### Consequence:

funding of **networks** on a national agenda

funding of **networking** on the international scale



## National activities

Most research programmes are **publicly funded** (in FR and SE charities actively collaborate)

Except for France, these programmes are not part of a **National Plan for Rare Diseases**, although some countries (EP, IT) such plans are discussed

In DE, FR, IT and EP the **programmes are specific** for rare diseases, whereas in the other countries programmes are „**generic**“ (for all types of diseases), objectives are health related and rare diseases are included

Research „goals“ exist, they differ among the partner countries (ranging from „increasing research on RD“ to „improve Health research“) but common priorities are:

- basic research such as identification of new syndromic entities,
- genotype phenotype correlation,
- identification and characterization of genes,
- (precompetitive) development of new drugs, therapies

Funding instruments for individual **projects** as well as **networks** exist

## National research activities (2)

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### France:

- individual projects and networking,
- access to infrastructure platforms (mouse clinic, small molecule screening, high throughput screening platform)
- organize access to small molecules from industry (ERDITI)

### Spain:

- funding of individual projects in generic „sub“programmes
- funding of multicenter projects
- funding of a consortium for translational studies, specific for rare diseases
- funding of clinical research on Orphan drugs

### Italy:

- Support for independent preclinical research: MoH/ISS call for proposals
- funding of clinical research on Orphan drugs and non-responders by AIFA

### Germany

- funding of national networks, to coordinate scattered resources (manpower, databases, material banks) infrastructures (e.g. diagnostic services) and to foster interdisciplinary research of basic and clinical researchers.



## „Generic programmes“

Do not define diseases to be addressed (nor prevalence), but are highly relevant for rare diseases:

### Examples:

NL: „translational gene therapy“

EP: „ Genetic Diseases, and Disease and Therapy Models“

DE: „Innovative therapies“ (including gene therapy, cell therapies etc.)

„molecular diagnostics“

„national human genome network“ (e.g. sarcoidosis, neuroblastoma)

„Competence networks“ (paedatric oncology)

- it is claimed that research on rare diseases is in a disadvantage during review processes compared to research on frequent diseases
- Analysis in the [Netherlands](#): the success rate of proposals on rare diseases was rather higher than lower compared to frequent diseases

## National activities (summary)

	GIS-IMR (France)	ISS (Italy)	ISCIII (Spain)	BMBF (Germany)	ZonMW Netherlands	TUBITAK (Turkey)	CSO MOH (Israel)
National Plan	In action 2005-2008	In preparation	In discussion	NO	NO	NO	NO
programme specific for RD	5-10 Mio. €	2004-2006 3,5 Mio. € 2006-2008 8,2 Mio. €	6-8 Mio. € /year	5-6 Mio. €	in preparation	NO	NO
generic programmes			6-8 Mio. €	> 9 Mio. €	ca. 2,5 Mio € per year	ca. 0,5 Mio € per year	variable
timeline of programmes	2002-2008	2004-2006 2006-2008	4 year programmes	2003-2008 2008-2016	unlimited	unlimited	unlimited
deadlines for applications	every year	ad hoc	every year	2-3 years	every year	every year	every year
funding for	projects and networks	projects and networks	projects, networks and net center CIBER	networks	project and networks	projects	projects



## An example to foster translational research: National Networks for Rare Diseases Germany

### goals of the call, tasks of the networks

- research on prevention, diagnosis and therapy of rare diseases
- the networks may include basic research, clinical research and health care research
- to coordinate scattered capacities in research and health care into an integrated approach, national top research groups, specialized clinical centres, specialized diagnostic laboratories,
- the networks should present themselves as interacting entities, not as “collections of individual projects”.
- the networks should achieve a critical mass in coverage of patients in Germany
- the networks should orient themselves towards European initiatives
- no preselection on disease types
- Budget: 30 Mio. € for 5 years, about 0,5 Mio. € per network per year

## Types of projects within the networks (1. funding period)

<b>Overall number of projects</b>	<b>91</b>
<b>built-up of infrastructure and communication</b>	<b>24</b>
network coordination	10
databases	13
tissue and DNA collections	6
<b>basic studies on the individual diseases</b>	<b>55</b>
identification of diseases genes	17
genotype-phenotype correlations	16
biochemical and cell biological experiments on pathogenesis	22
<b>clinical studies</b>	<b>25</b>
documenting disease progression	16
testing diagnostic procedures	7
therapeutic studies	2



## experience with national funding initiative

### 1. diversity of proposals:

most prominent disciplines were neurology, oncology, dermatology, cardiology, but a wide variety of medical specialties were addressed.

### 2. success rate in first selection:

55 initial applications

10 networks funded in 1. funding period

Conclusion: large potential, also among not selected proposals

### 3. Evaluation after 1. funding phase (2006) :

scientific output is very good to excellent

Internationale integration mostly established

clinical impact:

better diagnostics

treatment studies studies done in few networks,

preparatory work done: thorough description of natural history as basis for treatment studies

	<b>Accompanying funds from EU, NIH or other funders</b>
<b>Ichthyosis</b>	1. EU-CA für Genodermatosen (GENESKIN), Koordinator: Prof. G. Zambruno, IT 2. EU-STREP Skintherapy, Koord. Prof. Meneguzzi, IT
<b>Epidermolysis bullosa</b>	3. EU-CA für Genodermatosen (GENESKIN) Koordinator: Prof. G. Zambruno, IT
<b>Inborn deficiencies of hematopoiesis</b>	4. SCNI-Register für Patienten in USA, Europa, Kanada, Australien; Kodirektoren: K. Welte, Hannover; C.Dale, USA 5. ENERCA, Koordinator: Prof. Joan-Lluís Vives Corrons, Spanien; EU
<b>Skelettal Dysplasias</b>	6. ESDN-Network (EU-IP), Koordinator: Dr. Michael Briggs, UK 7. ANABONOS (EU), Koordinator: Professor Stuart Ralston, UK
<b>„GeneMove“, genetic movement disorders</b>	8. EUROSCA EU-Projekt (IP), Koordinator: O. Riess, Tübingen, DE 9. EUROWILSON (EU), Koordinator: Stuart Tanner, University of Sheffield, UK
<b>Muscular Dystrophies</b>	10. Myocuster EU-Projekt, Koordiantor: S. Trumann, IT 11. Eurobiobank, EU-Projekt, Koordinator: Lochmüller, DE 12. TREAT-NMD (EU-NoE), Koord: Kate BUSHBY & Volker STRAUB; in Verhandlung
<b>Systemic Skleroderma</b>	13. EUSTAR

# What is an ERA-Net?

ERA = European Research Area („Lisbon goals“)

ERA-Nets are a funding instrument of the European Commission  
within FP6 and FP7

It addresses national research funding agencies

It supports coordination of national programmes

It supplies grants for personal and travels

GOAL: transnational calls for proposals as  
„one stop shop“ for scientists who perform international projects

COM provides resources for coordination

The member states provide resources for the research project

## Coordination:

France: Institut National de la Santé et de la Recherche Médicale (INSERM)  
GIS-Institut des Maladies Rares  
Agence Nationale de Recherche

## Partners:

Belgium: Fonds National de la Recherche Scientifique (FNRS), Belgium

Germany: 1. Federal Ministry for Education and Research  
2. Projektträger im Deutschen Zentrum für Luft und Raumfahrt (PT-DLR)

Israel: Chief Scientist Office, Israeli Ministry of Health (CSO/MOH)

Italy : Istituto Superiore di Sanità (ISS)

Spain: Instituto de salud Carlos III /  
Fundación para la Cooperación y Salud Internacional Carlos III (FCSAI),

The Netherlands: Der Nederlandse Organisatie voor Gezondheidsonderzoek en  
Zorginnovatie (ZonMw)

Turkey: Türkiye Bilimsel ve Teknolojik Arastırma Kurumu (TÜBİTAK)



## History of the ERA-Net „E-RARE“

Started with three countries which already had programmes on rare diseases: DE, EP, FR

Other countries joined, which established programmes in the meantime or plan to do so

EU funded a preparatory action (1 year)

EU now funds a coordination action ( 4 years, starting mid 2006)

Transnational call launched in march 2007,

Deadline for proposals was in may 2007

Evaluation finished in october,

projects start in 2008 (13 projects, 10 Mio. € spent)

Next call planned!!

Broad spectrum of research addressed  
**NO PRESELECTION OF DISEASES**  
Bottom-up approach

- a) Collaborative research using or constituting cohorts of patients/families for:
  - Definition of new nosological entities, epidemiological studies, genotype/phenotype correlations.
  - Characterization of the genetic/molecular basis of specific diseases.
- b) Basic research on rare diseases including genetic and pathophysiological studies with clinical relevance.
- c) Research on diagnosis and therapies for rare diseases.  
biological targets, screening systems, model systems, gene or cell therapies.
- d) Patient oriented research in the area of social and human sciences - e.g. psychological, psychosocial and behavioural research – as well as health services research and health economy research in the field of rare disorders.



## experience with international funding initiative

### 1. diversity of proposals:

most prominent disciplines were neurology, hematology, metabolic diseases, dermatology, bone diseases, but a wide variety of medical specialties were addressed.

The spectrum is richer than in the national call

### 2. success rate in first selection:

125 applications

13 projects will be funded

Conclusion: large potential, also among not selected proposals

### Consequence:

Next call to be prepared,

?? Increase in available funds due to contribution of the European commission??

(ERA-Net plus scheme??)



# Summary

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1. There is a large scientific potential
2. Due to heterogeneity in type of disease and state of knowledge **bottom-up approach** of funding is most promising.
3. **Translation** of knowledge from basic science to patients must be improved (bench to bedside to bench to bedside)
4. translational research needs **interdisciplinarity** and therefore networking between (basic) researchers and physicians
5. efficient use of limited resources needs **networking** (e.g. access to technological platforms and facilities, sharing of databases)

Generic calls: include and encourage research on rare diseases!

Specific calls: mainly address networking!

Other issues addressed in the ERA-Net in the future will be:

access to infrastructures

rotational positions for clinical scientists



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# THANK YOU FOR YOUR ATTENTION

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**Most of which are in the audience today**



# Network Epidermolysis Bullosa



## Structures of the networks (1. funding phase)

<b>Title of network</b>	<b>number of centres</b>	<b>number of projects</b>	<b>coordination and central services</b>	<b>Data base</b>	<b>DNA and tissue collection</b>
<b>ichthyosis</b>	<b>13</b>	<b>7</b>	<b>3</b>	<b>1</b>	
<b>epidermolysis bullosa</b>	<b>15</b>	<b>9</b>	<b>3</b>	<b>1</b>	
<b>skleroderma</b>	<b>18</b>	<b>11</b>	<b>1</b>	<b>1</b>	
<b>SkelNet</b>	<b>12</b>	<b>7</b>	<b>2</b>	<b>1</b>	
<b>intersex</b>	<b>40</b>	<b>5</b>	<b>1</b>	<b>1</b>	
<b>hematopoiesis</b>	<b>5</b>	<b>12</b>	<b>2</b>	<b>2</b>	<b>2</b>
<b>leukodystrophies</b>	<b>14</b>	<b>11</b>	<b>2</b>	<b>1</b>	
<b>muscular dystrophies</b>	<b>21</b>	<b>18</b>	<b>4</b>		<b>1</b>
<b>GeneMove</b>	<b>19</b>	<b>9</b>	<b>3</b>	<b>3</b>	<b>3</b>
<b>metabolic screening</b>	<b>15</b>	<b>11</b>	<b>3</b>	<b>2</b>	
	<b>167</b>	<b>88</b>	<b>24</b>	<b>13</b>	<b>6</b>