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ERNs and Research: state of play from the European Commission perspective

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European Reference Networks (ERNs)

1) Background and recent history of ERNs

2) ERNs and Research from DG SANTE perspective

3) ERNs and medicinal product authorisation point of view

4) ERNs and Research from DG RTD perspective

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The context: Healthcare in the EU

- ***National competences and systems*** *(28 so far):*
  - Different rights and entitlements
  - Different organisational models
  - Beveridge (Public national healthcare systems) vs Bismarck (social security based models) and mixed models
- ***Subsidiarity*** *principle*
- *Healthcare collaboration based on* ***voluntary participation***
- ***Cross-border healthcare directive*** *(only legislation addressing healthcare at EU level) to facilitate mobility of patients across borders and to strength cooperation and added value*

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The European Reference Networks (ERNs)

Networks of healthcare providers aiming at **improving quality, and safety and access to highly specialised healthcare**

Patients affected by rare or low prevalence and complex diseases

Added value at EU level

Multidisciplinary approach (different specialities/areas of knowledge)

Need of cooperation:

- Scarcity knowledge
- Need education
- Complexity / high cost
- Effectiveness in the use of resources

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The rationale behind

- Many of those affected by a rare or complex condition do not have access to diagnosis and high-quality treatment.
- Expertise and specialist knowledge may be scarce because patient numbers are low
- No country alone has the knowledge and capacity to treat all rare and complex diseases.
- Important delay in diagnosis because lack of knowledge or right referal systems
- Lack of diagnostic capacity (no tests available) and treatments in many cases

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WHAT?

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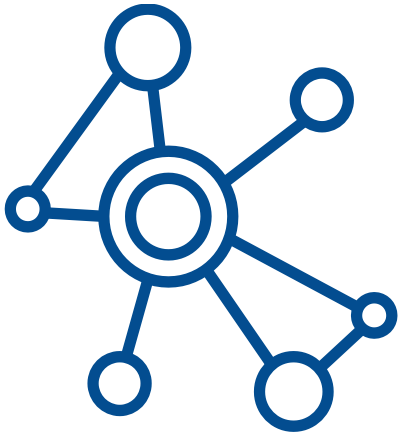
Networking is the basis:

"The knowledge travels, not the patient"

- **Exchange of expertise** and clinical **data on patient cases** through the network and across the EU
- Swift and smooth **contact between providers** and between patients and providers at a distance
- **Collaborative/cooperative actions** and systems
- Networking **activities,** specific network **tools** and IT solutions



Share. Care. Cure.

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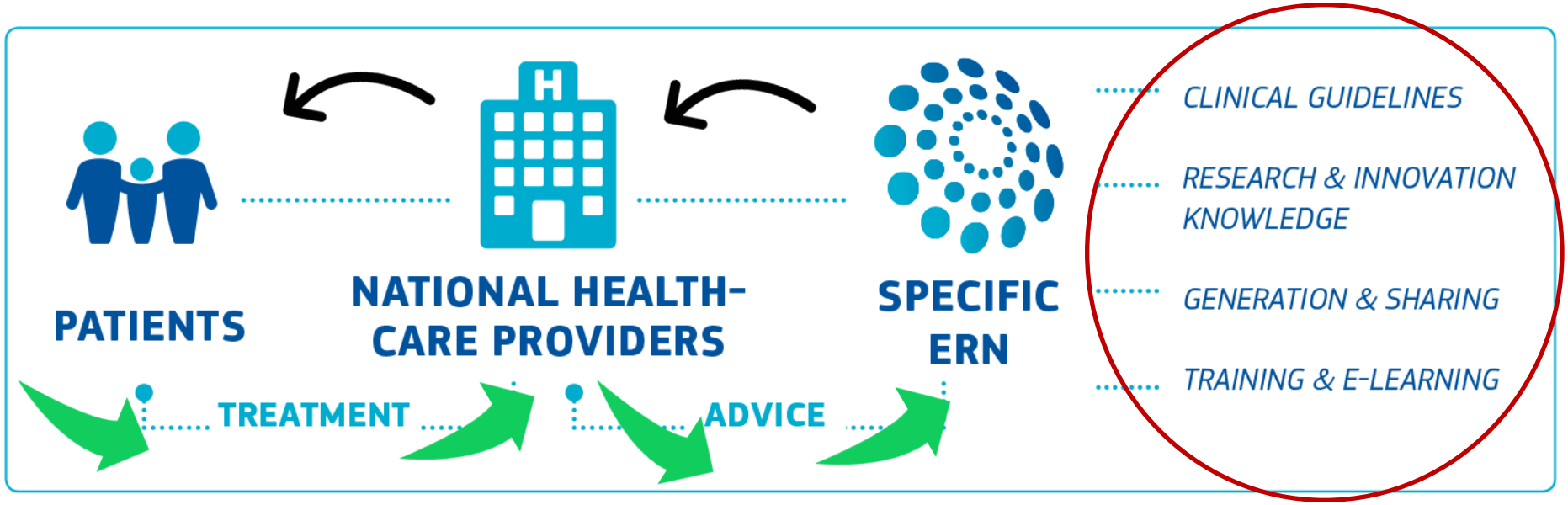

Clinical virtual care

Remote monitoring & follow-up

Remote guidance and diagnosis

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HOW?

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Telemedicine and other IT solutions and tools

Local healthcare provider

National referal Complicated case

Member or affiliated partner

Patient case

Enrolment of case

Virtual care

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Outcome call 2016

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24

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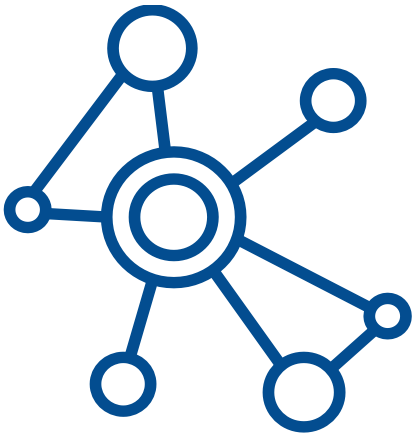

Networks

26 COUNTRIES

› 300 HOSPITALS

Full Member

Affiliated partner (late 2018)

› 900 HEALTHCARE UNITS

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AWARD CEREMONY

3rd European Reference Networks Conference

9 March 2017 - Vilnius, Lithuania

The 24 Networks approved

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ERN BOND	Bone Diseases
ERN CRANIO	Craniofacial anomalies and ENT disorders
Endo-ERN	Endocrine Conditions
ERN EpiCARE	Rare and Complex Epilepsies
ERKNet	Kidney Diseases
ERN GENTURIS	Genetic Tumour Risk Syndromes
ERN-EYE	Eye Diseases
ERNICA	Inherited and congenital anomalies
ERN-LUNG	Respiratory Diseases
ERN-RND	Neurological Diseases
ERN-Skin	Skin Disorders
ERN EURACAN	Solid Adult Cancers
ERN EuroBloodNet	Onco-Hematological Diseases
ERN EURO-NMD	Neuromuscular Diseases
ERN GUARD-HEART	Diseases of the Heart
ERN ITHACA	Congenital Malformations and Intellectual Disability
MetabERN	Hereditary metabolic diseases
ERN PaedCan	Paediatric Cancer
ERN RARE-LIVER	Hepatological Diseases
ERN ReCONNET	Connective Tissue and Musculoskeletal Diseases
ERN RITA	Immunodeficiency, AutoInflammatory and Auto Immune Diseases
ERN TRANSPLANT-CHILD	Transplantation in Children
VASCERN	Multisystemic Vascular Diseases
ERN eUROGEN	Urogenital Diseases

Phases of the ERN life cycle

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We are here

2011-14

Legislation and initial planning

- Directive
- Implementing decisions
- Awareness and communication

2015-16

Implementation: (Approval stage)

- Design and development Assessment tools
- Call for ERN
- Assessment of Network proposals
- Approval of ERNs

2017-18

Implementation: (deployment stage)

- Establishment
- Initial organisational phase
- Functioning (initial actions and services)
- Partial service production

2019-20

Consolidation

- Full service production
- Continuous monitoring
- Performance indicators and initial outcome assessment

2021

Evaluation and update

project cycle re-initiation

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Actors involved in the ERN implementation

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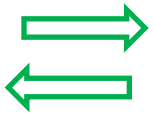
ERNs' Coordinators Group (ECG) and Working Groups



ERN Board of Member States (BoMS)

Commission expert group on rare diseases

RD ACTION DATA AND POLICIES FOR RARE DISEASES

JARC JOINT ACTION ON RARE CANCERS

Patients organisations

Professional / scientific organisations

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National Healthcare System

DG SANTE

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DG RTD
DG CONNECT
JRC

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ERN's IT Platform & tools

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IT tools

CLINICAL patient management System (CPMS)

- Web/video conferencing , Virtual clinical meetings
- Exchange of Images (Radiology), diagnostic tests & pictures (genetics, pathology etc., (PACS)
- Exchange of clinical information and patient data

Communication and collaboration

- Management / governance tools
- Communication / conferencing tools

Other modules

- eTraining / eLearning
- Public webpage / ERNs webs

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Funding / support

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THE THIRD HEALTH PROGRAMME 2014-2020
FUNDING HEALTH INITIATIVES

EUROPEAN UNION
STRUCTURAL FUNDS

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ERNs and Research from DG SANTE perspective

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Research, innovation & knowledge generation

Key Elements of ERNs

- A **framework for structured cooperation** to maximise cross-country expertise through joint research projects and clinical trials
- ERN provide an **opportunity** to build **top level translational and basic research** around shared strategies
- Dissemination of research results, **education & training activities**

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Directive 2011/24/EU (Article 12 on ERNs)

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- ***ERNs shall have at least 3 of the following objectives:***
- *(a) to help realise the potential of European cooperation regarding highly specialised healthcare for patients and for healthcare systems by **exploiting innovations** in medical science and health technologies;*
- *(b) to contribute to the **pooling of knowledge** regarding sickness prevention;*
- *(c) to facilitate **improvements in diagnosis** and the delivery of high-quality, accessible and cost-effective healthcare for all patients with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare;*
- *(d) to maximise the cost-effective use of resources by concentrating them where appropriate;*
- *(e) **to reinforce research, epidemiological surveillance like registries and provide training for health professionals;***
- *(f) to facilitate mobility of expertise, virtually or physically, and **to develop, share and spread information, knowledge and best practice and to foster developments of the diagnosis and treatment of rare diseases**, within and outside the networks;*
- *(g) to encourage the development of quality and safety benchmarks and to help develop and spread best practice within and outside the network;*
- *(h) to help Member States with an insufficient number of patients with a particular medical condition or lacking technology or expertise to provide highly specialised services of high quality.*

Registries, research and ERNs

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PATIENT CARE
Patient clinical unmeet needs (treatment/diagnosis)

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RESEARCH
Research question/gap
Prospective research
Translational/trials

Patient Data

Population Cohorts / Concentration of cases

Secured Databases

Clinical / Imaging / Biological Data

Genetics, Molecular Pathology

IT Solutions / Communication between HCP

- *common elements , principles and requisites*

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Towards collaborative efforts of ERNs in the area of Research

- Explore… interaction with EMA and clinical trials related initiatives, IMI initiatives, etc.
- But also potential and interest in non-commercial research projects (for example on effectiveness of treatments, impact of guidelines etc.)

BUT first of all:

- Start by mapping and building up research capabilities among ERNs:
  - **Internally to each of the 24 ERNs**
  - **As group of ERNs**

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Building up research capabilities among ERNs (1)

- **Within each ERN**:

- Thematic groups in terms of diseases,
- Transversal Working Groups on Research (and/or Registries)
- For a coordinated approach within the ERN

(building upon strengths and needs of all ERN members from that ERN – it could start by a mapping exercise…)

Building up research capabilities among ERNs (2)

- **For the whole group of ERNs**:

- Thanks to the Working Group on Research of the ERN Coordinators' Group

→ Different actions by different WG members since WG creation in 2017 (EJP, FP9, RD-ACTION Workshop with EMA…)

→ now moving towards a **more coordinated approach**, involving all WG members and supporting all ERNs

- With RD-ACTION Workshop today: survey on needs of ERNs regarding research (but views to be confirmed and consolidated)

Building up research capabilities among ERNs (3)

- **For the whole group of ERNs**:

- To be coordinated with the work of the Working Group on Ethics of the ERN Coordinators' Group

→ for example in the area of cooperation with industry

!! WORK IN PROGRESS !!

- To be coordinated with the work of the **ERN Board of Member States** and with **national policies**

Board of Member States (BoMS) (1) statement on ERNs & industry

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"In recognition of the importance of industry in improving our knowledge of rare conditions and developing clinical tools and therapies, **the Board of Member States agrees with engagement between ERN members and industry <u>where appropriate, for example in clinical trials and research projects</u>**.

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Board of Member States

Statement on European Reference Networks (ERNs) and industry

November 2016

In recognition of the importance of industry in improving our knowledge of rare conditions and developing clinical tools and therapies, the Board of Member States agrees with engagement between ERN members and industry where appropriate, for example in clinical trials and research projects.

However, there is no legal provision for the involvement of external stakeholders, including industry, in the operation and governance of ERN. To address this issue and to steer ERN in their thinking on engagement with industry, the Board of Member States offers the following guidance:

* Conducting some aspects of research and in particular clinical trials will be an integral task of ERNs which may require collaboration with industry. This requires defining in advance the relations with industry so that they will be organised in an open and transparent manner. In particular, access to the data from registries and biobanks has to be carefully defined respecting the patients' rights and relevant national and European legislation.

* A complete transparency policy should apply to the relationship between ERNs and industry.

* Industry stakeholders cannot have a place in the governance structure of an ERN.

* There must be no industry funding of any operational ERN activity (e.g. activities such as, but not exclusive to: the management and running of the network, meetings of the members, development of diagnostic guidelines etc.)

* Each designated ERN should establish a charter endorsed by all its members, to define its own Conflict of Interest Policy and ensure disclosure of all financial and non-financial conflicts of interest before any engagement commences.

* Conflict of interest policy must respect relevant national and European legislation and follow the recommendations and guidelines developed by independent organisations and recognised bodies.

* Each Healthcare provider (HCP) must respect and follow the national legislation relating to conflict of interest.

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* Conducting some aspects of research and in particular clinical trials will be an integral task of ERNs which may require collaboration with industry. This requires defining in advance the relations with industry so that they will be organised in an **open and transparent manner**. In particular, access to the data from registries and biobanks has to be carefully defined respecting the patients' rights and relevant national and European legislation.

* A **complete transparency policy** should apply to the relationship between ERNs and industry. […]

Board of Member States (BoMS) (2) statement on ERNs & industry

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[…]

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[…] "

! More on this by Board representative later today !

Statement available at:

https://ec.europa.eu/health/sites/health/files/ern/docs/statement_industry_conflictofinterest_en.pdf

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Towards collaborative efforts of ERNs in the area of Research – at different levels:

- **ERN community**:
  - Within each ERN
  - Coordinated approach for the whole ERN group, via the Working Group on Research and the ERN Coordinators' Group
- **Member States'** research agendas, Public Health policies, National plans on Rare Diseases etc.
- Other views:
  - Patients' organisations,
  - Professional associations (national, European, International)
  - Industry
  - Other stakeholders – e.g. IRDiRC

Citation: Clin Transl Sci (2018) 11, 21–27; doi:10.1111/cts.12500

REVIEW

Future of Rare Diseases Research 2017–2027: An IRDiRC Perspective

Christopher P. Austin[1,*], Christine M. Cutillo[1], Lilian P.L. Lau[2], Anneliese H. Jonker[2], Ana Rath[2,3], Daria Julkowska[4], David Thomson[5], Sharon F. Terry[6], Béatrice de Montleau[7], Diego Ardigò[8], Virginie Hivert[9], Kym M. Boycott[9], Gareth Baynam[10,11], Petra Kaufmann[1], Domenica Taruscio[12], Hanns Lochmüller[13], Makoto Suematsu[14], Carlo Incerti[15], Ruxandra Draghia-Akli[16,17], Irene Norstedt[18], Lu Wang[18] and Hugh J.S. Dawkins[19] on behalf of the International Rare Diseases Research Consortium (IRDiRC)

The International Rare Diseases Research Consortium (IRDiRC) was founded in 2011 with the conviction that rare diseases research had reached a critical juncture. Proof of principle existed that rare diseases could be diagnosed, new treatments successfully developed and approved, and improvements in quality and quantity of life achieved. Government research funders, companies, scientists, and patient advocacy groups had all demonstrated their commitment and effectiveness in contributing to progress in rare diseases research. However, the work was largely atomized, with each organization, each country, and the champions of each disease pursuing independent, often duplicative solutions. The scale of the "rare disease problem"—thousands of rare diseases, the vast preponderance of them with no approved treatment, and decades-long diagnostic odysseys for many patients—led to the realization that the time had arrived for global cooperation and collaboration among the many stakeholders active in rare diseases research, to capitalize on these proofs of principle, and maximize the output of rare diseases research efforts around the world. IRDiRC's initial aims were to aid in the achievement of two overarching objectives: to contribute to the development of 200 new therapies and the means to diagnose most rare diseases by the year 2020.[1] For more detailed information on the history, governance, and nascent stages of the Consortium, please refer to the accompanying piece on the first 6 years of IRDiRC.[2]

Due to the remarkable global surge in activity in rare diseases research over the last 6 years, including contributions by IRDiRC, the Consortium's 2020 goal for 200 new therapies was achieved in early 2017—3 years ahead of schedule—and the goal for diagnostics—the ability to diagnose most rare diseases by 2020—is within reach; these accomplishments were celebrated at the 3rd IRDiRC Conference in Paris in February 2017.[3] The 6 years preceding this 2017 conference have been truly extraordinary for the rare diseases research community and for rare disease patients. Major public-sector research initiatives focused in this area have emerged or expanded in many countries, most notably from the US National Institutes of Health (NIH), the European Commission (EC), and the newly formed Japan Agency for Medical Research and Development (AMED). Engagement and partnering among public funders, scientists, industry, and people living with rare diseases have gone from being the exception to commonplace. IRDiRC has been a major positive factor in raising public awareness about rare diseases, the need for more research to address them, and for collaborative tools which allow ethical data sharing for and with patients. It has also clearly led to increased investment of public- and private-sector research funds for rare diseases, in addition to the research funding raised by patients and patient organizations. IRDiRC has helped to catalyze several important initiatives that are improving collaboration among researchers and enhancing the ability of patients to engage as constructive partners in research.[2,4]

As gratifying as these developments are, those who lead much of the global rare diseases research community are well aware of the enormous challenges that lie ahead for all patients living with rare diseases to receive an accurate and timely diagnosis, to have approved treatments available, to get access to those treatments, and to realize improvements in their quality and quantity of life; in short, to be able to live the best life possible. Although the means to diagnose most rare diseases that are caused by mutations in the coding genome is on track to be achieved either via genotype-phenotype correlation or novel gene discovery, in practice most patients with rare diseases spend years in the

Expected impact of ERNs…. (1)

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… for patients and professionals

- ✓ improve **public and professional awareness** of rare and complex diseases
- ✓ increase the **likelihood of early and accurate diagnosis** and effective treatment where available.
- ✓ platforms for the **development of guidelines, training and knowledge-sharing.**
- ✓ facilitate **large clinical studies** to improve understanding and develop new drugs
- ✓ An **opportunity for networking** with likeminded experts from across Europe — **ending the professional isolation that many experts in rare diseases face.**

ERNs offer the potential to give patients and doctors across the EU access to the best expertise and timely exchange of life-saving knowledge, without having to travel.

Expected impact of ERNs…. (2)

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… for the Healthcare systems and society

✓**Innovation** in healthcare delivery is the cornerstone of the ERN system

✓Development of **new care models**, and innovative medical solutions and devices, changing the way in which treatment itself is delivered.

✓Incubators for the development of **digital services** for the provision of virtual healthcare.

✓Will help to **boost economies of scale** and ensure a more efficient use of resources, with a positive impact on the sustainability of national healthcare systems.

✓The networks are a visible demonstration of what solidarity can achieve in Europe.

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Thank you for your attention

Further information:

http://ec.europa.eu/health/ern/policy/index_en.htm

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