Response by the Chairman of ENETS, European Neuroendocrine Tumor Society, Dr WW de Herder, MD PhD
See: www.neuroendocrine.net

Q 1:Is the current EU definition of a rare disease satisfactory?

A: YES, of course better and universal codification and classification will be well-appreciated!

Q2: Do you agree that there is a pressing need to improve coding and classification in this area?

A: Certainly.

According to the recent publication:
Modlin IM, Oberg K, Chung DC, Jensen RT, de Herder WW, Thakker RV, Caplin M, Delle Fave G, Kaltsas GA, Krenning EP, Moss SF, Nilsson O, Rindi G, Salazar R, Ruszniewski P, Sundin A.Gastroenteropancreatic neuroendocrine tumours.Lancet Oncol. 2008; 9:61-72.
there is an increase in incidence of the rare carcinoid tumours, but since 1973 there has been NO change (no improvement) in survival from carcinoids!! (According to SEER database of the US National Cancer Institute)

For this purpose ENETS has recently published their:

ENETS Consensus Guidelines for the Management of Patients with Digestive Neuroendocrine Tumors Part 1 - Stomach, Duodenum and Pancreas in Neuroendocrinology 2006, Vol. 84, No. 3

ENETS Consensus Guidelines for the Diagnosis and Treatment of Neuroendocrine Gastrointestinal Tumors Part 2 - Midgut and Hindgut Tumors, in Neuroendocrinology 2008, Vol. 87, No. 1

As well as:

Rindi G, Kloppel G, Alhman H, Caplin M, Couvelard A, de Herder WW, Erikssson B, Falchetti A, Falconi M, Komminoth P, Korner M, Lopes JM, McNicol AM, Nilsson O, Perren A, Scarpa A, Scoazec JY, Wiedenmann B; and all other Frascati Consensus Conference participants (2006). TNM staging of foregut (neuro)endocrine tumors: a consensus proposal including a grading system. Virchows Arch. 2006;449: 395-401.

Rindi G, Klöppel G, Couvelard A, Komminoth P, Körner M, Lopes JM, McNicol AM, Nilsson O, Perren A, Scarpa A, Scoazec JY, Wiedenmann B.TNM staging of midgut and hindgut (neuro) endocrine tumors: a consensus proposal including a grading system.Virchows Arch. 2007; 451:757-62.

ENETS is also setting up EuroNETS an European neuroendocrine Tumour Registry

ENETS is a multidisciplinary organization with >400 members worldwide, both basic scientists and clinicians who are experts in the diagnosis and treatment of neuroendocrine

tumors (NETs) (of the gastrointestinal tract) and holding a once-yearly educational conference attended by 800 participants (see website: www.neuroendocrine.net)

Q3: Can a European inventory of rare diseases help your national/regional system to better deal with RD

A: Yes, certainly. See also answer to Q2, ENETS is putting a lot of effort in this field. ENETS is also starting with identifying 8-10 European centres of expertise in the field of neuroendocrine tumour disease. Also standards of care have been defined and will be published shortly. ENETS is also setting up "EuroNETS", a European neuroendocrine Tumour Registry

Q4:
Should the European Reference Networks privilege the transfer of knowledge? The mobility of patients? Both? How?

A: Yes, certainly.
ENETS is already supporting activities in this field e.g. patients are referred to other European centres for specific therapeutic interactions.
ENETS is training students and physicians and spreading knowledge in the field of neuroendocrine tumour management all over Europe.
ENETS has organised the first European patient meeting and is supporting patient support groups all over Europe
ENETS is participating in many trials initiated by the pharmaceutical industries but also organizes its own multicenter European trials.

Q5: Should on-line and electronic tools be implemented in this area?

A: Yes, see previous answers. Standardised laboratory tests e.g for chromogranin A determinations have become available. We are still in search for more specific tumour markers for different NETs and especially circulating prognostic markers. (Expensive) microchip technologies seem very promising in bringing NET research further. Specific reference laboratories might play an important role in this. Additional funding is necessary.

Q6: What can be done to further improve access to quality testing for RD

A: NETs can occur in the spectrum of the MEN-I (MEN IIa-b, von Hippel Lindau and tuberous Sclerosis genotypes. Guidelines for family screening have been set up for these disorders. For NETs in general, screening is currently not performed-available.

Q7: Do you see a major need in having an EU level assessment of potential population screening for RD.

A: Yes
Currently the prevalence of NET disease in Europe is not well known.
Preventive measures are only possible in patients with the MEN-I, VHL or TS phenotype
Best practices on NET care have been developed by ENETS
NET patients use a lot of orphan drugs not only for the treatment but predominantly for diagnostic purposes like: secretin, pentagastrin, but also ketoconazole and phenoxybenzamine and products for peptide receptor coupled radiotherapies.

Q8: Do you envisage the solution to the orphan drugs accessibility problem on a national scale or on an EU scale?

A: Preferentially on an EU scale

Q9: Should the EU have an orphan regulation on medical devices and diagnostics

A: Yes, see above
ENETs also provides a web-based forum where patients can ask specific NET-related questions and advise.

Q10: What kind of specialised social and educational services for RD patients and their families should be recommended at EU level and at national level

A: ENETS is setting up EuroNETS an European neuroendocrine Tumour Registry. National databases will be linked to this database
It has supported the formation of national networks and supported patient support groups in many European countries.
ENETS is setting up biobanks in various European countries-laboratories.

Q11:
What model of governance and of funding scheme would be appropriate for registries, databases and biobanks?

A: See answers to previous questions.

Q12: How do you see the role of partners (industry and charities) in an EU action on rare diseases? What model would be the most appropriate?

A: ENETS already supports national patient self-help groups. Charities and pharmaceutical industries currently provide financial support for ENETS activities. Until now it has not received funding from MS.

Q13: Do you agree with the idea of having action plans? If yes should it be at national or regional level in your country?

A: Preferentially at a national level, long-term support will be needed.

Q14: Do you consider it necessary to establish a new European Agency on RD and to launch a feasibility study in 2009?

A: Yes, it will not be easy though, as there is a wide variety of RD, expanding into different fields of medicine (internal medicine, endocrinology, oncology, pathology, nuclear medicine, radiology, gastro-enterology, surgery) and varying from acquired to inherited, juvenile to adult, sex dependent – non-sex-dependent.
An agency will be able to inform the EU about the state of the art with regard to developing its strategies in RD

Dr. W.W. de Herder, MD PhD
Department of Internal Medicine
Sector of Endocrinology
Erasmus MC
Room D430
‘s Gravendijkwal 230
3015 CE Rotterdam
The Netherlands
Tel: +31-10-7035950
Fax: +31-10-7033268
e-mail: w.w.deherder@erasmusmc.nl