

## **Eurordis Round Table of Companies 2<sup>nd</sup> Workshop** **Concept Paper**

### **New Methodologies for Clinical Trials in Small Populations**

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Among approximately 7000 rare diseases, many affect only a few thousand or even fewer than one hundred patients in the EU. In these circumstances, a trial enrolling several hundred patients may be neither practical nor possible. Accordingly, the design and the conduction of the clinical trial, the analysis and interpretation of the collected data are constrained by the prevalence of the disease itself.

In 2003, the Committee for Human Medicinal Products (CHMP) Efficacy Working Party (EWP) at the EMEA was given the task of with preparing a Discussion Paper concerning the problems associated with clinical trials when there are very few patients available to study. The paper, currently under public consultation until September 2005 (available at <http://www.emea.eu.int/pdfs/human/ewp/8356105en.pdf>), has been prepared in joint collaboration with members of the Scientific Advice Working Party (SAWP), the Committee on Orphan Medicinal Products (COMP) and the Paediatric Expert Group (PEG). The expertise within the group includes clinicians, epidemiologists and statisticians from National Regulatory Authorities and from universities.

The approaches outlined in the EWP-EMEA document, while they should not be interpreted as a general paradigm change in the evaluation of drug development, give nevertheless a new open vision on the advantages of applying alternative methodologies when the restrictions due to the nature of the rare disease do not allow a classical trial to be conducted.

Next July 8<sup>th</sup> 2005, Eurordis invites patients, scientists, regulators and pharmaceutical companies to analyse and discuss common important issues linked to the clinical development in small populations, such as:



- What is the impact of a restricted number of available patients on the clinical development?
- What is the impact of the little knowledge of the disease's natural history, in particular when associated to a small population of patients?
- Which alternative methodologies are available to overcome these problems?
- Are “regulators”, sponsors and clinical researchers ready to explore new methodologies?
- Are patients aware of the methodological constraints of Clinical Trials (feasibility/quality) and of the possible solutions offered by non-classical methodologies?
- Are there attempts or successes in conducting trials that apply new methodologies?
- Are Sponsors and Regulators ready to invest and take risks in trying alternative approaches required in situations where only very few patients can be enrolled in trials?

Such compromise positions will usually be at the cost of increased uncertainty concerning the reliability of the results and hence the reliability of the effectiveness, safety and risk–benefit of the product. However the example of several orphan products which have received market authorisation even though randomised controlled trials had not been performed, could be taken as important new steps towards the development of therapies for serious and life-threatening diseases.

In some circumstances, Randomised Clinical Trials (RCT) “Gold Standard” have their limits due to the great difficulties in adapting their design if necessary, once the trials have started. The new approaches may perhaps also lead to solutions to ease the conduct of more classical trials.