EURORDIS Contribution to the European Commission Public Consultation on the revision of the "Clinical Trial Directive 2001/20/EC

EURORDIS, the European Organisation for Rare Diseases, represents today 469 rare disease organisations from 45 countries, 25 of which are EU Member States, and thereby reflects the voice of an estimated 29 million patients affected by rare diseases in the European Union.

In response to the Commission's Public Consultation on "A concept paper on the revision of the 'Clinical Trials Directive' 2001/20/EC", EURORDIS is pleased to send its comments from the rare disease patients' perspective.

The responses provided in this document are based on the work performed and the experience gained by EURORDIS since its creation in 1997 in the area of clinical development. Since its inception, EURORDIS has been devoted to facilitating the development of therapies for small and geographically widespread specific patient populations, such as rare diseases, and to improving the quality of clinical development in all aspects. This includes involving patients' representatives in the decisions made for clinical development (i.e. clinical protocols, ethical aspects, information on studies and communication of results) and increasing their capacities by training them on the technical and regulatory aspects of drug development.

Given the demonstrated value of patients' contribution in the EU and national marketing authorisation processes, we trust that the European Commission and all other stakeholders will recognise the need to expand this role to include those activities regulating the conduct and authorisation of clinical studies.

Specific answers to European Commission public consultation:

Item n°1:

EURORDIS agrees with the proposal of a single submission. In our view, and in the light of the experience with other centralised procedures established at the EU level to facilitate medicinal product development, the single submission is the only way forward to finally reduce the administrative burden of the sponsors and to guarantee a real harmonisation of authorisation practices.

Item n°2:

EURORDIS agrees with the appraisal. A separate assessment performed by each Member State would not address the concerns raised by the current Clinical Trial Directive.

Item n°3:
EURORDIS welcomes the proposal for a Coordinated Assessment Procedure. However, as we further develop in some of the following answers, we expect the CAP addresses the real issues of reducing the burdens for the clinical development of medicinal products within the EU territory. In our opinion, this can only be achieved by equally covering the Ethical aspects related to informed consent, recruitment and reward in clinical trial application. (cf. items 4 and 5).

Item n°4 and Item n°5:
While EURORDIS welcomes the proposal for a CAP procedure, it does not agree to limit the scope of the CAP to the assessment of the risk-benefit and to the aspects related to the quality of the medicines and their labelling.

In particular, the European rare disease patient community that EURORDIS represents, also wishes to include within the scope of the CAP the Ethical aspects related to the informed consent, recruitment and rewards. In fact, and contrary to what is stated in the proposed concept paper, we do not agree with the general and too casual statement that "The ethical issues clearly follow within the ambit of the Member States".

If we could admit that cultural differences across EU can explain different approaches in some specific areas (e.g. acceptance of products derived from embryos or embryonic stem cells), the differences we observe today in the composition and the quality of work of the Ethics Committees are folkloric.

If it is true that until now we have observed some differences in the evaluation of the clinical trial ethical issues, these differences represent a real anomaly since Ethics are, by definition, aimed at being universal if we consider the Helsinki Declaration based on Kantian principles.

The ethics to be applied in the clinical development is simply the one of the Helsinki Declaration to which all EU MS have already adhered. Based on the same declaration, the fields of application of ethics are clearly defined and should be applied similarly across Europe: person protection, justice, autonomy, risk (benevolence and malfeasance).

Furthermore, the ethical issues to be analysed in the framework of a clinical study are intimately linked to the study methodology. Therefore, ethics committee evaluation cannot continue to modify the methodology of a study creating and sustaining a situation of non harmonisation that the revision of Directive 2001/20/EC aims to address.

It would be unethical to allow that such a confused situation in the area of Ethics Committee composition and performance translates into the non respect of the justice principle foreseeing the same opportunity for all patients to equally contribute to treatment developments.

- ➔ Not including the evaluation of ethical issues in the CAP would defeat the harmonisation efforts of the current directive revision.

Instead of continuing to maintain such an acceptable compartmentalisation of ethics, we should naturally and strongly work towards a convergent composition of the Ethics Committees and thus towards the same outcomes. The inclusion of the Ethical issues within the CAP would accelerate such logical and beneficial process.

EURORDIS proposes that each MS involved in a CAP coordinates the Ethics evaluation within its own country and brings to the centralised assessment one single opinion/comment on the ethical issues of that specific study. Divergent opinions on ethical issues should be discussed in the same way as the scientific opinions. Such a centralised Ethical evaluation would also be beneficial to help MS to harmonise their national Ethics Committees. Today even Ethics Committees in the same MS reach divergent opinions and request different study amendments.

- ➔ This is unacceptable and in particular from the point of view of those same patients that these Ethics Committees are meant to protect, following identical universally accepted principles.

Concerning the third area considered in a clinical trial application, while leaving the decisions regarding the suitability of the sites, the investigator and national rules to be agreed at national level, EURORDIS advises the single national evaluation of these local issues to be shared with the other MS involved in the trial. Such an exchange of information could help each MS in planning the technical improvements needed, at the level of the single national research centres, in order to increase their quality and would subsequently increase the standards of the entire European research infrastructure. In this way, the EU would become more attractive for non EU sponsors.

Item n°6:
EURORDIS believes that the first approach, allowing for "opt-out" of MS, is currently the most realistic option. Nevertheless, we advise that in the case of a divergent opinion by one or more MS, the EC (and/or the EMA) would then be involved in the analysis of the reasons for the opt-out and made responsible to make them public.

Item n°7:
In order to reach the objective of an increased quality and harmonisation of EU clinical trials, we think that the CAP procedure should be mandatory for all multinational clinical trials. While trials conducted in a single MS would be excluded from the CAP procedure, we suggest the same forms should be used for requesting national authorisations.

Item n°13:
EURORDIS agrees with the proposed appraisal. The present non-regulated situation of the non-IMPs, creates a climate of uncertainty and represents an additional burden for the development of medicines. We agree with the proposed narrowing of the definition of the IMP and with the introduction of proportionate provisions for the "auxiliary medicinal products" in the future revised Directive.

Item N°14:
As no intervention in humans is exempt from any risk, EURORDIS wishes to express its agreement for an indemnification by the MS. This option, while still guaranteeing the protection of the study subjects, would hugely reduce the cost of clinical trials and thus

support the development of clinical research in Europe and in particular that of academia and SMEs.

Item n°15:
Concerning the issue of sponsorship and considering the difficulties that academic clinicians encounter today to organise multicentre and multinational clinical trials, we think that the possibility to choose between Option 1 (Single sponsor) and Option 2 (multiple sponsorship) should be left to the parties involved in the trial. The possible disadvantages linked to multiple sponsorship, would possibly be overcome by advantages such as an increased opportunity for financial support at national level and an increased willingness by academic investigators to be involved in a trial once the responsibilities and the liability are shared in a contractually defined manner.

Item n°16:
EURORDIS very much welcomes the initiative to address the issue of Emergency Clinical Trials in the future revised Directive. Addressing this type of research would fill the present legislative gap which was often putting at risk those health practitioners intervening in emergency situations and would respond to the objectively urgent medical needs arising in such cases.