GPOH SUBMISSION TO EUROPEAN COMMISSION CONSULTATION ON THE

REVISION OF THE "CLINICAL TRIALS DIRECTIVE" 2001/20/EC

The "Society of Paediatric Oncology and Haematology" (Gesellschaft für Pädiatrische Onkologie und Hämatologie = GPOH) would like to thank the European Commission for the opportunity to contribute to the EU Clinical Trials Directive Consultation process. This answer includes comments from several German and international study groups who are launching childhood cancer clinical trials in Germany and across the EU.

CONSULTATION TOPICS

1. COOPERATION IN ASSESSING AND FOLLOWING UP APPLICATIONS FOR CLINICAL TRIALS

Consultation item no 3

1.2. It will be not possible to perform a total central assessment procedure, since the national ethical committees have to be considered. The most extensive work considering the application for clinical trials is the multiple appraisals of the ethical commissions (EC) (in Germany about 50 EC). **Only one EC per country should be necessary. This would reduce our workload a lot.**

Consultation item no 5

1.3 There will be a coordinated assessment procedure (CAP) anyway, regardless of what anyone comments. While far from ideal, this could be a major step forward compared to the current situation. It is unfortunate that there isn't anything making topics b) and c) any easier. Maybe we could suggest to at least open the "mailbox" into which things are to be sent for "CAP" in a way that ethics committees (b) and local regulatory bodies (c) can access it to perform a "Single submission with separate assessment" type procedure if they so wish. That would open things towards a completely voluntary harmonization for ECs and local governing bodies and might be an option to reduce waste paper production / dissemination.

Consultation item no 6

1.3.2. Disagreement with the assessment report

⇨ Member states will not allow anything but option "opt out".

Or: the matter could be referred to the Commission or the Agency for a decision at EU level.

Consultation item no 7

1.3.3. Mandatory/optional use

⇨ It MUST be mandatory for multinational trials, otherwise, we will have gained absolutely nothing, as some member countries are bound to "opt out" here too

Consultation item no 8

1.3.4. Type A trials

This is the only place where a risk based approach might be introduced into regulation, and it should therefore be applauded. The definition, however, needs to be refined. We should point out that a trial must not be considered ineligible for "type A" just because it involves treatment of children or treatment outside of the licensed indication (We assume that the "standard in one country" will not make it through the assessment process and we therefore need to make sure about kids!)

Consultation item no. 9

Yes, we should agree!

Consultation item no. 12

The letter states that there is confusion regarding the definition of SUSARs and SAEs between the member states. However, the definitions seem to be clear, but probability the implementation is very different. A potential solution for academic multinational phase III studies could be to exclude many SAEs from being reported - and limit reporting to true SUSARs and/or to ICU admissions, etc. In other words: to modify reporting requirements for safety based on risk and clinical relevance.

Consultation item no. 14

2.4.2. Policy options

We fear that, whatever we say, most of our pediatric trials will not be considered "low risk" (see below). Therefore, we should go for option 2. (Member states should be under obligation to provide for a compensation for damages incurred during clinical trials in their country according to their legal system.)

The proposals concerning the insurance are not very helpful for our GPOH trials. In case of reducing the insurance only for trials with drugs which are not "off label" (which is hardly the case in pediatric trials) or the treatment can be considered as a standard therapy (this implies not an additional risk for the patient), we don`t see any opportunity to avoid an expensive and not very useful insurance.

Consultation item no. 15

Realistically, one must agree with the appraisal, we have learned a lot about sponsorship. The EU should endorse efforts which make sponsoring an investigator initiated multinational trial attractive for academic institutions!

Consultation item no. 16

2.6 Emergency clinical trials

This is not only a problem in case of emergency. It is a problem for rare diseases. For these diseases (e.g. promyelocytic leukaemia 8 pediatric cases/year will be seen) more than 50 centers have to be initiated for a trial and most of them will never have such a patient. Therefore an initiation of the center should be possible after the patient accrual and after starting treatment, because no delay can be accepted.

18. April 2011 T. Klingebiel and U. Creutzig for the GPOH