Consultation item no. 1

The single submission has both its merits and limitations. It is true that it would reduce the administrative work of sponsors. However, its "price" should not be much more difficulty for the assessing national competent authorities. We should take it into account that, at present, there are still some administrative differences between member states regarding clinical trial submissions such as insurance, suitability of investigators and trial sites, etc. This means that, inevitably, there are some country specific requirements for submissions. If a harmonised format for the electronic submission is created that is also capable to handle these country specific requirements, one single submission package could be compiled by the sponsor and we see no real workload differences if it is sent to one single point or parallel to all concerned member states.

Consultation item no. 2

We could not agree with the appraisal completely. The rate and reasons of separate assessments leading to contradictory decisions has not been analysed in detail.

Consultation item no. 3

We do agree with the appraisal that a centralised assessment would not be feasible.

Consultation item no. 4

The catalogue in the Concept Paper is complete (if fees remain in the national competence). However, it is questionable that all "aspects under point a) would be suitable for the CAP". The crucial point is the assessment of "the characteristics of the intervention compared to normal clinical practice". "Normal clinical practice" is still not fully harmonised over the member states. Its simplest form (that gave rise to negative decisions in our country in the past) is that the comparator product had not the indication to which the trial was conducted, approved in Hungary. (It should be emphasised that divergent decisions originated from non-harmonised indications are *not* the consequence of different clinical trial assessments but that of the will of the marketing authorisation holders of the comparator products, failing to harmonise the SmPCs over the EU and the weaknesses of the Community-interest referral system!)

Consultation item no. 5

We do agree to include aspects under a) (only those) if the harmonised submission has a mandatory chapter in which the applicant states and explains he analysed the "normal clinical practice" concerned (the approved indications of the comparator product included, if applicable) in all member states where the application is valid and found no differences.

Consultation item no. 6

As the last word, only the "opting out" justified on the basis of a "serious risk to public health" is acceptable. Any referral would lengthen the process and making the European clinical trials much less attractive then at present. Moreover, existing objective differences between member states (see e.g. that in no. 4) may not be eliminated by "voting and simple

majority", the rather because Ethics Committee opinions (and the subsequent divergent decisions) could not be harmonised by such a voting.

However, this issue is much more complicated then indicated in the Concept Paper. Authorities rarely make a "yes-or-no" decision they rather require slight modifications or ask questions. As indicated above, there may be differences between member states in this field. The sponsor is then to decide whether accepts the modification and/or answers the questions or withdraws the trial from that country. The indicated "accepting the CAP positive decision or opting out" is not lifelike.

Consultation item no. 7

We'd prefer if CAP would be optional. (e.g. there's no point in CAP if the trial is to be conducted in only one memberstate). The EU(or EMA) can issue some guidance about when it is recommended to use CAP.
We'd not suggest making CAP mandatory – especially until there's no experience with it. The VHP project started two years ago and the procedure is still under modification based upon the recent experiences. Moreover, less then 5% of all applications are submitted via VHP. Based on these experience we believe it would be risky to make a very new procedure mandatory from the first moment.

Consultation item no. 8

The indicated pre-assessment would be ideal. However, it is not workable! For instance, definition Type A is very similar to a Phase IV trial ("minimal risk trial"). In the recent past, withdrawals of the marketing authorisations of certain medicinal products were the consequences of results of such trials. How should we explain to the public that they were "minimal risk" ones? In general, how to explain if a trial classified as a "minimal risk" one causes serious adverse effects? Surely the assessors have a perception on the risk of a given trial when evaluating the non-clinical (and/or previous clinical) data but it is just a perception, if the risk could be foreseen exactly, conducting the trial would be superfluous!

Moreover, the assessor should go through the documentation. The time needed for it is the same for all trials. If there is a pre-evaluation of the perceived risk, the time gained by the later shorter assessment is counterbalanced by the time needed for the pre-assessment!

Consultation item no. 9

First let us point out that the present definition of a "non-interventional trial" only states that it is not a clinical trial. However, it is nowhere stated that it is also not a "biomedical research". Thus, in Hungary, non-interventional trials need ethics committee approval plus authorisation (in one step) based on the general "biomedical research" rules (not less complicated than a clinical trial). Not addressing this issue but changing the scope of the "non-interventional trial" would by no means simplify the issue.

In theory, emphasising also that the definition of the "non-interventional trial" should be in line with the new pharmacovigilance regulation, we do agree with this appraisal.

Consultation item no. 10

We agree with the appraisal. From the patients' safety point of view, we see no difference between commercial and non-commercial ("academic", "investigator-initiated", etc.) trials. (Remark: there is no civil service fee for the latter in Hungary, it is the only difference.)

Consultation item no. 11

Ideally the presented solution might work. In practice, in the real life – we have some definite doubts; see our answer to item 8.

Consultation item no. 12

Harmonisation of the format of electronic clinical trial submissions over member states is suggested.

Consultation item no. 13

In theory, the difference in the definitions of IMP and non-IMP could be of value, although it has already been reflected in the relevant guidance.

In practice, it has an implication which is outside the scope of the clinical trial authorisation. Namely, Insurance Administrations in some member states are very keen on excluding the scope of reimbursement/financing any medicinal product that is connected with the conduct of a clinical trial (e.g. rescue medication covered). A too strict (i.e. legal) differentiation between medicinal products used in a clinical trials may have unexpected drawbacks in national legislations.

Consultation item no. 14

We do not agree with policy options one or two either. First, risks can not be totally excluded from clinical trials; consequently, all trials should be covered by insurance. Second, it is not up to the Community law-maker or member state authorities to decide on the perceived risk, its probability and its compensation; it is up to the insurers! The present legislation not requires the same insurance for all clinical trials, the insurance fee (and the insured compensation) depends on the risk. Thus, in practice, the issue is solved.

Consultation items no 15.

The Concept Paper is completely right; in some languages the same (or similar) term(s) describe both "responsibility" and "indemnity".

We prefer to maintain the concept of the single sponsor, at least one single ("responsible") sponsor per member state.

Consultation item no. 16

The conditions described here are too general. The first two ("the subject is not in the state..." and "the physical or mental conditions… are necessary characteristics of the research population") are valid for all incapacitated subjects (see Article 5 of the Clinical Trial Directive). The third condition: the "urgency" is very broad; there is a big room for its

interpretation. The forth condition is not “lifelike”; there is no Civil Code provision to “objection to conducting a clinical trial on me in an emergency situation”.

The emergency trial provision should be tightened mostly to oxyology trials. Any wording to facilitate this would be welcome (the present one is not!). Moreover, in the Hungarian legislation there is an additional provision to emergency trials: “to all possibility, it will serve the interest of the patient”.

Consultation item no. 17

Agreed!

Consultation item no. 18

We have no additional comments.