12.15 Joint Statement by the CP and the European Federation of Pharmaceutical Industries' Association (EFPIA)

Adopted in Athens, April 1995
(CP 95/016 Rev. 2)

The medical profession, represented by the Standing Committee of European Doctors (CP) and the pharmaceutical industry, represented by EFPIA, each aware of its responsibilities vis-à-vis patients and society, consider it essentiel to establish a framework for their relationship, particularly in the fields of information, advertisement, medical press, clinical trials and continuing medical education for doctors.

These two independent organisations have agreed to meet regularly, in order to seek, jointly and with due regard for patients interests, greater efficiency and the independence of each party, the best approach in each of these specific fields. Their work will be geared to the following objectives:

Clinical trials and pharmaco-epidemiological studies
The cooperation between the pharmaceutical industry and the medical profession in conducting clinical trials and pharmaco-epidemiological studies is essentiel to the development of medicinal products as well as to their through knowledge and their optimal use.

Each trial or study must pursue a scientific and therapeutically relevant aim without being developed primarily for promotional purposes. This aim must be stated beforehand. Protocols must be drafted in such a way as to ensure that this aim is achieved and to ensure the validity of the conclusions of the study.

In the performance of these trials and of pharmacological studies, ethical and professional rules (namely the Helsinki Declaration) as well as scientific principles and quality assurance (namely codes of good clinical practice) must govern the relationship between the investigator and the promoter, and the investigator and the patient.

Medical information
To ensure that medicinal products are used appropriately, both from a clinical and a scientific viewpoint, the prescribing doctor needs to be well informed about the full range of therapeutic means available to him.

Due to the body of knowledge it accumulates, namely through its collaboration with the medical profession, the pharmaceutical industry is an important source of information to doctors.

Doctors must be in a position to obtain objective, complete and unbiased information on issues relating to drugs' effects.

This information must be governed by strict codes and ethical principles in accordance with existing legislation and Codes of good practice. The latter need to be emphasised and widely distributed.

Continuing medical information
The pharmaceutical industry has traditionnaly supported medical training. Co-operation in this field shall be transparent, conducted according to professional codes and shall safeguard the independence of continuing medical education.

12.16 Good Clinical Practice, CP Comments

(CP 96/138 Final)

Re: Draff Directive on the approximation of provisions laid down by law, regulation or administrative action relating to the implementation of Good Clinical Practice in the conduct of clinical trials on medicinal products for human use.

(Comments of the CP transmitted to Mr *DeBoyser* [DG III], 26 September 1996)

Introduction
The draft directive on the implementation of Good Clinical Practice has a clear goal: to harmonize the ethical and scientific review and approval of clinical pharmaceutical research in the EC. Its encompasses phase I to IV studies, mono or multi-centre trials in one or more EC countries.

In order to reach this goal several new elements are introduced:

- in the case of multi-centre trials a single opinion of an ethics committee shall suffice for a particular member state (art. 3.1.)
- the scientific evaluation of a multi-centre trial in more than one member state can be performed by one of the competent authorities involved (art. 5.2.)
- approval by a competent authority for any pharmaceutical trial is needed before starting the trial (art. 5.2., 5.3. and 5.4.)
- the starting of a database concerning approved trials, accessible only by the competent authorities (art. 6.1.)
- a system of inspection of research sites (art. 10.)
- a system of clinical safety reporting (art. 11.).

Comment
In general it can be applauded that additional rules are being developed regarding the implementation of Good Clinical Practice. It is of major importance that some of the current problems are addressed. These problems can be identified as:

1. the absence of one 'location' for the ethical and scientific review of multi-centre studies within member states
2. the absence of information on clinical trials in progress, their results, those withdrawn or stopped (and the reasons why) and the safety risks involved

3. the lack of control on the compliance with the provisions of GCP by inspection at research sites
4. the absence of clinical safety reporting in ongoing trials.

Hence, several elements of the proposed draft can be strongly supported such as the scope (including phase I to IV studies) and both the control and safety reporting system (art. 10 and 11), although the latter invokes some specific comments.

However, the medical profession have a number of specific comments on the solutions proposed in the draft text.

Preamble

In the preamble three important instruments are indicated to ensure the trial subject's protection (i.e. control of clinical trials by ethics committees, control by competent authorities and the protection of individuel data). It is strongly suggested to make clear that these means all have the same weight, for instance by making an indention in the text. E.g.

– 1) control of clinical trials by competent authorities
– 2) control of competent authorities
– 3) protection of individuel data.

Article 1

With regard to the glossary in article 1 two recommendations are

– 1) in the definition of clinical trials it should be emphasized that clinical trials may be mono- and multi-centre trials.
– 2) in the definition of an ethics committee it is stated that it should also consist of 'non-medical/ non-scientific members'. This should not imply that so-called lay members of an ethics committees cannot have an academic education. We recommend that the text says "an ethical committee should also consist of non-medical members".

Article 2

In this article the role of ethical committees is defined. The term 'opinion' used to indicate the conclusion of an ethics committee cannot be accepted, since it has no effective power. We recommend the word 'advice' to be used instead since it would then create a need to justify any deviation from that advice.

In article 2.1. it seems to be the case that sometimes trial subjects have to pay for participating in the trial. This, however, must be rejected. If patients are willing to participate in a study – thereby accepting the burden and risks attached to that – it is unethical to ask for payments in addition.

Article 3

Article 3.1. states that each member state shall establish a procedure 'whereby a single opinion of an ethics committee shall suffice for that member state'. This article tries to find a solution for the lack of one 'location' in the case of multi-centre trials. The problem is, however, that it is very specific in its solution, leaving out good alternatives. It is not always necessary to have a single opinion of one particular ethics committee for a member state, provided all member states create a procedure to harmonize the workings of the committees of all the involved research sites. Hence it is suggested to change the second part of article 3.1. so that all member states shall "establish a procedure by which harmonization of all involved ethics committees in this Member State occurs". Therein one of the ethics committees (preferably that of the principal research site) might act as a coordinator for the procedure. Where advice from a single ethical committee is accepted for a Member State, it is strongly felt that that should be contained in the principle research site. It would have the responsibility of examining all the evidence. Other ethical committees would retain the power to either approve or disapprove that research in its own site, in principle on the basis of a summary of the evidence, taking into account the specific conditions of that site.

Article 5

In this article the scientific review is regulated, including an obligatory approval by a competent authority, which shall be valid for the Community.

The current draft of the guideline introduces a maximum amount of control, without a clear analysis of the pro's and con's of such a system. Although it is clear that more information is needed on trials before they make it to the registration phase (if ever), it is not clear whether this proposal will be effective. Importantly however, is that there is no information gathered efter completion of the trial. Since negative results are less frequently published, a serious form of publication (and information) bias is known to occur. Reporting the reason why a trial was ended, exist and a summary of the positive and negative findings to the competent authorities, is clearly necessary to improve the current situation.

A second point is the degree of bureaucracy involved by using an approval system throughout the Community.

Hence, it is strongly suggested to steer a different course, by introducing a compulsory notification system which consists of a notification at the beginning and at the end of any trial to the competent authorities of the involved member states. The competent authority will have a particular time period (e.g. two to four weeks) to respond. If no negative response is given within this time period, then the trial can be started. Obviously clear criteria should be developed for motivating a negative responset. Moreover, efter ending the trial, the reasons therefore, and a summary of the results must be made available to the competent authority, respecting the confidentiality of the data. Such a system would contain strict penalties for non compliance.

Article 11
In this article a system of clinical safety reporting is proposed. Essentially the system implies that:

- adverse events are reported to the sponsor (art. 11.2.)
- serious adverse events are immediately reported to the sponsor except for those events identified as not requiring immediate reporting (art. 11.1.)
- serious unexpected adverse reactions are to be reported to the member state in whose territory the reaction occurred within 7 to 15 days (art. 11.4.)
- each twelve months a line risting of all suspected serious adverse reactions, and a summary overview of the subjects safety, will be provided by the sponsor to the competent authorities (art. 11.6.)
- each member state shall notify the Agency of reports on suspected serious adverse reactions (art. 11.7.).

Concerning this article some comments can be made:

- it is not clear whether an ethics committee should ever be informed. As a minimum ethics committees should be adequately informed about serious adverse events and/or reactions, including of course cases of death. Ethical committees have responsibilities to those involved in any trial.
- it is not clear what criteria might be used to identify serious adverse events that need not be reported to the sponsor immediately. We consider all serious adverse events and reactions must be reported to the sponsor and the ethics committee as well. Cases to be reported to the competent authorities immediately need to be specified.
- 'unexpected adverse reactions' is not defined in art. 1.
- we fear that the frequency and amount of information concerning suspected serious adverse reactions to the competent authorities (line risting each twelve months) is insufficient and must be strengthened and made consistent with current pharmacovigilance systems.

Summary
In summary, the medical profession as represented by a working group of experts of the Comité Permanent, welcomes this initiative by the European Commission. In addition to our overall comments on the draft, we have identified specific proposals with regard to Articles 2, 3, 5 and 11. We would be happy to elaborate these views and comment on any future draft produced by the Commission.

CP Ad Hoc Working Group on GCP

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12.17 Motion on CP as an International Association

Adopted at Rhodes, November 1995
(CP 95/131 Rev. 1)

The CP at its meeting in Rhodes:

– considers that an International Association has to be constituted;
– the statutes of this association will correspond to the rules of the CP orders;
– each National Delegation shall have one representative on the Board;
– the Associated Organisations shall have observer status within CP;
– the CP requests the group of jurists to examine the most convenient legal statutes, according to the Belgian law or any other one;
– the CP requests that the draft statutes and supplementary rules of such an association be submitted at the next meeting.

12.18 Self Medication in Europe

Adopted at Athens, November 1996
(CP 96/36 Final)

Common position of the CP, UEMO, UEMS

Definitions
Self-medication is the use of over-the-counter medicines by patients (or their parents/guardians where appropriate e.g. minors) without either diagnosis- or symptom-oriented advice by a physician or a pharmacist.

Guided, pharmacist-assisted self-medication is the use of over-the-counter medicines after symptom-oriented advice by a pharmacist.

Treatment is the use of over-the-counter and prescription medicines after the diagnosis-oriented advice by a physician.

The aim of self-medication and of guided pharmacist-assisted selfmedication is the prevention, relief or the healing of symptoms or signs associated with minor ailments. Another aim of self-medication maybe towards substitution therapy (such as vitamins and mineral substances).

The aim of medical treatment is the prevention relief or the healing of diseases.

Responsibility
In the case of guided, pharmacist-assisted self-medication, the pharmacist bears the full legal responsibility for advice and/or products dispensed. Where in the case of "Treatment" it is the physician who has the responsibility.