〈抄録〉 第 22 回 日本臨床薬理学会年会 2001 年 12 月 14~15 日 横浜
招待講演 1

Implementing the New European Good Clinical Practice Directive-Opportunities and Challenges

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The EU comprises 15 member states with a population of 370 million people. A fundamental objective of the EU is to guarantee the free movement across national borders of people, capital, goods and labour.

In the pharmaceutical area-medicines constituting goods-moving towards a single market has brought about a number of major undertakings, increasingly in cooperation with other major players such as the United States and Japan. Most activities have been directed to establishing the legal framework and guidelines for drug development, drug approval and drug surveillance acknowledging the significant contribution by the International Conference on Harmonisation (ICH) guidelines. Since 1995 there is in place a European Community (EC, the legislative body) system for drug approval and surveillance allowing the pharmaceutical industry the possibility to obtain European authorisations valid in all member states without having to spend resources on a country to country approach.

Contrasting the situation for the drug approval process, there is yet no EU system in place for the approval of multi-centre clinical trials (CT) protocols for studies to be conducted in more than one EU country. All CT protocols are handled nationally, the systems vary between countries and there is no cooperation across borders.

Since the 1960ies Independent Ethics Committees (IECs) have been established in EU, now operating

in accordance with ICH guidelines. However, there are national differences pertaining to operational procedures. Most notably, the coordination of multi-centre CTs ranges from decisions by the IEC of the principal investigator valid for all sites to consensus decisions at the national level.

There is no approval process for CT protocols by the drug regulatory authority in Germany or the Netherlands. In the United Kingdom an approval is needed for phase II-III studies but not for phase I studies. In other countries there are different kinds of approval or notification processes to be complied with prior to commencing a trial.

In the Good Clinical Practice (GCP) area the EC issued a legally binding directive in 1991 which incorporated earlier recommendations on the proper conduct of clinical trials according to GCP. The ICH GCP guideline took this process further recognising the need to conduct many trials on a global scale and that accordingly drug regulatory authorities (DRAs) have to assess data from a variety of geographical regions. In addition to the technical requirements both sets of documents outlined what would be expected from the IRBs/IECs in the drug development process in order to meet drug approval requirements in the major regions.

Early in 2001 the European Community adopted a more elaborate GCP guideline with the intention to harmonise scientific standards as well as administrative and documentary procedures in the conduct of CTs in the EU, while ensuring the safety of trial participants. In particular should be noted that time limits will be introduced for both the assessment of

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a clinical trial by a DRA and an IEC respectively. In both instances the time limit has been set to maximum 60 days but for trials involving gene therapy, cell therapy products and genetically modified organisms (GMO) there is the possibility for an extension by 30 days and by a further 90 days if a separate technical consultation is deemed necessary. With regard to multi-country multi-centre CTs there shall be only one IEC decision per country.

The directive shall be implemented in two years time. Considering the huge implications for many countries system- and resourcewise it will be a challenging task. On the other hand the directive should be seen as an important first step forward to improving the efficiency of the regulatory and ethics review procedures much needed in order not

to lose the competitive edge in international clinical drug development. The long-term objective clearly being to arrive at a harmonised EU system for the handling of CTs minimising the number of decision levels, providing EU decisions on interstate protocols and a logical link to the EU approval system.

There is an increasing understanding of the importance of conducting CTs in the EU countries not only to the benefit of EU based pharmaceutical industry but also in order to attract US and Japanese CT investments. Overall these activities are regarded crucial for maintaining and extending a solid clinical research base in EU. In addition the carry-over effect of GCP to clinical practice in general with positive consequences for the quality of patient care is acknowledged.