The European Pharmacopoeia was inaugurated in 1964 through the Convention on the Elaboration of a European Pharmacopoeia. The present Fifth Edition of the European Pharmacopoeia is therefore published at the time where the 40th Anniversary of the Pharmacopoeia can be celebrated. The work on the Pharmacopoeia has gone through a remarkable development since the first difficult years.

Elaboration and approval of monographs and other texts proceed by an effective and smoothly running process producing public quality standards that keep pace with scientific progresses. The work is remarkable because of its volume: the Fifth Edition presents close to 2000 monographs and other texts - and because all technical requirements have to be adopted by the European Pharmacopoeia Commission by unanimous decision. The monographs of the Pharmacopoeia are legally enforced in the countries being signatories to the Convention on the Elaboration of a European Pharmacopoeia. In addition to the 31 European countries and the European Union now being parties to the Convention, the work on the Pharmacopoeia is followed by 16 European and non-European countries and the WHO as observers. The quality standards of the European Pharmacopoeia have, therefore, an impact on the quality of medicines, which goes far beyond the European region.

The Fifth Edition of the European Pharmacopoeia will become effective on 1st January 2005. Like the Fourth Edition, the present main volumes will be added to by three annual supplements implementing the decisions of each of the three annual Sessions of the European Pharmacopoeia Commission. The presentation of the Pharmacopoeia in a main volume and three annual supplements was initiated by the publication of the Fourth Edition. The intention was to increase the flexibility of the publication scheme and, in particular, to shorten the time span between adoption and enforcement. The shortening of the time span, which has indeed been successful, is possible only thanks to a very flexible attitude by those countries that make national translations of the European Pharmacopoeia monographs. A very low number of rapid revisions implemented in the past three years is another result of the new publication scheme. The Fourth Edition is completed with the publication of Supplement 4.8 since it is impracticable to work with more than the eight supplements. The Commission decided therefore to proceed to the Fifth Edition by consolidation of the Fourth Edition after three years, only. The change from First to Second Edition was caused by major changes in the general methods, while the change from Second to Third Edition was due to the wish to consolidate the work achieved and to change the form of presentation from a loose-leaf format into a main volume followed by annual supplements. The change from Fourth Edition to Fifth Edition continues the work of making the publication of the Pharmacopoeia as user-friendly as possible. It is assumed that the publication of this Fifth Edition will proceed by publication of supplements over the next three years.

The eight founder countries of the Convention realised in 1964 that manufacturing and quality control standards for medicinal products on the European market had to be harmonised for reasons of public health and to facilitate the free movement of medicines. Since 1964 the world has changed and the market for medicinal products has become global. Accordingly, international harmonisation among the three major pharmacopoeias of the world, the European Pharmacopoeia, the Japanese Pharmacopoeia and the United States Pharmacopoeia, has been in progress since 1990 when the Pharmacopoeial Discussion Group was set up to co-ordinate the harmonisation work. In the first years, the work was focused on the harmonisation of monographs on widely used excipients. In the absence of harmonised general methods this was a difficult work, which has now been speeded up by ‘harmonisation by attribute’ meaning that there may be tests that cannot be fully harmonised before the concerned general method is harmonised. At the stage where the monographs are harmonised, detailed information will be provided in the monograph and in a chapter of the Pharmacopoeia devoted to information on international harmonisation. In recent years, harmonisation of a wide range of general methods has been in progress, partly because of an impact from the International Conference on Harmonisation (ICH). Implementation in the Pharmacopoeia of harmonised general methods, for example for a dosage form specification, needs careful consideration because the specification must be met by products already on the market as well as new products submitted to the regulatory process.

The European Pharmacopoeia Commission supports strongly the international harmonisation. It is not the harmonisation work itself that gives rise to the greatest problems, rather the implementation, which has to be decided in mutual agreement with the registration authorities. The links between the European Pharmacopoeia Commission and European regulators have been steadily strengthened during the years, as have the links with the pharmaceutical manufacturers and their associations.

The new European Directives 2001/82/EC and 2001/83/EC on medicines for human use and veterinary use maintain the mandatory character of the European Pharmacopoeia monographs in the preparation of dossiers for marketing authorisation of medicines, which was instituted in the first directive 75/318/EEC in 1975. It means that the monographs of the European Pharmacopoeia must therefore be updated to keep pace with products on the market, with scientific progress, and with regulatory developments. In the field of active pharmaceutical substances, the European Pharmacopoeia Commission decided at its March 2002 Session that the principles and terminology of the revised ICH Q3A impurity testing guideline Impurities in new drug substances should as far as possible be implemented in the monographs on active substances, both new and already published. A change in terminology has been introduced in the Impurities section of monographs published in Supplement 4.6 and later where the term ‘specified impurities’ is used for impurities that have a defined individual acceptance criterion. A revision of the general monograph Substances for pharmaceutical use (2034) was also presented in Supplement 4.6 to implement the threshold values for reporting, identification and qualification of organic impurities in active substances of the revised ICH guideline. For the Fifth Edition a new chapter, 5.10. Control of impurities in substances for pharmaceutical use has been developed with great assistance by the chairs of the chemical Groups of Experts and other experts from the Commission, and by consultations of the Groups of Experts. The next step will be revision of monographs to ensure that they contain related substances tests and lists on specified and other detectable impurities. Monographs containing a related substances test based on TLC will be considered for revision. Major revision work will thus proceed during the coming years. Hopefully, these revisions can be completed with the publication of the Sixth Edition. In the meantime, users of the Pharmacopoeia must consult the new Chapter 5.10.
on impurity control for the interpretation of monographs published in the past and therefore adapted to a style that has now been changed as described above. Users can in addition find information on representative chromatograms, reagents and columns used in drafting the monographs on the EDQM web site.

The aim of the revision is to ensure that the related substances test and impurity lists reflect the purity of pharmaceutical substances being authorised for the European market. The goal cannot be met without close collaboration with the registration authorities and consultations regarding the specifications for impurities. A procedure for co-operation with the CPMP/CVMP Quality Working Party has been established. It will certainly contribute to ensure the validity of the European Pharmacopoeia monographs. The Certification of Suitability of Monographs of the European Pharmacopoeia might be a valuable source of information on the purity of pharmaceutical substances. The procedure is, however, confidential and will be kept so. In cases where a new impurity is present and calls for revision of the monograph, this can be done only when the manufacturer provides the concerned Group of Experts with the information required for updating.

The growing number of monographs on pharmaceutical substances and the need to keep them updated means a great workload on the Groups of Experts. In 2001, the number of chemical groups was increased and some reallocations of experts between the groups took place. There is, however, still a need for more experts with access to experimental facilities as permanent members of the Groups of Experts or as members on an ad hoc basis. In addition to the reorganisation of the system of Groups of Experts and Working Parties the working procedures for the elaboration of monographs have been expanded. In addition to Procedure 1, the traditional elaboration by a Group of Experts, and Procedure 2, adaptation of national monographs, which is now considered almost complete, Procedures 3 and 4 have been established in recent years. Procedure 3 applies to substances produced by only one manufacturer and which are close to patent expiry. The manufacturer and the national pharmacopoeia authority of the country where the substance is produced carry out the preliminary drafting stages and check the requirements experimentally. The draft is reviewed by the working party also responsible for the adaptation procedure and then processed in the usual way by public inquiry. Procedure 3 has proved successful. The Commission decided in 2002 to establish a modified version, Procedure 4. This procedure implies collaboration between the manufacturer of the substance and the EDQM on the draft monograph and experimental checking by the EDQM laboratory and laboratories of national pharmacopoeia authorities before publication for public inquiry. At present, Procedure 4 is run as a pilot project supervised by members of the European Pharmacopoeia Commission. It is the aim of the Commission to have a full coverage of monographs on substances no longer subject to a patent and being present on more than one European market. It requires the collaboration with the innovators and manufacturers of active substances, which has been established during recent years.

The Fifth Edition of the European Pharmacopoeia has a number of excipient monographs containing a non-mandatory section on functionality-related characteristics. The aim is to provide users with a list of physical and physicochemical characteristics that are critical to the typical uses of the concerned excipient, and to give the general methods required to assess these characteristics. The section does not necessarily give acceptance criteria for the concerned properties; this is usually left as an option for labelling by the manufacturers and where specified, the values are indicative only. This is a new development which is in agreement with the policy of the European Pharmacopoeia Commission to make monographs and other texts appropriate to the needs of regulatory authorities and manufacturers of starting materials and medicinal products. The intention is to provide manufacturers of excipient materials and manufacturers of medicinal products a "common language", to facilitate the establishment of product-specific specifications, and to provide regulators with data generated by methods that have been independently assessed.

It is the intention of the European Pharmacopoeia Commission to continue the work by drafting sections on functionality-related characteristics in monographs on excipients available in more than one physical grade. Introduction of the concept of functionality-related characteristics presupposes that the relevant general methods are available in the Pharmacopoeia. The European Pharmacopoeia Commission has therefore established a Working Party on synthetic polymers to investigate the need for general methods for polymers and a Working Party on powder characterisation methods. The provision of the needed general methods, for example in the field of powder characterisation, is also included in international harmonisation among the pharmacopoeias.

The achievements of the European Pharmacopoeia Commission during the past three years would not have been possible without the participation of the great number of experts from industry, academia and national authorities, who have given their time and expertise to the work of Groups of Experts and Working Parties. The Commission is indebted to all these experts whose work is given on a voluntary basis. The Commission is equally indebted to the Chairs of the Groups and Working Parties who have the responsibility of guiding the work through and bringing it to term according to tight time limits. The Chairs are thanked for their contributions within the Groups and also for their advice and counsel to the Commission itself.

The work of the European Pharmacopoeia Commission is strongly dependent on an effective Secretariat. The role of the Secretariat is to obtain and process all the information and reports needed for the Groups of Experts, Working Parties and for the Commission, to undertake laboratory work to support the experts and to ensure the availability of all the reference standards needed to allow the requirements in the monographs to be tested. The prompt publication of the Pharmacopoeia main volumes and Supplements and the on-line electronic version is possible, only, because of dedicated and hard work by the staff at the Secretariat.

Along with the growing volume of the European Pharmacopoeia and its adjustment to the regulatory process, the use of the Pharmacopoeia and its interpretation has become rather complex. The journal of the European Pharmacopoeia, Pharmeuropa, is a valuable source of information. General chapters for information will appear in the Pharmacopoeia during the publication of the Fifth Edition as a result of the international harmonisation, and because the European Pharmacopoeia Commission has agreed on the elaboration of other chapters for information. During the past two years, the staff at the EDQM have offered training courses to users of the Pharmacopoeia. The Commission is grateful to the EDQM for having taken this initiative, which also strengthens the role of the Pharmacopoeia and the links to its users. The links to users of the Pharmacopoeia are also strengthened by
the frequent workshops and conferences organised by the EDQM. This activity is highly valued by the Commission as it gives the opportunity to Commission members to exchange viewpoints and to discuss new developments with experts from authorities, industry and academia. The EDQM website is another valuable source for information on the work programme and other activities of the Commission, its Groups and the EDQM.

During the past three years I have had the honour to serve the European Pharmacopoeia Commission as its elected chair. The task has been challenging but, certainly, rewarding because of the insight it has given me into the many quality aspects of the development, manufacture and marketing of medicinal products. I wish to thank members of the European Pharmacopoeia Commission for their support and collaborative spirit within and in between the Sessions of the Commission. The two vice-chairs of the Commission are thanked for good collaboration and support during the years we have joined the Presidium. I will also thank the staff at the EDQM, in particular the secretaries to the Groups, for their kindness, enthusiasm and hard work for the benefit of the Pharmacopoeia. Finally, I wish to express warm thanks to the Director of EDQM, Dr. Agnes Artiges, and her deputy as secretary to the European Pharmacopoeia Commission, Mr. Peter Castle. I have appreciated our collaboration during the three years and wish to express heartfelt thanks to both for their support to the chair and for the tremendous work they are doing to develop the European Pharmacopoeia and its role in the European regulatory system.

Professor, Dr. Henning G. Kristensen
Chair of the European Pharmacopoeia Commission