ABSTRACT. Regulations and guidelines on radiopharmaceuticals are under development within the European Economic Community. Implementation in national legislation will take place during the next few years. Regulations on medicines in the European Community (EEC) are being further developed particularly in relation to the 1993 open market. The nineties present a further challenge to radiopharmacy.

1. INTRODUCTION

Radioactive substances used for diagnosis and therapy in nuclear medicine and research (radiopharmaceuticals) were recognized as medicines in some European countries more than 20 years ago, while in other countries this will not happen until the first of January 1992, when European Community directives require national regulations to be established. This paper confines itself to the conditions for the 12 European member countries of the EEC. Radiopharmacy activities were in the earlier days of the sixties and seventies particularly developed in the nordic countries and in the United Kingdom. The first production of radiopharmaceuticals according to pharmaceutical principles was carried out in Norway already in the fifties. Nordic radiopharmacists prepared a GMP guide for radiopharmaceuticals (1) and the Nordic pharmacopoea published the first monograph on radiopharmaceuticals in Europe (2). Such work was later continued by the Nordic Council of Medicine which has prepared reports that have been used as the basis for more general European work (3,4). Good Radiopharmacy Practice (GRP) has been further developed in the United Kingdom (5,6).

Numerous are the unpublished contributions by pharmacists, chemists and other in Europe that has formed the basis of European radiopharmacy as expressed at this and the 3 previous symposia on radiopharmacy and radiopharmaceuticals (7,8,9)

Through this work there is a basis that, if further developed, will form a solid basis for a reasonable uncomplicated introduction of regulations on radiopharmaceuticals.
2. PHARMACOPOEA STANDARDS

Standardisation of medicines was first introduced through pharmacopoeaeas. A convention on a European pharmacopoea was signed by a number of European countries in the sixties as the basis for the European pharmacopoea published in 1973. Most European countries are now members of this pharmacopoea. An expert group has developed monographs for radiopharmaceuticals. Including those under preparation a list of monographs now cover more than 30 radiopharmaceuticals (10). A new area which should be useful to cover in a pharmacopoea is radiopharmaceuticals for Positron Emission Tomography (PET), as these, in most cases, are substances without any measurable pharmacological effect and where the quality standard is the main problem for National authority approval. This should be an area where a fruitful cooperation between Ph. Eur. and USP could be established as the USP has already published a monograph on F-18 fludeoxyglucose (11).

3. EEC-REGULATIONS ON MEDICINES

Quality, Safety and Efficacy of medicinal products have been of great interest to the European Economic Community since 1965:

"The primary purpose of any rules concerning the production and distribution of medicinal products must be to safeguard public health. However this objective must be achieved by means which will not hinder the development of pharmaceutical industry or trade in medicinal products within the community" (12).

In 1965 the first council directive on "The approximation of provisions laid down by law, regulations or administrative action relation to proprietary medicinal products (65/65-EEC)" was approved. This started a procedure that finally within the next few years will lead to a European registration of new drugs. In the mid-seventies some guidance on the registration of drugs was published but it was not until the eighties that a real breakthrough in European work in this field took place. Many guidelines were published and many more are now under preparation. Table 1 gives a list of most of the guidelines published. These give the basis for harmonization of the system in different countries (13).

Within the framework of a multistate application procedure common ideas have also been developed by the CPMP (Committee for Proprietary Medicinal Products). During the last few years a substantial number of cases has been referred to this committee for an opinion.

This committee has also functioned as the scientific body for the obligatory concertation procedure which was established for high technology medicinal products in 1987, particularly those derived from biotechnology. The system may also be used for other new products if the manufacturer so wishes. In all such cases no National authority may make any decision on an application for registration before consulting the CPMP however the final decision is always made by the national authorities. This directive also applies to radiopharmaceuticals but has so far only been used in a few cases for radiolabelled monoclonal antibodies and a single radioactive therapeutic agent.