Regulations and Education of Radiopharmacy/Radiopharmacists (Europe)

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• “The direction in which education starts a man will determine his future life”
  Plato (427-347BC), The Republic

• “Laws are like sausages. It’s better not to see them being made”
  Otto von Bismarck (1815-1898)

Regulation (History)

• EU conglomerate of growing number of sovereign states
• In the pantheon of Greek mythology, Europe was a princess, daughter of Phoenician king. One day, while she and friends frolicked on beach, Zeus, highest Greek god, saw her and immediately fell in love with her. To seduce her, Zeus took the form of a kind and peaceful bull. Europe, confident, began to caress the bull and sat down on its loin. That was the moment that Zeus was waiting for. Suddenly, he rose and galloped toward the sea, taking her away with him. The bull Zeus didn’t stop swimming until he arrived in Crete. Once in this Mediterranean island, Zeus assumed again his human form and had three children with Europe, one of them, Minos, king from Crete and “Dux Europaeus”.

Regulation (History)

• There is a risk of seeing the European integration process as an isolated process, exclusively centred in the period after World War II. This view reveals a clear misunderstanding of the great transformations that shaped a reality known as Europe.
The Roman Empire constituted the first great effort to integrate an important section of the European continent and lands surrounding the Mediterranean.

Middle Ages brought the idea of unification under the common banner of Christendom.

Ascendancy of euro-centrism and the superiority of the European civilization.

Without Renaissance and Enlightenment we cannot understand the ideas of tolerance, freedom, respect of human rights and democracy that constitutes the foundation of the European construction.

In 1923 the Austrian Count Coudenhove Kalergi founded the Pan-European Movement. In 1926 he managed to bring together diverse political figures in the First Pan-European Congress held in Vienna.

1946, former British Prime Minister Winston Churchill gave a celebrated speech at Zurich University (Switzerland). It was considered by many as the first steps towards European integration in the postwar period:

“I wish to speak to you today about the tragedy of Europe ... Yet all the while there is a remedy which, if it were generally and spontaneously adopted by the great majority of people in many lands, would as if by a miracle transform the whole scene, and would in a few years make all Europe, or the greater part of it, as free and as happy as Switzerland is today. What is this sovereign remedy? It is to recreate the European Family, or as much of it as we can, and to provide it with a structure under which it can dwell in peace, in safety and in freedom. We must build a kind of United States of Europe ... The first step in the recreation of the European Family must be a partnership between France and Germany.”

European Council instituted in 1975 as a periodical meeting of Heads of State.

In 1979 the European Monetary System (EMS) came into force.

End of military dictatorships in Greece (1974), Portugal (1974) and Spain (death of Franco in 1975) made possible the inclusion of these nations. Greece, in 1981, and Spain and Portugal, in 1986, became new members of the EEC.

In 1984 a group of European MPs, chaired by the Italian Altiero Spinelli, introduced to Parliament a new Treaty of the European Union.

They intended to obtain approval for a new treaty to substitute the original document that was signed in Rome and constituted the first advancement towards European integration.
• On 22 July 1964, Belgium, France, Germany, Italy, Luxembourg, Netherlands, Switzerland, UK sign a European convention "on the elaboration of a European Pharmacopoeia"
• Contains monographs on radiopharmaceuticals

In 2003 EANM proposed Guidelines for Radiopharmacy
• In 2005 EANM published Good Radiopharmacy Practices Guidelines
• Disparity between practises within Europe
• Variation from “on the bench” manufacturing to total GMP

• UK leading European countries in terms of GMP
• 1976: Breckenridge Report recommended that preparation of IV injections be carried out in pharmacy departments rather than on wards
• NHS Pharmaceutical Quality Control Committee recognised need for standards for aseptic preparation

• From 1995, MCA (now MHRA) recognise that all IV injectables have to be manufactured within the most stringent environments with strict quality assurance regimes
• In 1999 audits identified a need for strict standards to include products for short-term use (up to 24 hours from preparation)
• Radiopharmaceuticals part of latter regulations
Regulation

- Aseptic preparations are exempt from MHRA licensing requirements if following conditions are met:
  1) Preparation is carried out by, or under supervision of, pharmacist who takes full responsibility for quality of product
  2) Preparation use closed systems
  3) Licensed sterile medicinal products are used as ingredients, or sterile ingredients are manufactured in licensed facilities
  4) Products allocated shelf-life of no more than one week

Regulation (Current Practise)

- Virtually all radiopharmacies in the UK are MHRA licensed facilities
- No need for a pharmacist to run licensed facility, but required to have proven record of education/knowledge of aseptic preparation

Regulation (Definitions)

- Clean room: room in which number and concentration of viable/non-viable airborne particles controlled (temperature/humidity controlled too)
- Closed procedure: where sterile pharmaceutical is prepared by transferring sterile ingredients/solutions to pre-sterilised sealed container without exposing solution to external environment

Regulation (Practical Issues)

- Facilities: all operations performed only in a controlled workstation conforming to EU Guide grade A (laminar flow cabinet or pharmaceutical isolator)
- Workstation to be in either EU grade B or C/D workspace environment
Regulation (Personnel)

- The pharmacist or scientist in charge of the radiopharmacy should be knowledgeable in all aspects of aseptic preparation, including:
  1) GMP as defined by the EU guide
  2) Formulation
  3) Validation
  4) Aseptic processing
  5) Quality assurance
  6) Quality control

Regulation (Monitoring)

- Monitoring should include: environment and clean-air devices, the aseptic process (including staff validation with universal operator validation tests) and finished products
- Programme of monitoring to include:
  1) Finger dabs (sessional)
  2) Settle plates (sessional)
  3) Surface sampling (weekly)
  4) Active air sampling (quarterly)

Regulation (Peripheral/other issues)

- Controlled cleaning of the workspace
- Product approval
- Storage and distribution
- Internal/external audit
- Capacity/contingency planning
Education

• In Europe, radiopharmacist and radiopharmaceutical scientist used interchangeably
• Skills required: working knowledge of microbiology, chemistry, physiology/pharmacology and radiation physics

Education

• Productions of radiopharmaceuticals permitted in two ways:
  1) Under terms of Manufacturing (Specials) License, necessary to identify Production Manager and Quality Control Manager (one or other could be a clinical scientist and not a pharmacist)
  2) Without a license, this can be performed under direct supervision of a radiopharmacist/pharmacist

Education (Pharmacist training)

• Four-year degree course, followed by one year postgraduate attachment to qualify for membership of professional society (i.e. Royal Pharmaceutical Society)
• During final year one gains radiopharmacy experience
• Postgraduate course for PTQA includes radiopharmacy modules

Education (European Training: VirRAD)

• Started in 2002; virtual learning platform
• Difficulty to teach radiopharmacy since disparate group from many backgrounds
• EANM has specialisation certificate in radiopharmacy with courses in Germany, Switzerland, France and Slovenia (see later)
## Education
### (European Training: VirRAD)
- See www.virrad.com
- Make radiopharmacy training accessible
- VirRAD is international consortium including radiopharmacy representatives from UK, Belgium, Portugal, Canada and USA
- Platform divided into:
  1) Virtual learning community
  2) Multimedia learning resource containing course ware
  3) Virtual radiopharmacy laboratory

## Education
### (European Training: INSTN/EANM)
- Jointly run European Radiopharmacy Course under auspices of EANM (Vienna, Austria) and Institut National des Sciences et Techniques Nucléaires (Saclay, France)
- Objectives:
  1) To improve radiopharmaceutical knowledge and training
  2) To be recognised as a radiopharmacist/radiopharmaceutical scientist

## Education
### (European Training: INSTN/EANM)
- Modular comprehensive course covering:
  1) European regulation and directives (radiopharmaceuticals, radiation protection, waste management)
  2) Production (isotopes, preparation of short-lived SPECT and PET pharmaceuticals)
  3) Quality control (physical, chemical, biological, pharmaceutical and equipment)
  4) Radiopharmaceutical preparation/manufacturing
  5) Pharmacokinetics
  6) Imaging problems linked to radiopharmaceuticals

## Education
### (European Training: INSTN/EANM)
- Research and development applications (radiopharmacology, biopharmacy of radiopharmaceuticals, toxicology, new trends, clinical trials)
- Medical applications (diagnosis, imaging techniques, metabolic therapy, radioecology)
Education (European Training: ETH, Zürich)

- Course run by ETH in Zürich, in conjunction with Institute of Pharmaceutical Technology (Frankfurt-am-Main) and Institute of Pharmacy (Leipzig)
  1) Module 1: Pharmacy 1 and legislation
  2) Module 2: Radiopharmaceutical chemistry
  3) Module 3: Pharmacy 2 and nuclear medicine

Education (European Training: postgraduate degrees)

- University of London offers two-year MSc in Radiopharmaceutics and PET Radiochemistry
- Universität Aachen (Jülich campus) offers two-year programme Nuclear Techniques in biomedical sciences for graduates of chemistry, physics, biology and biomedical engineering