New PET Radiopharmaceuticals: From Clinical Needs to Pharmaceutical Quality

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Positron Emission Tomography (PET) has become an established method for medical research and clinical routine diagnostics on patient individualized basis. Development and availability of new radiopharmaceuticals specific for particular diseases is one of the driving forces of the expansion of clinical PET. Clinical need is indeed the driver for this development.

Although 18F-fluorodeoxyglucose (18F-FDG) is still the most widely used positron emission tomography (PET) radiotracer, there are a few well-known limitations to its use.

The last decade has seen the development of new PET probes for in vivo visualization of specific molecular targets. Important technical advances in the production of positron-emitting radionuclides such as 68Ga has opened a new, brilliant future in the expansion of PET in oncology. Preclinical and clinical data for new prostate specific membrane antigen (PMSA)-based radiopharmaceuticals are particularly promising (1,2,3) also considering the extremely high incidence of this disease. Important progress in developing new radiopharmaceuticals for oncological PET has been also achieved, at least in preclinical studies, using long-lived radionuclides (124I and 89Zr) for labelling monoclonal antibodies.

Significant advances in the area of Alzheimer disease (AD) has been achieved by developing 11C-PIB-derived-18F-labelled radiopharmaceutical for imaging β-amyloid (4). More recent advances include the development of PET radiotracers for imaging aggregates of hyperphosphorylated tau protein in neurofibrillary tangles, a process that occurs late in the disease process (5).

As with any other medicinal product, it is of utmost importance to ensure by scientifically accepted procedures that quality and safety of new PET radiopharmaceuticals is adequate for their intended use. To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance incorporating Quality Control and Quality Risk Management. Albeit the current efforts for a worldwide harmonised regulation in the field of medicinal products for human use, legal requirements for preparation and use of radiopharmaceuticals both in clinical and research applications often differ from country-to-country. Furthermore, European regulations are interpreted in very different ways in the different countries of the EU. There has been a tendency to extend the cGMP regulations to all PET radiopharmaceuticals. It should be stressed that the application of European GMP for in-house small-scale preparation radiopharmaceuticals is a substantial hurdle for the development of clinical research in the academic environment. Recently, the European Parliament approved the new Regulation on clinical trials on medicinal products for human use (6), repealing the old Directive 2001/20/EC, reporting very relevant changes as compared with the previous Clinical Trial Directive. This new regulation will be of benefit for the nuclear medicine community, allowing the use of radiopharmaceuticals in clinical trials in an easier way than before.

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