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SPOTLIGHT

Spotlight on: guideline on current good radiopharmacy practice (cGRPP) for the small-scale preparation of radiopharmaceuticals published in EJNMMI Radiopharmacy and Chemistry (2021)6:8

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Radiopharmaceuticals play a central role in nuclear medicine imaging. Their binding properties and pharmacokinetics are a major determinant of the obtained PET or SPECT image.

Since radiopharmaceuticals are considered as medicines, their preparation is subject to the same legislation as for other drugs. One of the requirements is the application of Good Manufacturing Practice (GMP) which in the European Union is described in Eudralex Volume 4—Good Manufacturing Practice Guidelines.

Radiopharmaceuticals are either produced by industry or in hospitals. Industrially produced radiopharmaceuticals are often on a relatively large scale and are shipped to hospitals according to demand. Therefore, in this case, companies apply full GMP as they have sufficient resources to comply with GMP guidelines.

In hospitals, radiopharmaceuticals are often prepared on a much smaller scale and are used locally for only a few patients. Usually, these radiopharmaceuticals contain short-lived radionuclides locally produced using a cyclotron or eluted from a generator. Moreover, the commercial interest for such tracers is often limited and they are therefore not commercially available. The combination of the specific characteristics of locally small-scale prepared radiopharmaceuticals with the fact that in hospitals resources is much less compared to industry makes full compliance with regular GMP guidelines very challenging.

Therefore, the EANM Radiopharmacy committee has developed a set of guidelines for the small-scale preparation of radiopharmaceuticals according to current good radiopharmacy practice (cGRPP). With this set of guidelines, EANM offers hospital radiopharmacies guidance on how to ensure high-quality standards appropriate to the specific conditions for the small-scale preparation of radiopharmaceuticals (SSRP).

The recently published guideline is an update of the previously published guidance [2] and also refers to other documents that have since been published by the EANM: Guidance on cGRPP for SSRPs using automated modules: a European perspective [1], Guidelines on the labeling of leucocytes with ^{99m}Tc-HMPAO [8], EANM guideline on the validation of analytical methods for radiopharmaceuticals [4], and Guidance on validation and qualification of processes and operations involving radiopharmaceuticals [7]. Furthermore, this guideline refers to the current legislative documents issues by the European Union [3], Pharmaceutical Inspection Co-operation Scheme (PICs) [6], and IAEA [5].

The guideline provides a useful point of reference for hospital radiopharmacies, bringing together several documents published during the last 10 years to aid in the in establishment of quality standards for production of their radiopharmaceuticals. The guideline is in three parts: Part 1 contains general guidance with respect to quality assurance, personnel, premises, equipment, documentation, production, quality control and outsourced activities which applies for all diagnostic and therapeutic radiopharmaceuticlas. Part 2 contains guidance on the preparation of radiopharmaceuticals from licensed components (generators, radionuclide precursors and kits). Part 3 contains detailed guidance on the preparation of radiopharmaceuticals from non-licensed components, including the production of

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PET-radiopharmaceuticals from cyclotron-produced radionuclides using synthesis modules and other specialized equipment.

The following topics are addressed:

In part 1, the use of a risk-management approach in the quality assurance (QA) system is emphasized. Furthermore, the requirement of having a responsible person for radiopharmaceuticals (RPR) is promoted, whereas in the general EU GMP guidelines, a qualified person (QP) is mentioned. It must be highlighted here that the requirement for certification of radiopharmaceuticals by a QP is dependent on the type of product and applicable national legislation. Furthermore, the importance of having systems for handling deviations, changes, out of specification results (OOS) and corrective and preventative actions (CAPA) is stressed. Regarding personnel, it is described that sufficient staff must be available who have appropriate education and training. This can be offered by EANM/ESMIT at different levels, from e-learning to postgraduate courses and advanced courses. It is also stressed that, for outsourced activities, such as cleaning, monitoring, tests and qualification, written contracts should be in place.

Overall, in part 1, it is described how a high level of quality assurance can be maintained in a small hospital radiopharmacy.

In part 2, which covers preparation from licensed components, the following topics are explicitly described: premises and equipment, production, and quality control.

For production of SSRPs from non-licensed components, as described in Part 3, a dedicated quality management system is recommended. Furthermore, besides the RPR, a separate production manager and quality control manager should ideally be available. For these radiopharmaceuticals, automated synthesis systems are often used. Conditions for the use of such systems along with validation of production processes are described. Specifically mentioned are bioburden tests and identification of critical steps that can affect microbiology. Vendor qualification is discussed and it is recommended to perform supplier audits. EANM has taken the initiative to organize joint audits under the SASAI initiative.

In conclusion, the newly published guideline offers a comprehensive and up-to-date overview with reference to other applicable publications, and gives practical advice for hospital radiopharmacies with respect to the small-scale preparation of radiopharmaceuticals.

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