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Federal Department of Home Affairs DHA
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Division Radiological protection

Tc-99m radiopharmaceutical kits:

Aseptic technique related to preparation and quality controls

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Aseptic technique related to Tc-99m kits preparation: the situation in Switzerland

- One of the tasks of the Radiationprotection division protection of the Swiss Federal Office of Public Health is to regularly perform audits in the medical sectors involving the use of ionizing radiations
- An audit campaign on the preparation of Tc-99m radiopharmaceutical (RPH) kits was started in Switzerland end of 2012
- In the preliminary phase of this audit, it came out that both the existing infrastructures and the aseptic techniques used in the preparation of the RPH kits were quite heterogeneous
- At present, the Swiss ordinance stipulates that the preparation of RPH products has to be carried out following the Guidelines on Current Good Radiopharmacy Practice* (cGRPP), with some adpatation

*EANM, march 2007, www.eanm.org/publications/guidelines/gl_radioph_cgrpp.pdf

Cleanrooms, classifications

- **ISO 14644-1 cleanroom** standards
- US FED STD 209E cleanroom standards
- BS 5295 cleanroom standards
- **GMP EU classification**

Class	ISO 14644-1 maximum particles/m³						FED STD 209E equivalent
	≥0.1 µm	≥0.2 µm	≥0.3 µm	≥0.5 µm	≥1 µm	≥5 µm	
ISO 1	10	2.37	1.02	0.35	0.083	0.0029	

Class	GMP EU maximum particles/m³			
	At Rest	At Rest	In Operation	In Operation
	0.5 µm	5 µm	0.5 µm	5 µm
Class A	3,520	20	3,520	20
Class B	3,520	29	352,000	2,900
Class C	352,000	2,900	3,520,000	29,000
Class D	3,520,000	29,000	n/a	n/a

Cleanrooms, technical solutions

- From GMP (Good Manufacturing Practices): Grade A air (preparation area) in grade D air (environment).

- To stand-alone Biological safety cabinets: various norms, mainly defined by the number and quality of filters (preparation area), no specification regarding the environment.

Situation in Switzerland vs cGRPP: Preparation area

	cGRPP recommendations	Present situation in Switzerland
Workstation	• laminar flow HEPA-filtered grade A air or • a total containment workstation	• heterogeneous, from no specific measures related to clean air control to cGRPP recommendations.
Environment	• grade D air or • curtain of filtered grade A air	• heterogeneous, from simple air flow without special filtering to cGRPP recommendations.
Tc-99m generator	• should be placed in a grade A environment	• heterogeneous, from location in the environement of the laboratory without special filtering to cGRPP recommendations.

- The requirements in Switzerland are presently being revised, the cGRPP recommendations will presumably be followed

Situation in Switzerland vs cGRPP: Monitoring of aseptic conditions

cGRPP recommendations	Present situation in Switzerland
• workstation and environment should regularly be monitored with respect to microbiological quality (swabs or contact plates for surfaces, settling plates or dynamic air samplers for air quality). • new personnel have to be qualified for media fills and all personnel requalified at regular intervals. • sterility should regularly be controled on a random sampling following decay of radioactivity.	• heterogeneous, from no monitoring to full implementation of cGRPP recommendations.

- Possibilities offered to small institutes (usually isolated and not aware of state of the art practices) to apply the cGRPP recommendations by setting up a collaborations with larger institutes at cantonal hospitals accomodating bacteriology departments is under study.

Situation in Switzerland vs cGRPP: Training

cGRPP recommendations	Present situation in Switzerland
• only trained people should be responsible for and participate in the preparation and quality control of RPHs • personnel should be trained in quality systems, GRPP and regulatory requirements, in particular preparation, release, quality control and analytical techniques, cleaning, transport, calibration of equipment, working practices in the radiopharmacy, preparation of the individual doses, documentation, hygiene and pharmaceutical microbiology, microbiological monitoring	• heterogeneous, from no specific training related to aseptic techniques received during the course for radiology technicians to training related to cleanroom process techniques

- Possibilities offered to small institutes to get an external training and setting up of a course with the appropriate content in collaboration with larger institutes is at present carried out.

Situation in Switzerland vs cGRPP: Clothing and equipment

cGRPP recommendations	Present situation in Switzerland
• personnel should appropriately apply aseptic techniques throughout the handling of radiopharmaceuticals for injection, including the radiolabelling of kits • use of special clothing, sterile gloves, sterile vials, sterile syringues, sterile needles and sterile diluents	• heterogeneous, from use of no special clothing and partial use of sterile equipment to full implementations of cGRPP recommendations.

- Possible adaptations to combine the use of cheaper, regular equipment (for example gloves) and complementary work practices (disinfection prior to use, etc..) to achieve sterile conditions are being examined.

Situation in Switzerland vs cGRPP: Quality controls

cGRPP recommendations	Present situation in Switzerland
• according to the European Pharmacopeia or other Pharmacopeia. • final activity, labelling yield and/or radiochemical purity should be checked prior to any injection. • parameters such as particle size (if applicable), sterility, pH, and isotonicity should be controlled at regular intervals.	• usually performed • some lack of training or misinformation causes sometimes the use of unappropriate techniques or reactants • sometimes only performed per batch, not for each individual kit.

- A training in quality control is being organised to make up for the lack of experience or information.

Situation in Europe: ERPAN survey of 27th March

- Answers received from 5 countries
- In the majority of the countries, the authorities responsible for the Radiation safety and those in charge of the supervision of the Medical products are two different entities. Consequently, sparse information was received during the survey.
- Slovenia: the Radiation safety authority is not responsible for the requirements regarding the hygiene, no detailed information received.
- Sweden : following the cGRPP recommendations, with the exception that the Tc-99m generator should be in a grade C environment and that the safety bench should be a class II workstation (protection of the product and the user).

Situation in Europe: ERPAN survey of 27th March

- Norway (preparation of RPH not under supervision of Radiation protection authorities): following the cGRPP recommendations, with the exception that the safety bench should be a biohazard safety cabinet.
- France (preparation of RPH not under supervision of Radiation protection authorities): following the cGRPP recommendations.
- Germany (preparation of RPH not under supervision of Radiation protection authorities): special clothing must be used.

- SFOPH would be grateful to receive the contributions of the other countries in order to get a better view of the situation in Europe.