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PLANNING MEDIA FILL TEST AND ENVIRONMENTAL CONTROLS IN FILLING OF POSITRON EMISSION TOMOGRAPHY (PET) DRUGS

A.L. Viglietti[1], A. Davit[1], G. Perlo[1], M. Longo[1], R. Giuliano[1], A. Biggi[1]
[1]Nuclear Medicine Unit, Department of Radiology, AO S.Croce e Carle of Cuneo, Italy

BACKGROUND-AIM

PET drugs are produced by aseptic processing to have the final product free of microorganisms and endotoxins. The validation, after the sterilization with grade filter, of the filling process is mandatory to guarantee the sterility and the apyrogeniciy of the radiopharmaceuticals administered to the patients.
The aim of the study is to define a protocol to perform the Media Fill Test and environmental controls that, in accordance with the European regulation, fit our PET radiopharmaceuticals' filling method.

METHODS

We planned the following activities:
1. identification of the team (responsible of production, of quality control and of quality assurance) for the feasibility evaluation;
2. analysis of operational steps to be simulated, taking into account the worst case: the possibility of purchasing the radiopharmaceuticals;
3. identification of the critical aspects of the process and evaluation of the microbiological risk;
4. preparation of the flow chart reporting number and type of samples to be prepared during Media Fill;
5. identification of microbiological sampling points (settle plates, volumetric air and surface sampling as contact plates) in isolators and in the environment;
6. supply of the bottles and plates containing culture medium;
7. reading mode of the produced samples;
8. identification and training for the operators to be involved;
9. drafting of documents (worksheet for Media Fill – worksheet for environmental controls – report of data – report of investigation and corrective action)
10. definition of the acceptance criteria

RESULTS

Our analysis proved the need of simulating, in addition to the dose fractionation, the transfer of the purchased radiopharmaceutical from the primary vial to the one suitable for our dispensing system situated in isolator A; this phase is particularly critical since it involves the introduction in an isolator B of the vial containers, that coming from outside, breaking the contamination's class. As the transfer and the fractionation of radiopharmaceutical is performed using a closed system in isolators, the activity can be considered at low microbiological risk; we therefore decided to simulate the activities of a work-shift per operator.
To make the validation representative of aseptic manipulations occurring during clinical routine, we simulated, for each work-shift, the transfer of the radiopharmaceutical from two purchased vials (worst case) and the fractionation of 18 doses. The microbiological sampling, performed in accordance with the critical aspects emerged during planning, included: filter room, PET radiochemistry room, passbox, isolators A and B.

CONCLUSION

The team's work has led to an accurate analysis of all aspects of the process, with a final drafting of a working protocol representative of aseptic manipulations performed during routine activities as required by law and literature. In the light of the results obtained in validation of 8 operators, we think that the approach used to set- up the activities of aseptic process validation is positive because it would permit to analyze efficiently any deviation, allowing effective corrective actions.