QUALITY CONTROL AND ASSURANCE OF Tc-99m GENERATORS AND KITS APPLIED IN SAEC LABORATORIES

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Abstract

A briefe description of quality assurance and quality control system applied in SAEC laboratories for production of ^{99m}Tc- radiopharmaceuticals, is provided. The system includes documentation, procedures, releasing of the products and responsibilities. The system described here undergoes a continues development.

INTRODUCTION

Syrian Atomic Energy Commission had established a laboratory for production of Tc-99m Kits and generators in order to cover the demands of local hospitals. The products of this laboratory such as MDP, DTPA and PHYTATE kits and the eluate of the produced generators, are used in human being for diagnostic purposes, there fore any impurities or undesired forms of complexes which might affect the human health, image quality or localization of the radionuclides in the target organs should be controlled . in other word , in order to insure the efficacy and safety of products, several factors affect the quality should be controlled during preparation process and several properties should be tested after preparation. Precaution is taken to insure that all steps of process are carried out in accordance with the rules of GMP and GRP.

In order to achieve the requirements of the quality, a severe quality assurance system should be established and implemented. Such system should be written and revised by responsible persons and all the procedures to be applied and records of all relevant data must be documented.

THE ESTABLISHED QUALITY ASSURANCE SYSTEM
DESCRIPTION OF THE SITUATION

The radiopharmaceutical laboratory in SAEC has been designed and established in Co-operation with IAEA, where the rules for GRP were considered in the design and installation process. The area of the laboratory is about $100m^2$ which is divided in to three major parts which are: kit preparation, generator production and quality control laboratories.

The kit preparation lab consists of: clean room with LAF cabinet insuring class 1 environment, freeze drier, balances and filtration devices. laboratory for preparation of glassware and chemicals which contains equipments such as autoclave, pH meters, ultrasonic cleaners...., All spaces related to this lab . are considered controlled area.

Tc-99m generator laboratory contains: two hot cells which are provided with accessories and UV lamps for sterilization, in order to ensure higenity of internal environment , radio chemical hoods, isotope calibrator, working bench's, LAF for preparation of cold generator before loading it with Mo-99 in hot cell.

The quality control laboratory consists of radiochemical purity, sterility and pyrogenity tests, chemical purity test labs which contains gamma spectroscopy isotope calibrator, LAF cabinet, incubator and equibments for chromatography.

Quality is defined in different ways, but here we consider the quality as that products should satisfy the requirements specified by international standards. Quality assurance is defined in the guide of GMP as:' 'the sum total of the organized arrangements made by the object of ensuring that products will be of the quality required by their intended use.'' Quality control therefore can be defined in this context as" the verification of the quality of products to satisfy the predefined standard specification'' then the products can be accepted or refused according to these verifications.

Hence the quality assurance system specified in our laboratories consider xxII USP as standard specifications, and the quality control programme applied is a conformity control. The system of quality assurance consider all procedures from receiving raw materials to releasing final products, with emphasis on the qualifications and safety of the staff involved in the preparation and quality control process as, in accordance with guides of GMP and GRP, in order to ensure good quality products. The most important steps involve:

- Disinfection of premises, glassware. And equipment's.
- Calibration and verification of instrument in use.
-Testing of chemicals and raw materials.
- Documentation of procedures and records.
- Determination of responsibilities.

DOCUMENTATION

The Standard procedures for all aspects starting with cleaning and disinfecting processes , preparation, QC.. ending and releasing of final products are described in written forms and documented with related records. The Records for all procedures should be signed by the persons involved. All QC Mecords should be signed by QC manager and the certificate of releasing the product should be signed by quality control manager and the head of the laboratory.

About 10 procedures and about 30 records are specified for the preparation and quality control of the Kits. Also similar numbers of procedures and records are expected for generators production.

THE QUALITY CONTROL SCHEME FOLLOWED IN THE LABORATORY

As mentioned before the radio pharmaceutical production laboratory in SAEC has been designed and established in co-operation with IAEA guide lines of GRP considered in the design and installation process. Although all procedures are carried out according to predescribed

procedures and all necessary precautions are considered during preparation process, products are undergone tests for quality with accordance to specified procedure and the results of these tests are compared with defined limits(Standards) in order to confirm the validity of the products (conformity tests).

Both prepared Kits and generators are undergone specified tests where they share some of them and here we will review each of them. Freeze-dried Kits are sealed under vacuum and them they are tested for physical chemical and radio chemical purities. Then the investigations are continue for sterility, pyrogenity and biodistribution in rats. In very rare cases bioscan investigations are carried out on rabbit. The main tests applied for quality control for generators are: the performance, the elution efficiency, the Mo-99 break through, the radionuclidic purity, the chemical purity, the radiochemical purity, physical purity, as well as sterility and pyrogenity.

Physical properities include appearance, color and pH value. Chemical purity in the Kits concentrate on the stannious content and in the eluate of generators concentrate on the alumina and (sodium chloride) contents. Stanious is determined iodometrically while aluminum is determiened by complexing with chromazurol-S.

Radiochemical purity for both Kits and generators eluates. are investigated using ascending chromatography, where the proportions of pertechnitate, hydrolyzed reduced technetium and technetium complexes are determined and compared with the allowed limits. Biodistribution of the Tc-99m labeled complexes in rat were investigated by intravenous injection of about technetium complexes are determined and compared with the allowed limits. Biodistribution of the Tc-99m labeled complexes in rat were investigated by intravenous injection of about 0.1-0.5 mci of Tc-99m in the tail. After about two hours from the injection the rat is scarified and the relevant organs are counted in fixed geometry. The biodistribution is calculated as the ratio of the activity in the organ to the total activity. In the case of DTPA Kits, the rat is counted after one hour from the injection and after one day, then the rat is scarified and the relevant organs are counted.

Sterility measures are considered for all steps of preparation by sterilization of all equipments and reagents in use, but also further tests are carried out on the final products.

The sterility tests were carried out using two media which are fluid thioglycolate and Soya bean casein. Incubation is carried out for two weeks at 35C° for FTM and at 25C° for SCD. Negative results indicate the sterility of the products.

Test for pyrogen is carried out using limulus amebocyte lysate (LAL) test where positive and negative standards are used for comparison .

Radionuclidic purity of generators eluate and the Mo-99 breakthrough are assayed using a precalibrated gamma spectroscopy while the efficiency of the generator is determined using isotope calibrator.

CONCLUSION

As mentioned above quality of control Tc-99m radiopharmaceuticals and generators produced in SAEC laboratories undergoes long series of tests to ensure their validity for human use. The overall system of quality assurance applied also undergoes continuos development via research and training in order to keep our products competitive with others.

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