QUALITY CONTROL AND ASSURANCE OF RADIOISOTOPES AND RADIOPHARMACEUTICALS

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Routine - In the Centro de Radiofarmácia (CR) of IPEN, several quality control essays are performed on the final products ranging from primary radioisotopes to radiopharmaceuticals (labeled molecules) and ready-to-use kits for labeling with technetium-99m. In order to determine biological and physicochemical characteristics of the products as predicted by international pharmacopoeias and in accordance to the Current Good Manufacturing Practices (cGMP) for pharmaceutical production, the following quality controls are performed:

Biological Tests - Sterility, pyrogenicity, biological distribution, toxicity, and stability.

Physicochemical tests - Physical appearance, humidity determination, particle size and pH as well as chemical, radionuclidic and radiochemical purities.

Accessories, water, solutions, and environment are also subject to quality controls.

Development - The guide to cGMP defines Quality Assurance as the "total sum of organized routine made with the purpose of ensuring that products will be with the quality required". Great emphasis is placed on the process control in the assurance of final product quality. According to ISO 9001:2000, the quality policy is the continuous improvement of the quality of products and services. In this focus, analyses have been developed to obtain more safety and accuracy in the quality control tests as described bellow.

Radiochemical purity - In ready-to-use kits, primary radioisotopes and labeled molecules, radiochemical essays are performed by paper chromatography and gamma counter detection.

Determination of aluminum in ^{99}Mo-^{99m}Tc generators - Aluminum impurity in ^{99}Mo-^{99m}Tc generators has been determined by UV-VIS spectrophotometry.

Radionuclidic purity of ^{123}I, ^{131}I and ^{201}Tl - The presence of radionuclidic impurities: ^{124}I in ^{123}I, and ^{200}Tl and ^{202}Tl in ^{201}Tl production are determined in a high purity Ge detector.

Determination of tellurium, thallium, lead, zirconium and tin - Tellurium is a possible chemical impurity in Iodine-131. Its determination is carried out by a spot test using stannous chloride salt and atomic absorption spectrophotometry. Control quality of lead ion impurity in ^{201}Tl production is also determined by atomic absorption methodology and thallium ion by a colorimetric method with Rhodamine B. The determination of zirconium in eluate of ^{99}Mo-^{99m}Tc Generator with Gel Column is carried out by spectrophotometric method, in which the complexing dye is xylenol orange. In the production of freeze-drying kits ready to label with 99mTc, stannous chloride salt ($SnCl_2.2H_2O$) is used. The determination of the ion stannous in the salt is performed by titrimetric method with cerium(IV) and by atomic absorption spectrophotometry. A polarographic method where tin speciation is possible, is being developed.

Animals for biological distribution in freeze-drying kits - As the animals are of a special lineage, improvements were made in the laboratory in order to follow the cGMP. A great deal of the radionuclides used in the production is imported, so there is an effort to develop some production processes in this Center. Many essays have been performed to validate the following nationalized products: ^{201}Tl; ^{131}I and ^{99}Mo-^{99m}Tc Generator with Gel Column.

Quality Assurance - There is a group responsible for control, maintenance and improvement of data generated in the production and quality control process and all documents from the CR Quality System. The accompaniment of non-conformities generated in the system and the attention to the fulfillment of ISO 9001 are also attributions of this group. The Quality Assurance Division coordinates the validation process and determines the expiration date of the products. After performing necessary tests to each batch of the products, the Pharmacist responsible for the Quality Assurance Division decides about the approval or rejection and liberates the final product to the user. The Certification ISO 9002:1994 has been changed in 2002 to Certification ISO 9001:2000, and then many documents have been revised in accordance to it.