Radiopharmaceuticals quality control: analytical methods validation

L. Carvalheira[1], T. G. Mello[1], M. A. V. Bastos[1], A. M. S. Braghirolli[1], E. A. L. Sampaio[1], L. C. M. Aleixo[1], J. L. da Silva[1], R. F. Silva[1], C. A. Custódio[1], E. A. L. Andrade[1], H. O. K. Hernandes[1], R. C. Nunes[1]
e-mail: luciana@ien.gov.br

[1] *Division of Radiopharmaceuticals – IEN*

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The quality control of radiopharmaceuticals depends on the kind of radiopharmaceutical to be administered. Injectable radiopharmaceuticals, for example, require more rigorous assays than oral administered ones. Generally, this quality control is a set of chemical, physicochemical and biological methods performed regularly. These assays indicate the level of impurities in the final product. An excess of impurities can cause adverse reactions for the patient or result in poor image quality, for example, If these substances do not exceed established limits, the product is approved for safety usage. Therefore, the quality of measurements is essential to assure data reliability.

The method of validation is a process used to confirm, through supporting evidence, if the analytical method is suitable for its intended use [1]. At the Nuclear Engineering Institute (IEN), the method validation will provide reliability for the analytical methodologies used in the radiopharmaceuticals quality control. Furthermore, this process will attend part of the good manufacturing practice guidelines which was established by the National Agency of Sanitary Vigilance (ANVISA). This regulatory agency provides a specific method validation guideline [2] that should follow a validation master plan (VMP). According to Amer [3], "the VMP is a scope document, which is intended to define and to enumerate critical systems to be validated and also the appropriate approach to validate them."

The IEN produces ^{18}F-fludeoxyglucose (^{18}FDG), ^{123}I-*meta*iodobenzylguanidine (^{123}I-*m*IBG) and ^{123}I-sodium iodide (Na^{123}I). The current formalized VMP is applied for the validation of analytical methods used in the quality control of these radiopharmaceuticals. According to this document, the qualification of instruments and laboratory glassware and the acquisition of reference standards were performed. The method validation for the aminopolyether assay completed in October 2011. This substance is also an impurity in the ^{18}FDG final product. The Table 1 displays the methods that have been validating since 2012. This schedule comprises the following steps: (a) pre-validation experiments test, protocol elaboration and formalization, (b) protocol adjustments and experiments execution, and (c) the evaluation of results and the elaboration of a validation report.

Table 1: Schedule for methods validation.

	2012		2013					
^{18}FDG	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**Ma**	**Jun**
Bacterial endotoxin	a	a	b	b	b	c	c	
Radiochemical purity			a	a	b	b	c	c
Radionuclidic purity		a	b	b	b	c	c	
Residual solvents	a	a	b	b	b	c		
Sterility	a	a	b	b	b	b	c	c
	2012		**2013**					
^{123}I-mIBG	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**Ma**	**Jun**
Bacterial endotoxin	a	a	b	b	b	c	c	
Radiochemical purity		a	a	a	b	b	b	c
Radionuclidic purity		a	b	b	b	c	c	
Sterility	a	a	b	b	b	b	c	c
	2012		**2013**					
Na^{123}I	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**Ma**	**Jun**
Radiochemical purity			a	a	b	b	c	
Radionuclidic purity		a	b	b	b	c	c	

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