Validation of an in-house process for the production of Sodium [^{18}F]fluoride radiopharmaceutical

Marija Atanasova Lazareva[1,2], Maja Chochevska[1,2], Katerina Kolevska[1,2], Maja Velichkovska[1], Filip Jolevski[1], Ana Ugrinska[1,3], Emilija Janevik-Ivanovska[2]

[1]University Institute of Positron Emission Tomography, Skopje, Republic of North Macedonia
[2]Faculty of Medical Sciences, Goce Delcev University, Stip, Republic of North Macedonia
[3]Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Republic of North Macedonia

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Background

- An original in-house method for the synthesis of Sodium [^{18}F]fluoride radiopharmaceutical was designed and developed.
- The process validation of [^{18}F]NaF radiopharmaceutical production was performed with the aim to confirm the reproducibility of the process to produce a final product with consistent quality.

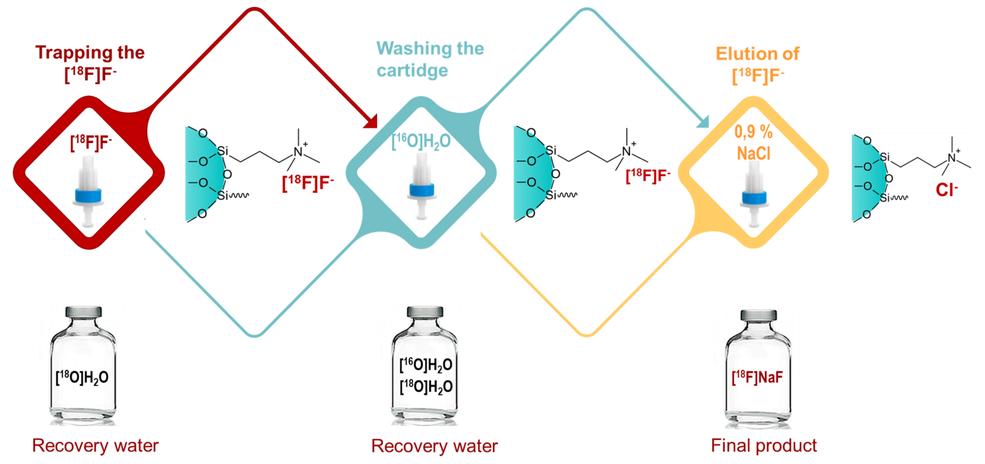
Materials and methods

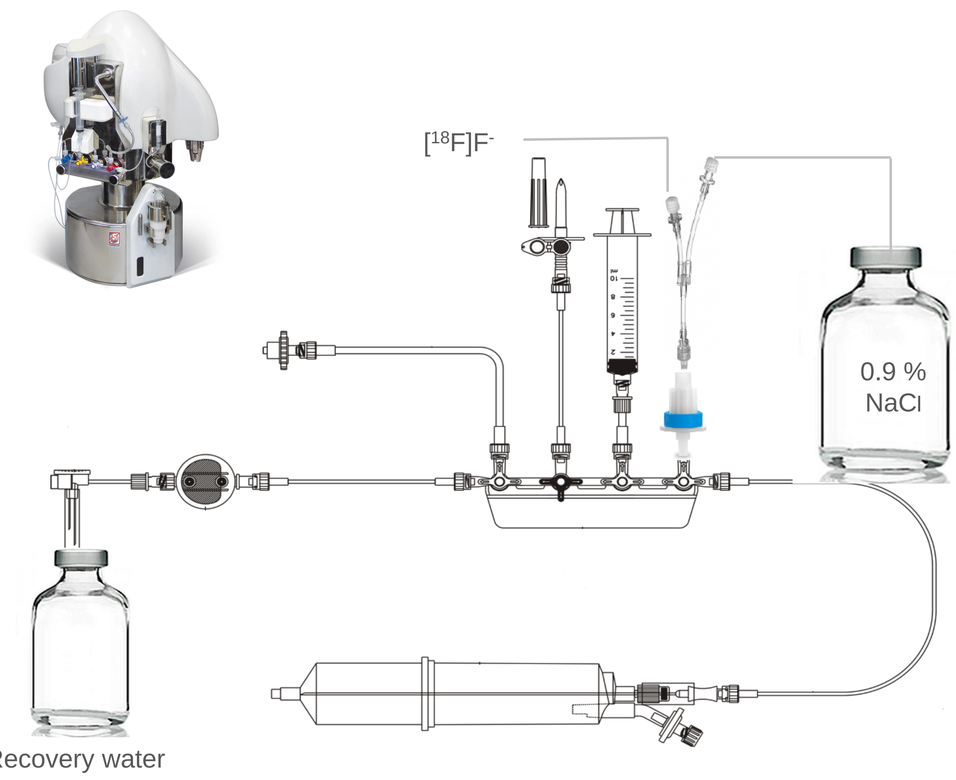
- The protocol for process validation was developed following the recommendations outlined in FDA Guidance for Industry Process Validation and EANM Guidance on validation and qualification of processes and operations involving radiopharmaceuticals.
- Three consecutive batches of [^{18}F]NaF were produced on different days under the same predetermined conditions.
- The production process (synthesis and dispensing) was carried out on the dispensing module Clio, using a modified single-use kit for dispensing. The modification involved installing a Y-connector and QMA cartridge on the kit.
- The quality of the final product should be in accordance with [^{18}F]NaF monograph of European Pharmacopeia.

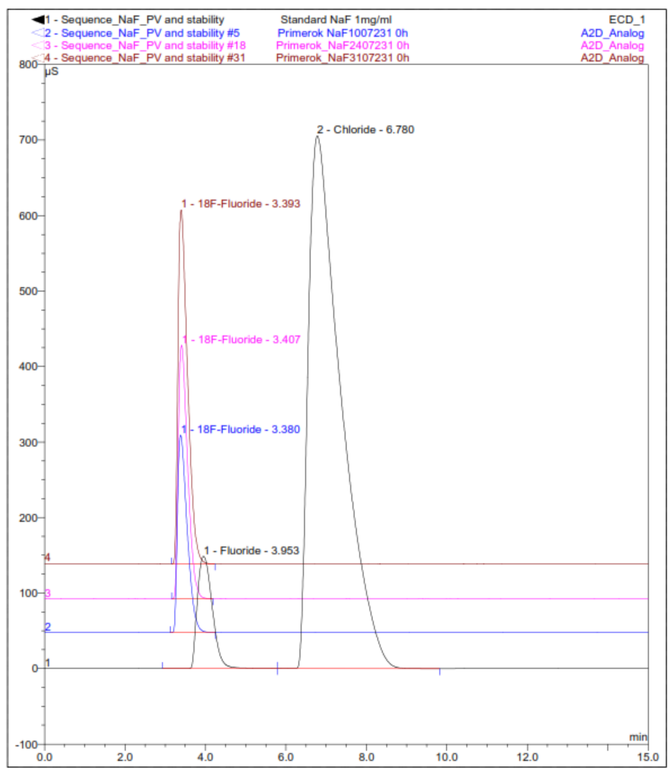
Results

- The results of tested quality parameters for the three batches were within the defined acceptance criteria.

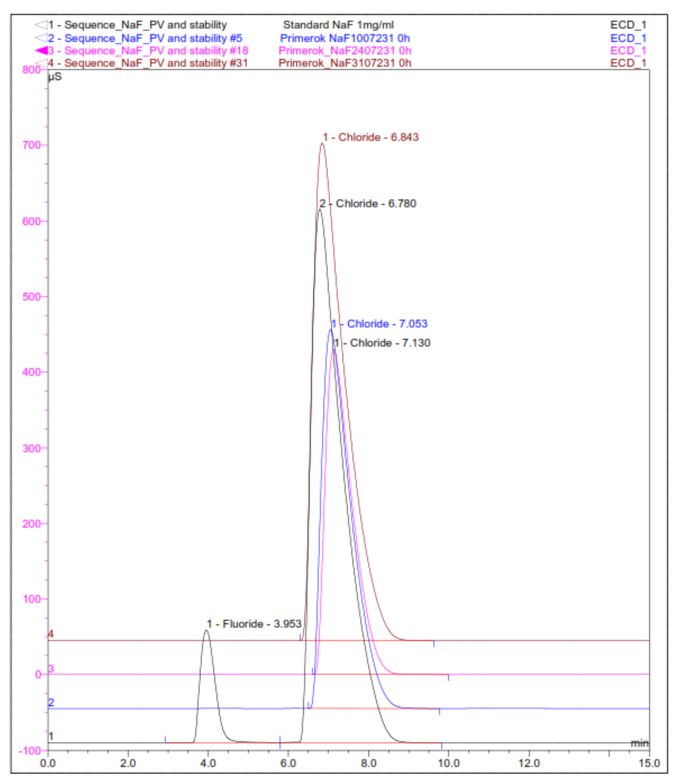
Test		Method	Acceptance criteria	Results		
				1 batch	2 batch	3 batch
Pre-release tests						
Appearance		Visual inspection	Clear, colorless solution	Clear, colorless solution	Clear, colorless solution	Clear, colorless solution
Identification	Half-life determination	Radioactivity measurement	1.75-1.92 hours	1.80	1.84	1.82
	Difference in retention time	HPLC	≤ 40 s	33.18	32.76	33.82
Approximate pH value		pH strips	5.5 - 8.0	6.5-7.0	6.5-7.0	6.5-7.0
Chemical purity: fluoride (F^-)		HPLC	≤ 0.452 mg/mL	≤ 0.452	≤ 0.452	≤ 0.452
Radiochemical purity: [^{18}F]fluoride		HPLC/gamma detector	min 98.5 % of the total activity	100	100	100
Release tests						
Bacterial endotoxins		Chromogenic LAL method	≤ 17.5 IU/mL	<5.00	<5.00	<5.00
Sterility		Test for sterility (Ph. Eur.)	Sterile	Sterile	Sterile	Sterile
Radionuclidic purity: radionuclidic impurities		Gamma-ray spectrometry	max 0.01 % of the total activity	8.83×10^{-05}	1.71×10^{-06}	1.63×10^{-06}







Radiochemical purity



Chemical purity

Conclusion

The process validation results confirmed that the in-house designed production process for manufacturing [^{18}F]NaF radiopharmaceutical is capable of consistently producing a product that fulfils the quality requirements defined in the European Pharmacopoeia monograph (Ph. Eur. 01/2008:2100).