11th Balkan Congress of Nuclear Medicine

Development and implementation of [18F]NaF radiopharmaceutical production at University Institute of Positron Emission Tomography

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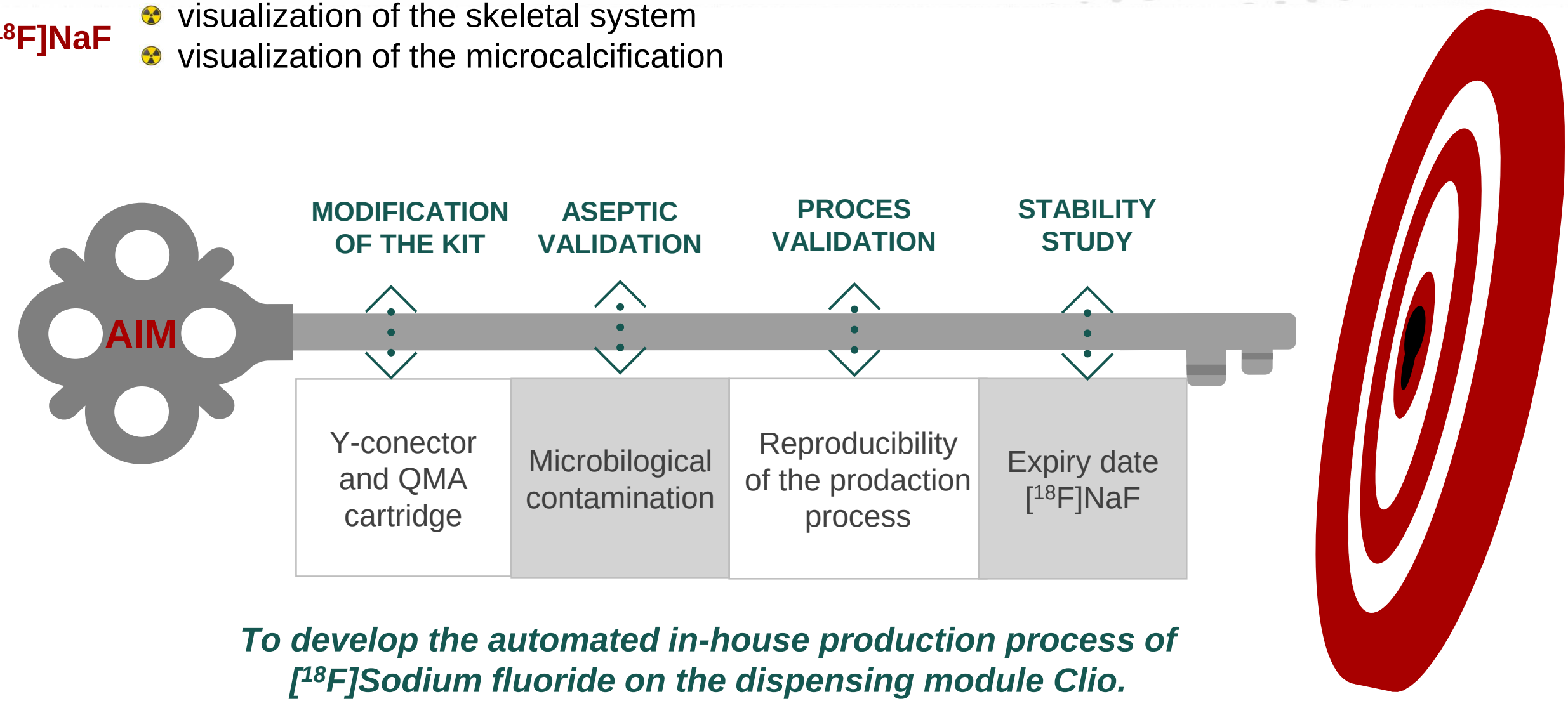
INTRODUCTION

[^{18}F]NaF

- visualization of the skeletal system
- visualization of the microcalcification



To develop the automated in-house production process of [^{18}F]Sodium fluoride on the dispensing module Clio.

[18F]NaF production

Dispensing module **Clio**

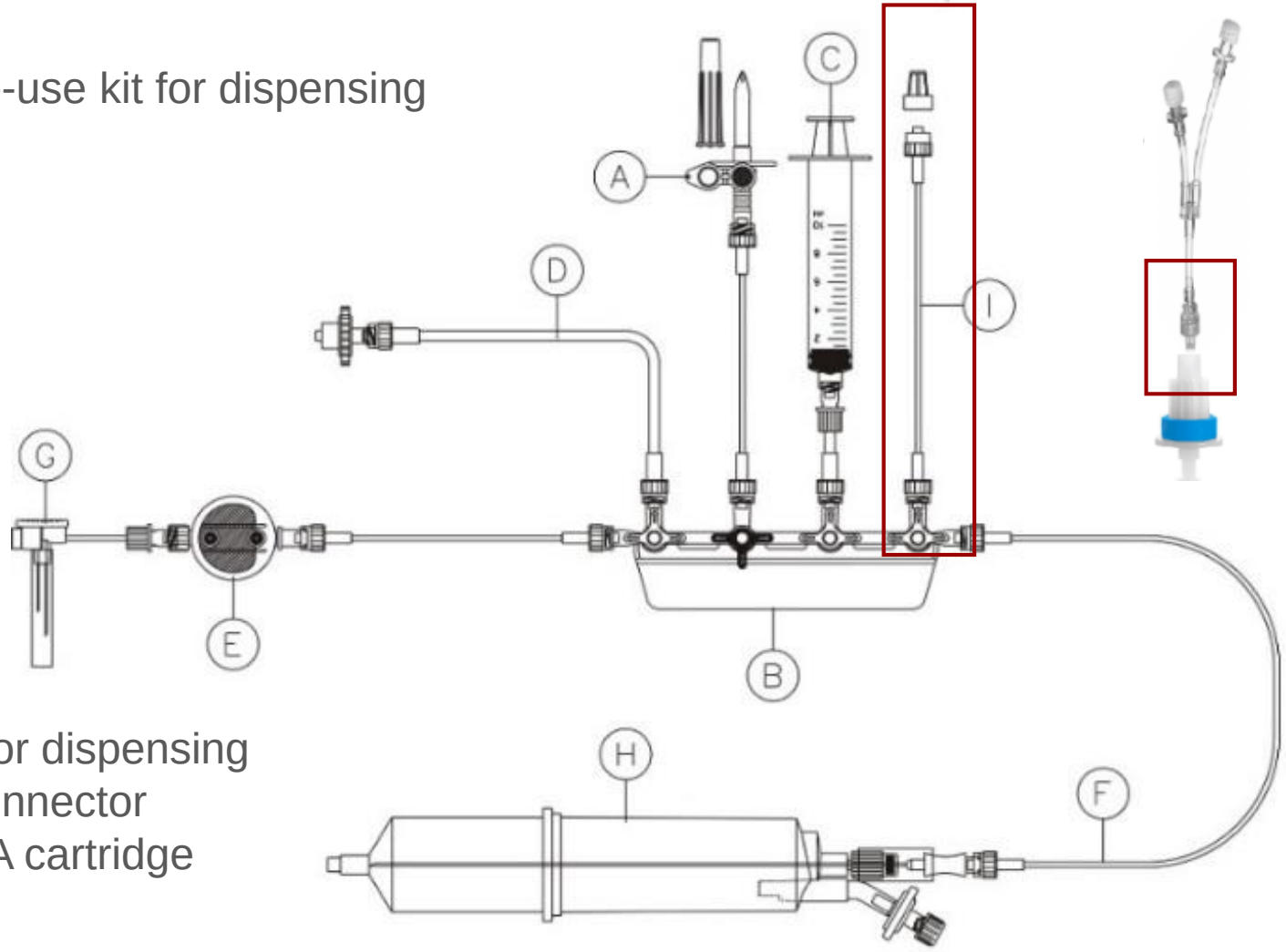
Dispensing of doses

- Single-use kit for dispensing doses

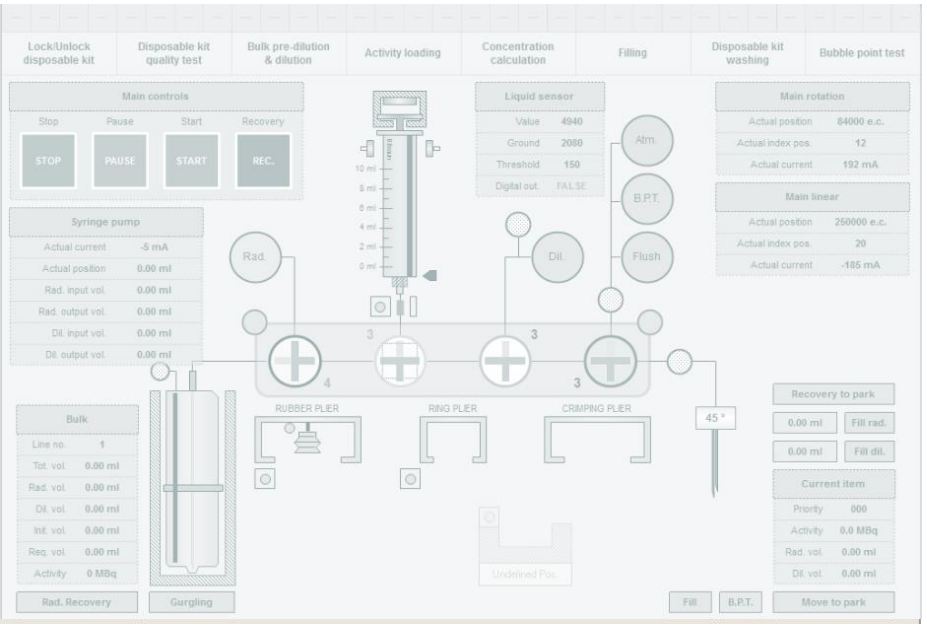
Synthesis and dispensing of [18F]NaF

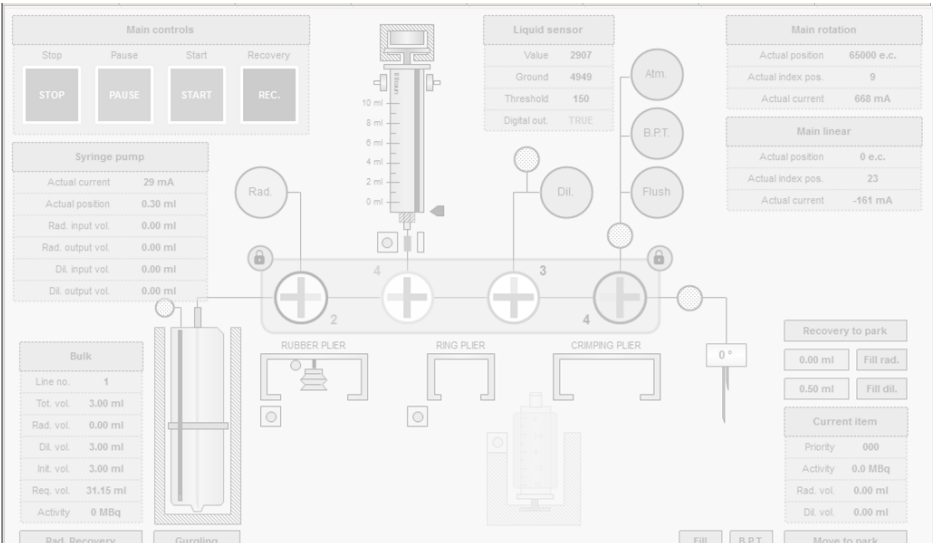
- Kit for dispensing
- Y connector
- QMA cartridge

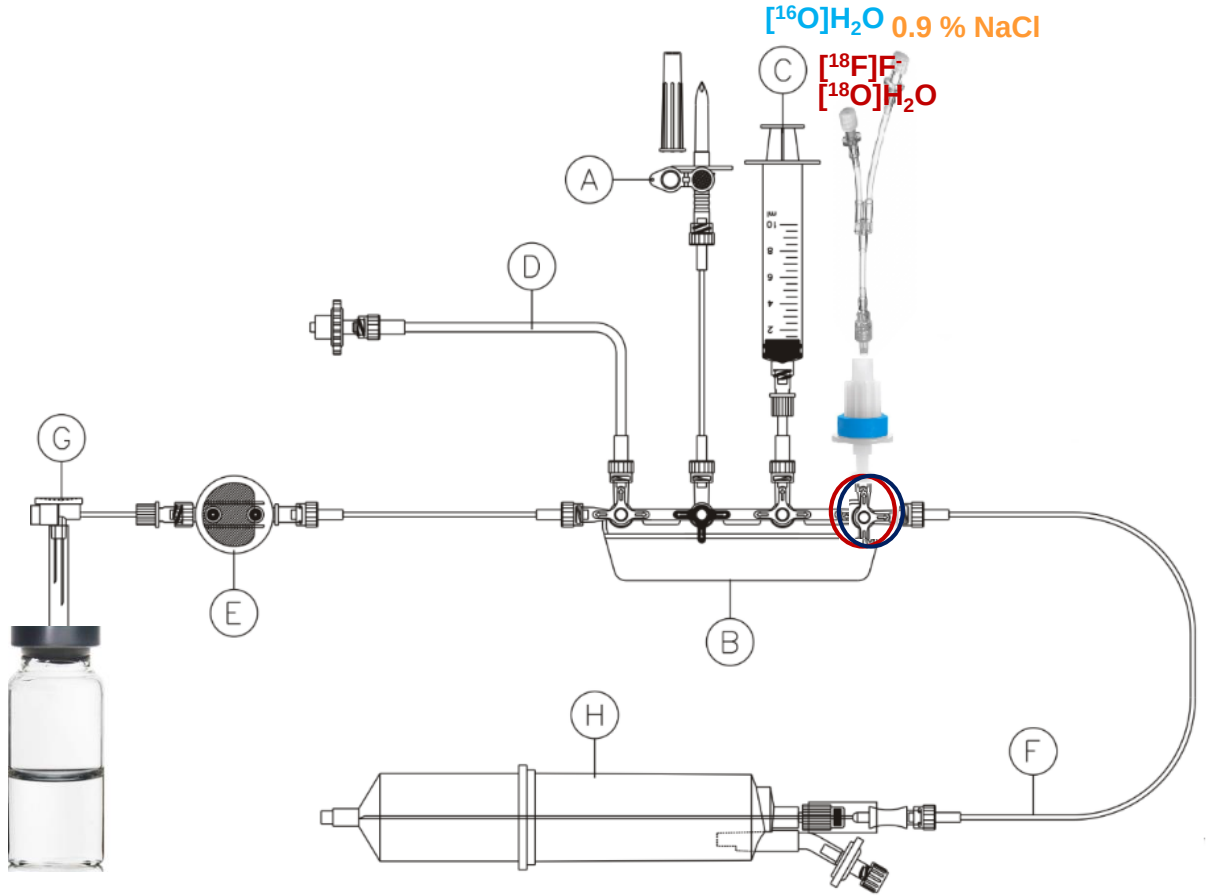
[18F]F-



[18F]NaF production







Quality control

RELEASE TESTS

01 Appearance

02 Identification

03 Approximate pH value

04 Chemical and radiochemical purity

POST-RELEASE TESTS

05 Sterility

06 Bacterial endotoxins

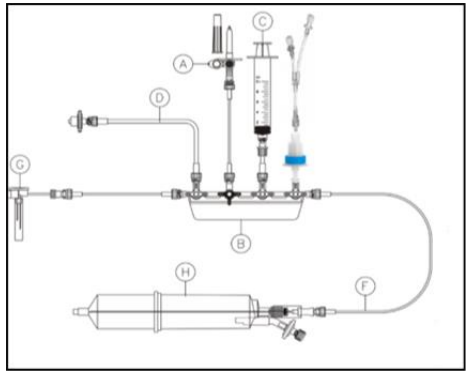
07 Radionuclidic purity

Aseptic validation

Aseptic validation

Bioburden

Simulation without filter for final sterilization



Media fill

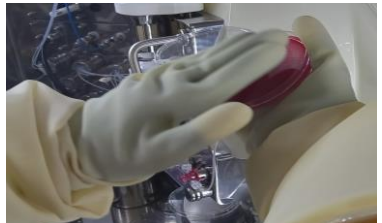
Simulation with microbial growth medium

Airborne particle and microbial monitoring

Particle counting in class A

Settle plates

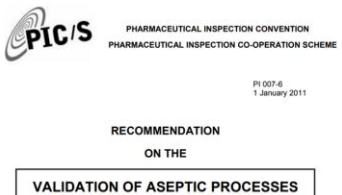
Glove print



Worst case scenario

Without radioactivity

Opened door between pre-chamber and chamber



Process validation and stability study

Tested parameters after 2, 4, 6 and 8 hours

- pH-value
- chemical purity
- radiochemical purity

3 batches
1000 MBq/mL

EOS → 02 → 04 → 06 → 08 → 10

- sterility
- radionuclidic puruty

Tested parameters: end of synthesis(EOS) and after 10 hours

- pH-value
- identification
- chemical purity
- radiochemical purity
- bacterial endotoxins

European Medicines Agency

August 2003
CPMP/ICH/2736/99

ICH Topic Q 1 A (R2)
Stability Testing of new Drug Substances and Products

European Medicines Agency
Inspections

London, 26 November 2008
Doc. Ref. EMEA/CHMP/QWP/306970/2007

COMMITTEE FOR HUMAN MEDICINAL PRODUCTS (CHMP)

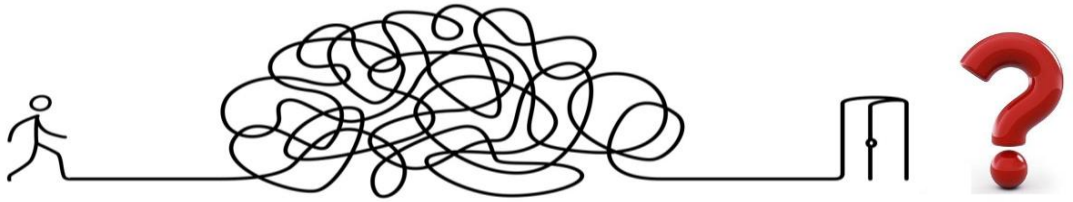
GUIDELINE ON RADIOPHARMACEUTICALS

Results

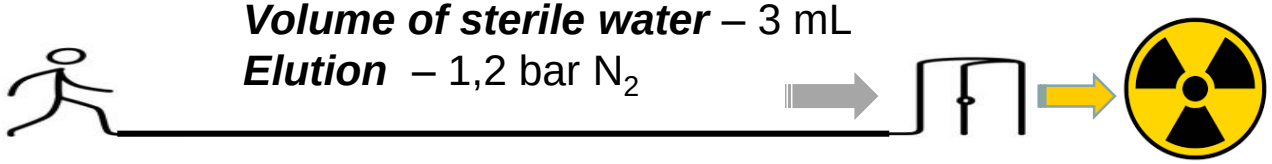
„COLD“ productions

Washing volume? Inert gas pressure?

Delivering time? Elution?



Delivering time – 2 minutes
Volume of sterile water – 3 mL
Elution – 1,2 bar N_2



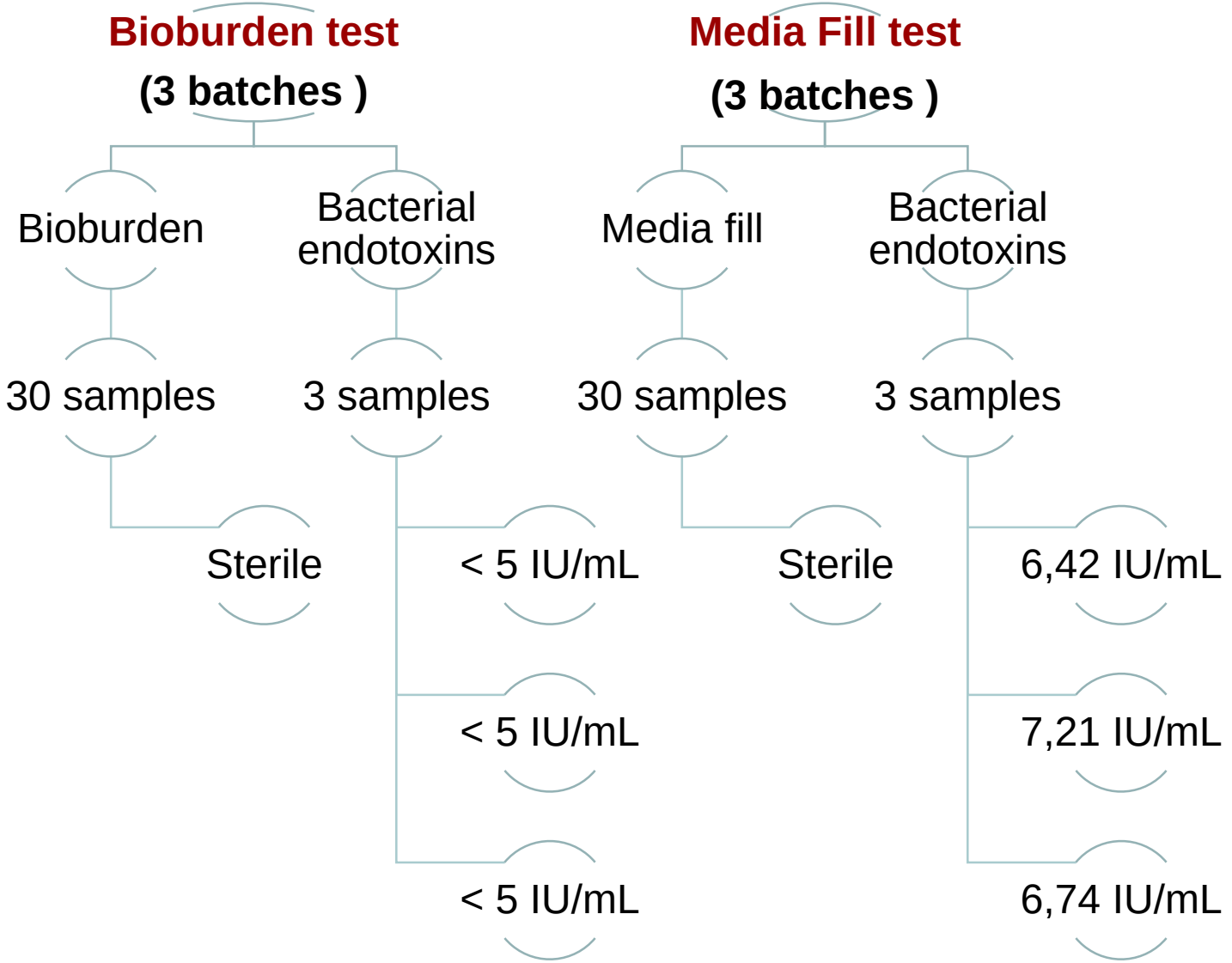
Batch	Retained activity on QMA cartridge (%)
	Elution
	5 mL 0,9 % NaCl
Batch 1	0,282
Batch 2	0,112
Batch 3	0,588
Batch 4	0,112
Batch 5	0,721
Batch 6	0,243
Batch 7	0,184
Batch 8	0,245
Batch 9	0,212
Batch 10	0,152

< 0,6 %

After the development of in-house method for synthesis, the process optimization was carried out, 10 production batches were performed, with **a yield higher than 98%, decay-corrected**.

Results

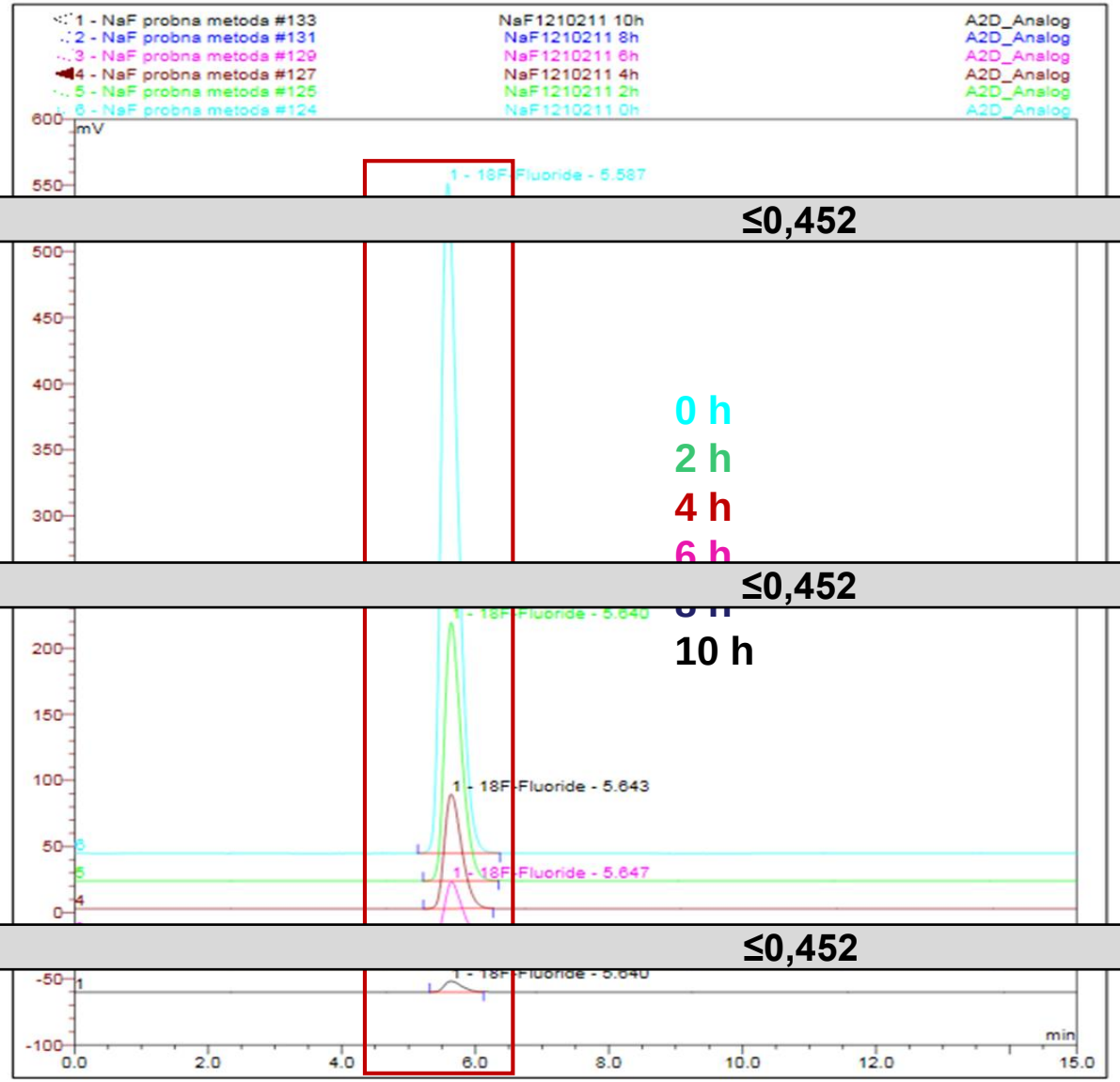
Aseptic validation of production process



Results

Process validation and stability study

Chemical purity (≤ 0,452 mg/L) ≤0,452



0 h
2 h
4 h
6 h
8 h
10 h

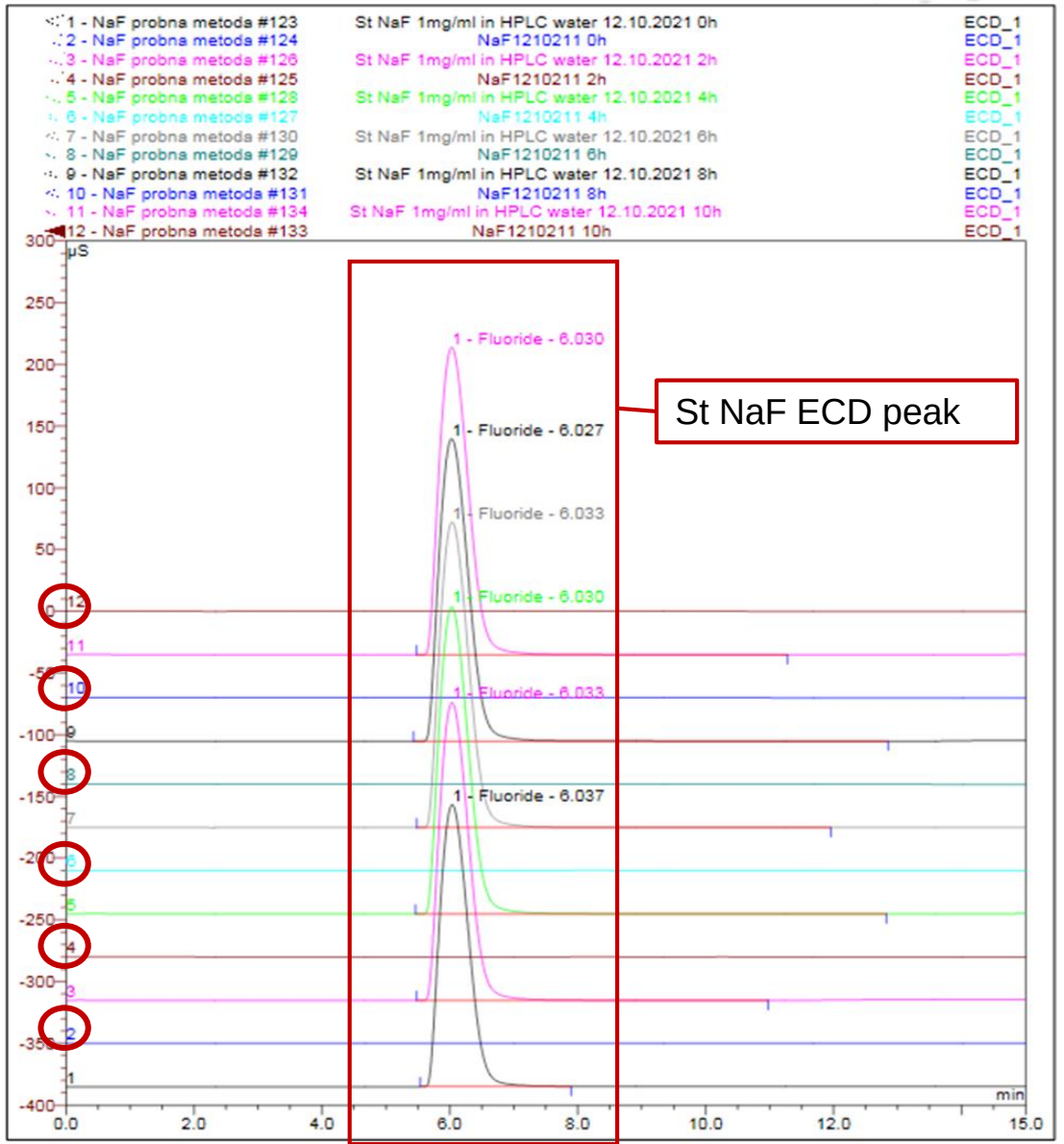
Chemical purity (≤ 0,452 mg/L) ≤0,452

Chemical purity (≤ 0,452 mg/L) ≤0,452

Acceptance criteria
≥ 98,5 % of total radioactivity

Results

Process validation and stability study



Acceptance criteria

≤ 0,452 mg/L

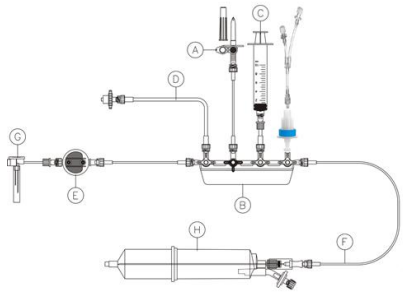
Results

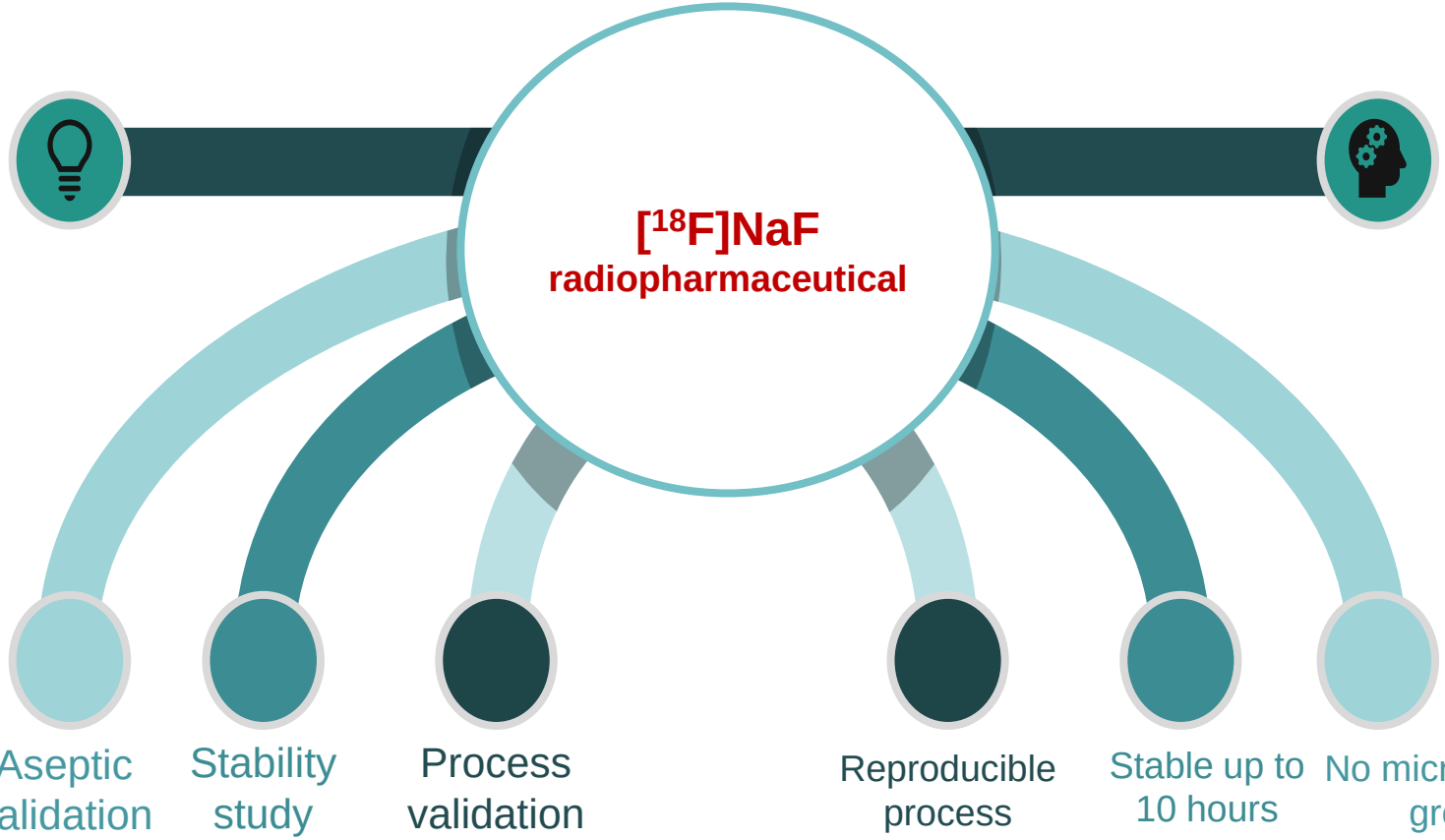
Process validation and stability study

	Tests	EOS	2 h	4 h	6 h	8 h	10 h
Batch 1	Difference in retention times (<40 s)	27,42	22,98	23,4	24,18	23,76	24,36
	t\2 (1,75-1,92 h)	1,82	/	/	/	/	1,83
	pH (5,5-8,0)	6,5 - 7,0					
	Radiochemical purity (>98,5%)	100					
	Chemical purity (≤ 0,452 mg/L)	≤0,452					
	Bacterial endotoxins (<17,5 IU/mL)	<5,00	/	/	/	<5,00	<5,00
	Sterility (sterile)	Sterile sample					
	Radionuclidic purity (<0,1%)	0,00001192					
Batch 2	Difference in retention times (<40 s)	26,76	24,36	23,82	22,98	23,64	24,24
	t\2 (1,75-1,92 h)	1,84	/	/	/	/	1,84
	pH (5,5-8,0)	6,5 - 7,0					
	Radiochemical purity (>98,5%)	100					
	Chemical purity (≤ 0,452 mg/L)	≤0,452					
	Бактериски ендотоксини (<17,5 IU/mL)	<5,00	/	/	/	<5,00	<5,00
	Sterility (sterile)	Sterile sample					
	Radionuclidic purity (<0,1%)	0,000060731					
Batch 3	Difference in retention times (<40 s)	27	23,58	23,22	23,16	23,64	23,4
	t\2 (1,75-1,92 h)	1,81	/	/	/	/	1,86
	pH (5,5-8,0)	6,5 - 7,0					
	Radiochemical purity (>98,5%)	100					
	Chemical purity (≤ 0,452 mg/L)	≤0,452					
	Bacterial endotoxins (<17,5 IU/mL)	<5,00	/	/	/	<5,00	<5,00
	Sterility (sterile)	Sterile sample					
	Radionuclidic purity (<0,1%)	0,0002834					

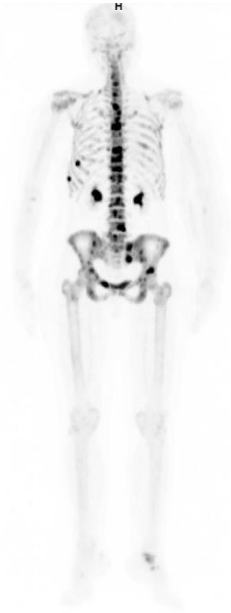
Conclusion

Originally designed in-house production process





Implemented into a clinical practice



THANK YOU FOR YOUR ATTENTION!

BCNM
2024

11th Balkan Congress of Nuclear Medicine

MACEDONIAN ASSOCIATION OF NUCLEAR MEDICINE

30.05. - 02.06.2024
Hotel Holiday Inn, Skopje, North Macedonia