Supporting Information

Synthesis of [^{68}Ga]Ga-PSMA-11 using amide™ microfluidic platform

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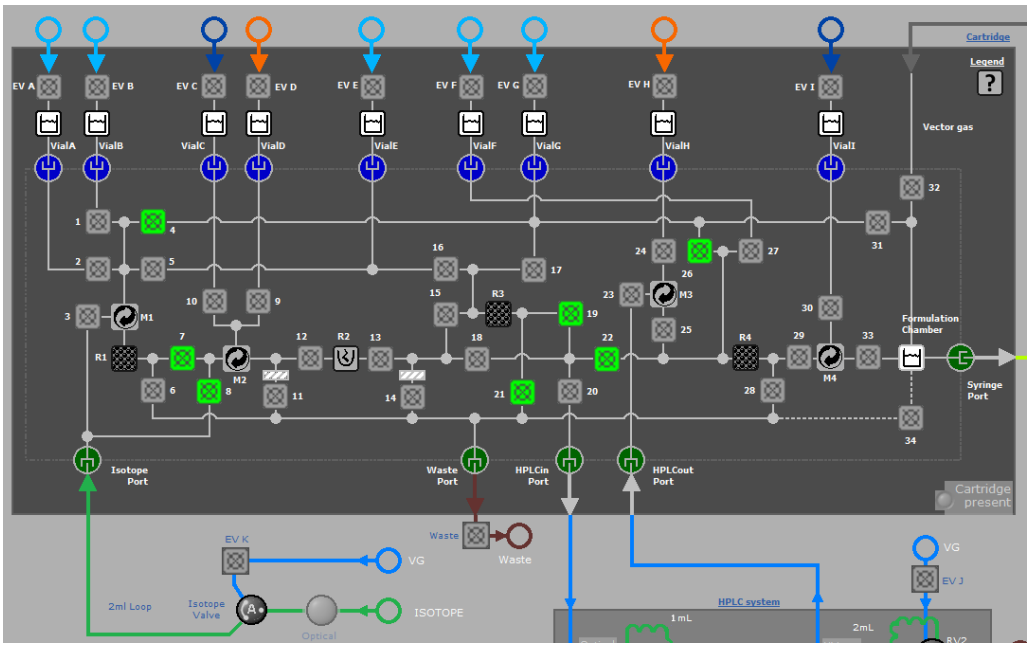
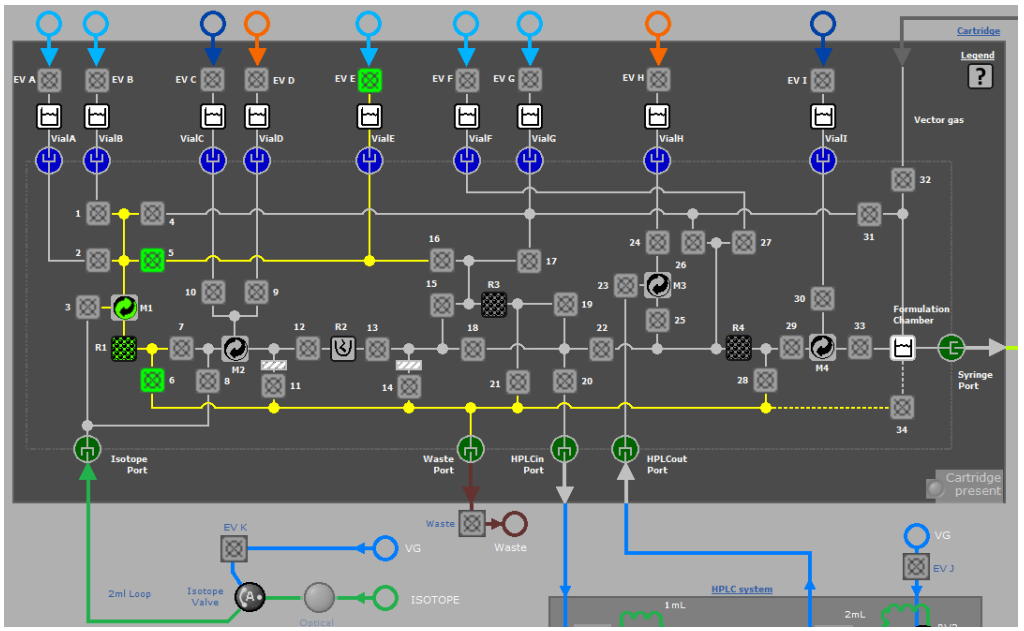
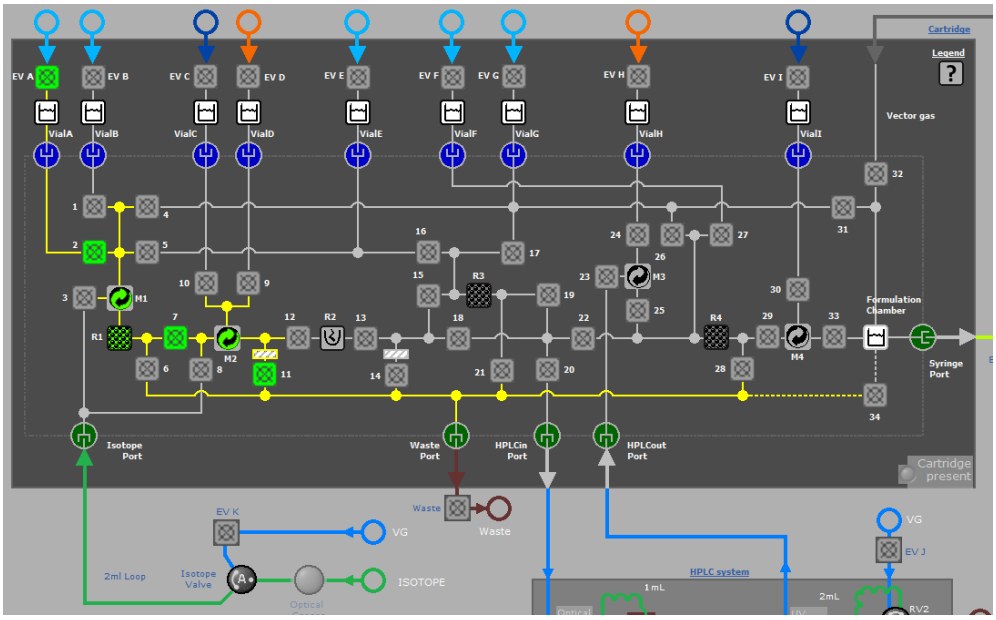
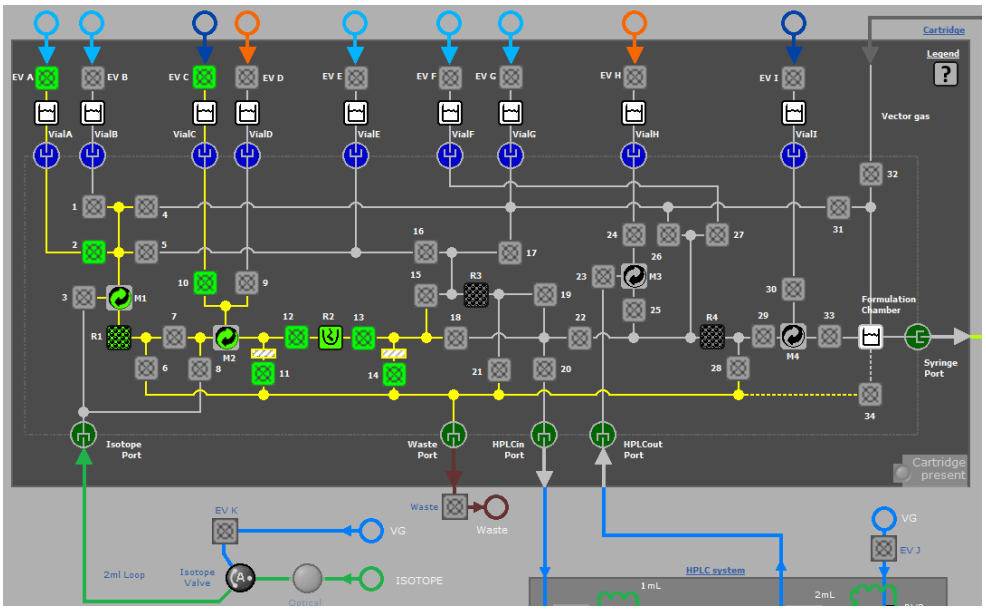
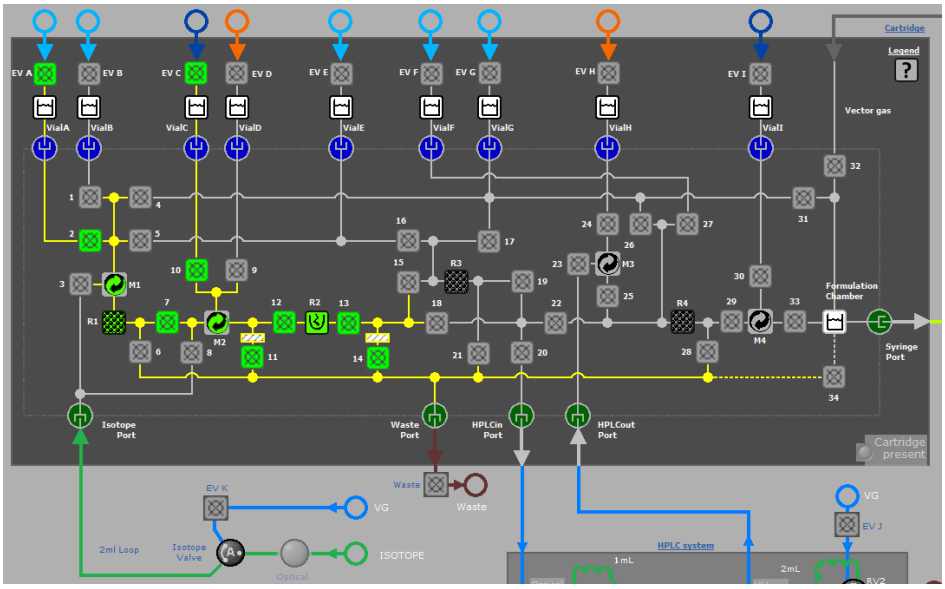
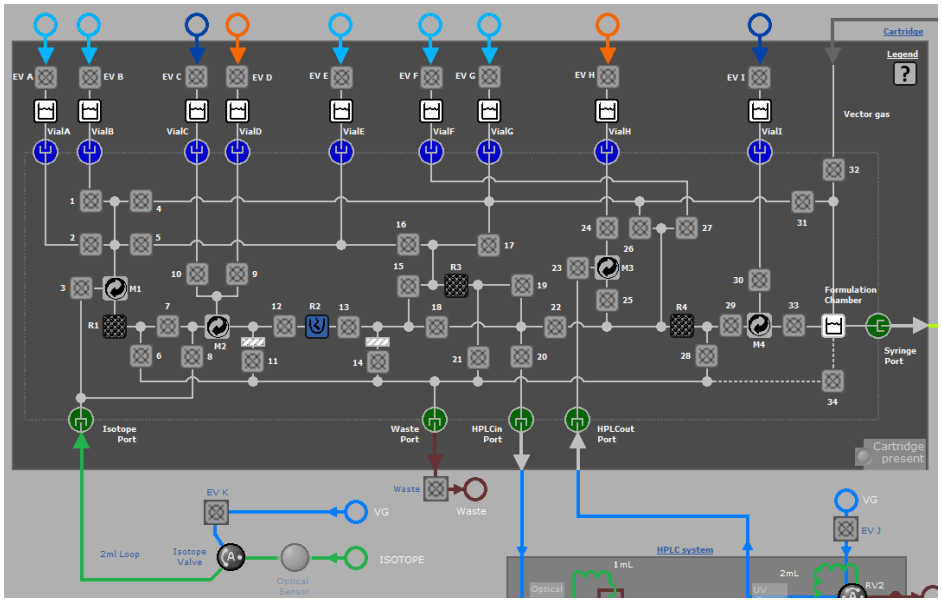
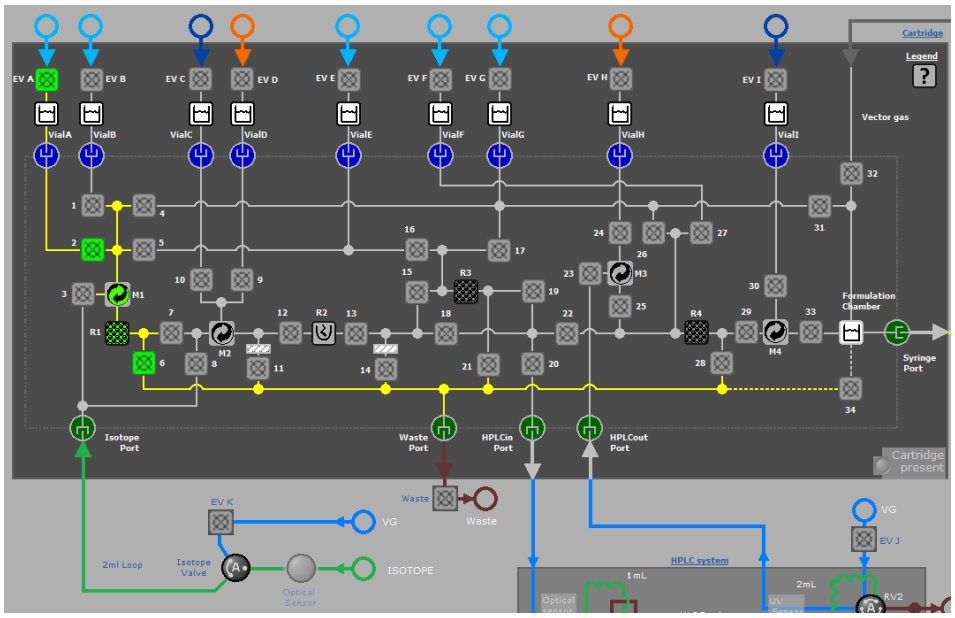
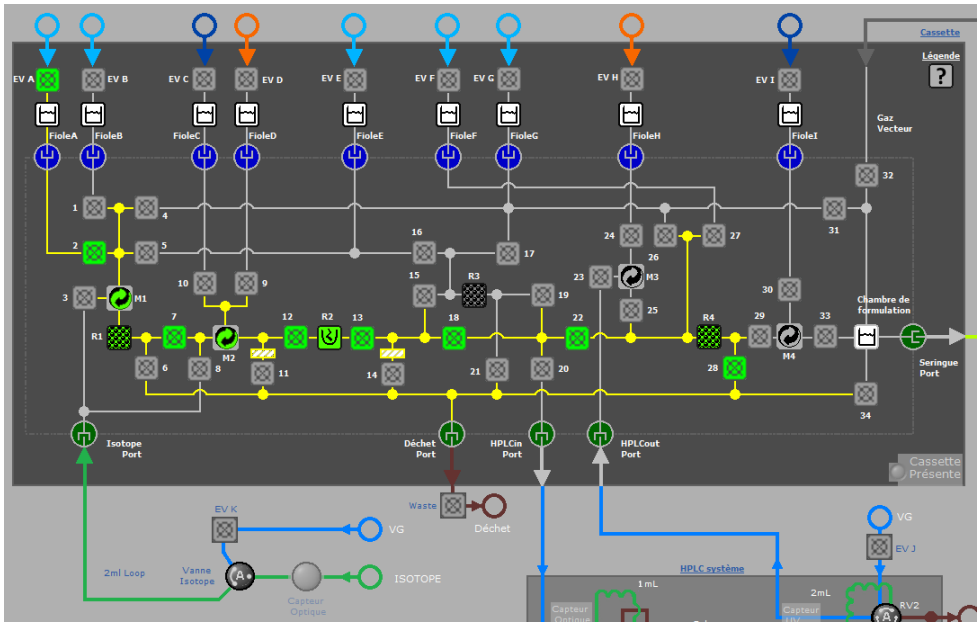
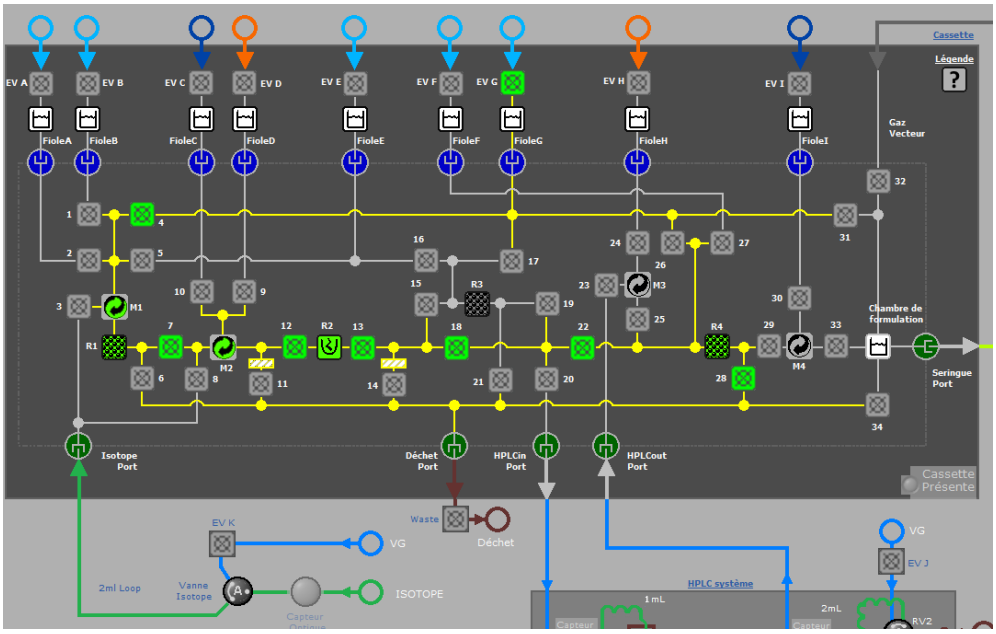
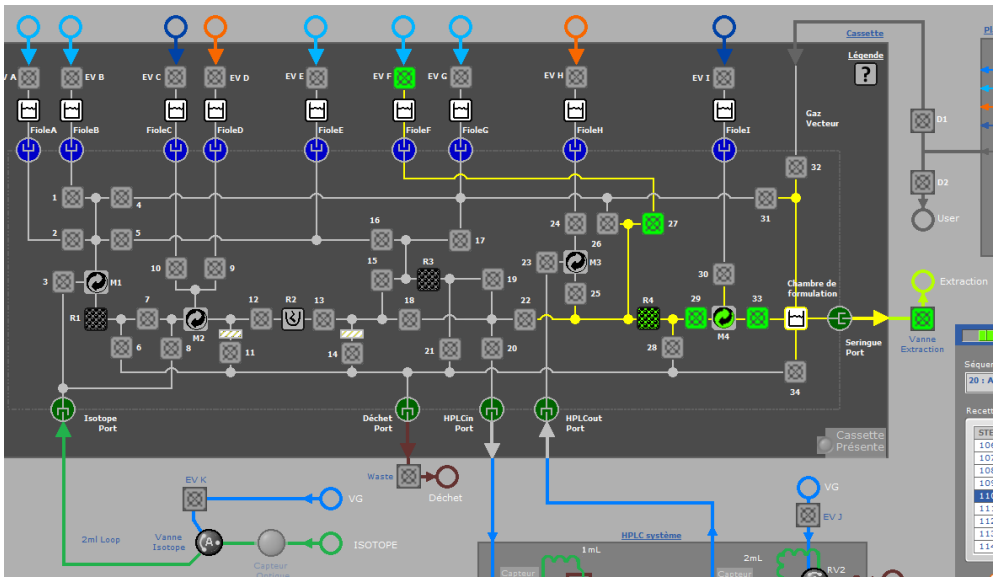
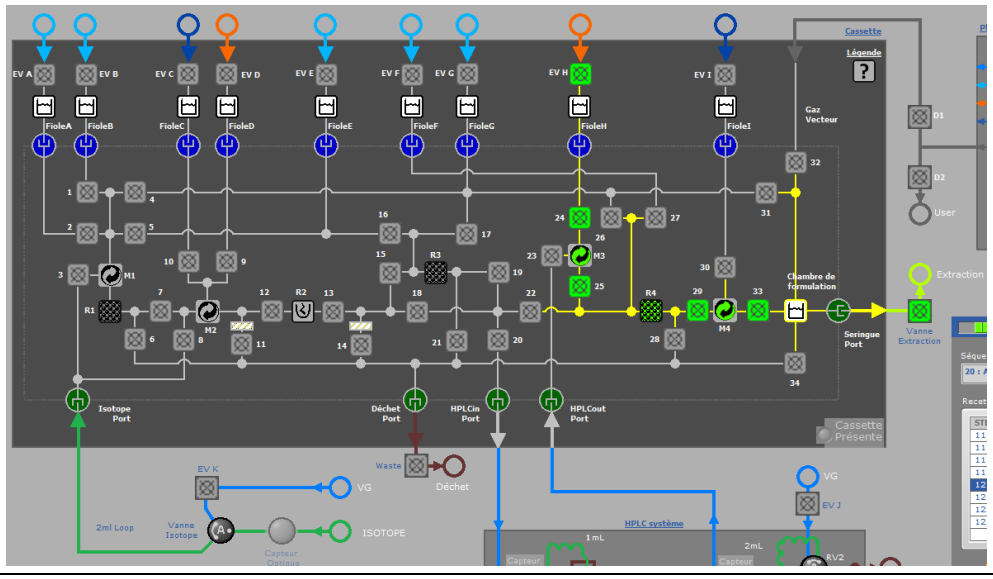
Table 1. : Schematic representation of the steps used for the production of [^{68}Ga]Ga-PSMA-11 on the iMiDEV cassette

- Vial A (4 mL): 5 M NaCl (130 µL) + 0.1 M HCl (220 µL) for MCX
- Vial C (0.3 mL): 0.8 M AcONa (140 µL) + PSMA-11 (10 µL)
- Vial E (4 mL): empty
- Vial F (4 mL): EtOH (0.8 mL)
- Vial G (15 mL): H_2O (4 mL)
- Vial H (15 mL): NaCl 0,9% (8 mL)
- External Vial with isotope (10 mL): $^{68}GaCl_3$ (1.5 mL)
- Collection vial (15 mL): empty

	Radiolabelling steps	
1	Reverse Injection of isotope on R1 filled with PSH+ or MCX Delay : 120 s	
2	Drying R1 with N_2 flow (Vial E) Delay : 60 s	

3	Pre-elution of ^{68}Ga (R1) with eluant (Vial A) to MFV* 11 (gas evacuation through the vent) Delay : 5 s followed by closing all MFV	
4	Sending precursor (Vial C) to M2 Delay: 1 s	
5	Simultaneous injection Vial A + Vial C to R2 Delay : 15 s (gas evacuation through the vents)	

6	Labelling at 95 °C (set temperature) Delay : 60 s – heating and 90 s - cooling	
7	Emptying Vial A to Waste Delay : 30 s	
8	Sending the reaction crude from R2 to R4 with Vial A Delay: 60 s	

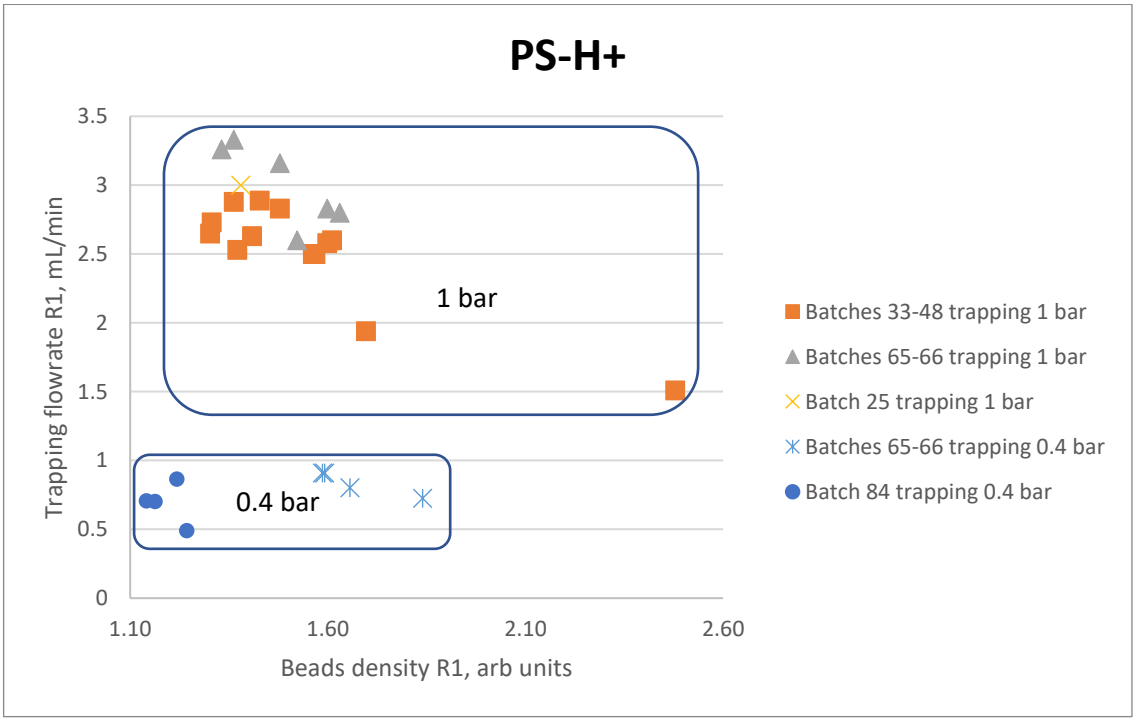
9	Washing of R2 and R4 with H_2O (Vial G) Delay: 150 s	
10	Elution of ^{68}Ga-PSMA-11 from R4 with Vial F to the formulation chamber Delay: 90 s	
11	Rinsing R4 with NaCl 0,9% (Vial H) and delivery of formulated [^{68}Ga]Ga-PSMA-11 through the extraction valve Delay: 240 s	

Open MFVs and EVs represented in green.

Table 2. Details on manufacturing changes in beads filling of different batches of cassettes iMiDEV

Details on manufacturing changes	**Beads filling***
Batch < 33	Manual filling of the beads, some voids are observable. Lack of stability and repetability
Batch 33 to 48	Automated filling of the chamber with vibrations, filling cycles and no control
Batch > 49*	Automated filling of the chamber with vibrations, filling cycles and control on the flowrate through the chamber

*The beads are filled during cassette manufacturing by gravity, then pushed with compressed air, and helped to settle with ultrasonic vibration before final testing, packaging, and gamma irradiation.



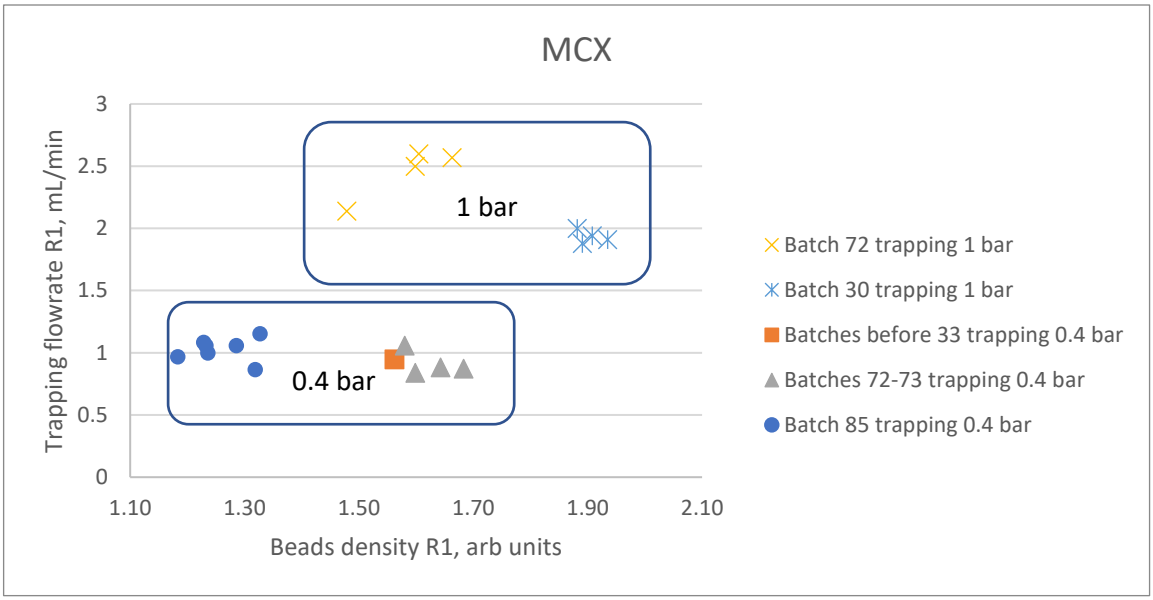


Figure 1. Distribution of cassettes batches as function of their bead's density and trapping flowrate in R1 chamber: top image – cassettes with R1 filled with PS-H+ resin; bottom image – cassettes with R1 filled with MCX beads.

Table 3. Results of pH measurements for mixtures of sodium acetate solution 0.8M and acidified sodium chloride solution 3M/5M prepared and measured off-cassette; the A+B combinations providing the good pH for complexation yields are highlighted in green and blue.

Volume A (NaCl+HCl)	Volume B (0,8M AcONa)	pH A+B (A : 3M NaCl + 2.5% $HCl_{30\%}$)	pH A+B (A : 5M NaCl+0,1M HCl)
0%	100%	7,7	7,87
10%	90%	5,99	6,67
20%	80%	5,51	6,27
25%	75%	5,36	6,12
30%	70%	5,24	6
40%	**60%**	**4,95**	5,76
45%	**55%**	**4,82**	5,61
50%	**50%**	**4,65**	5,5
55%	**45%**	**4,55**	5,39
60%	**40%**	**4,38**	**5,25**
70%	**30%**	3,9	**4,99**
80%	**20%**	1,15	**4,65**
90%	10%	0,39	3,71
100%	0%	0,14	0,92

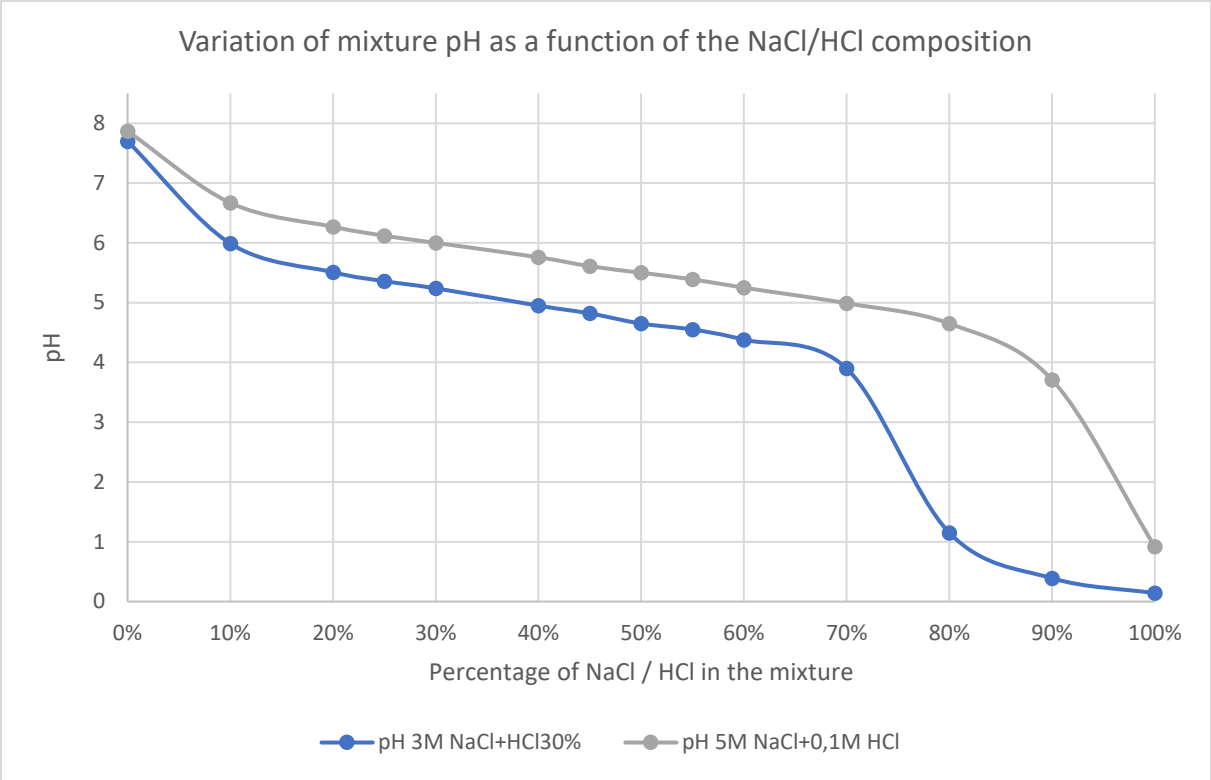


Figure 2. Variation of the mixture pH as a function of the eluent composition

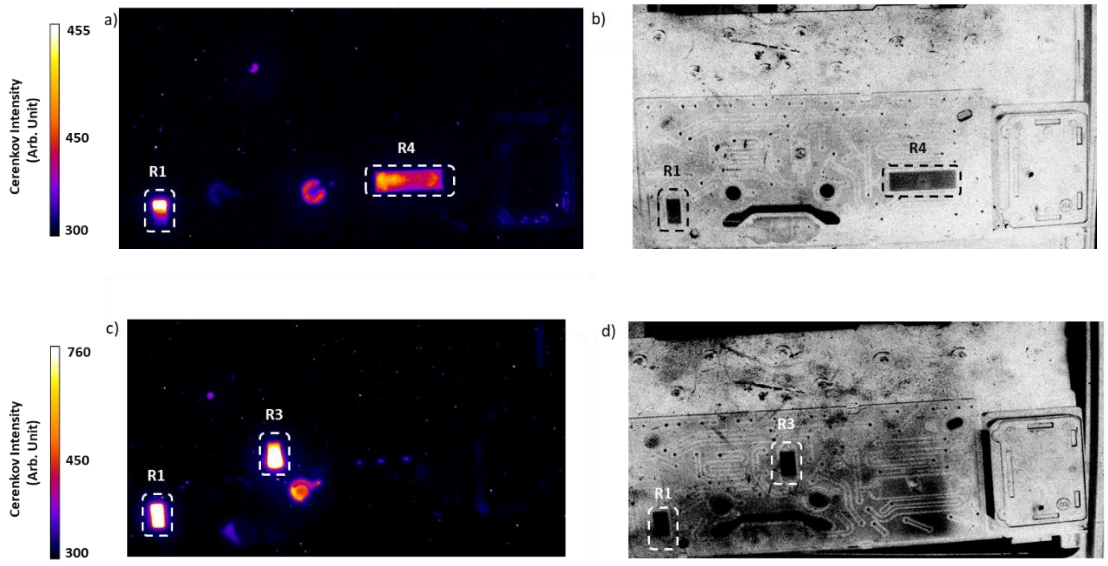


Figure 3. Cerenkov and white light images obtained after the [^{68}Ga]Ga-PSMA-11 production using the cassette with formulation in R4 (a, b) and in R3 (c, d) chambers.

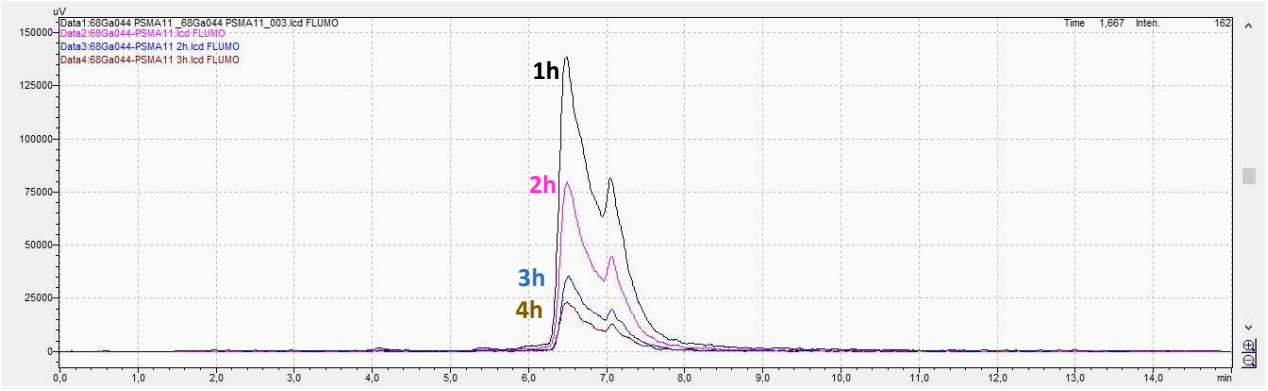


Figure 4. Overlayed radiochromatograms of [^{68}Ga]Ga-PSMA-11, demonstrating its stability within 4 h from the final product delivery.