DE-SC0019565
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Purification of Lutetium-177

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Technical Objective

Objective

- Rapid chromatography for purification of lutetium-177

Why?

- State of the art processes are time consuming

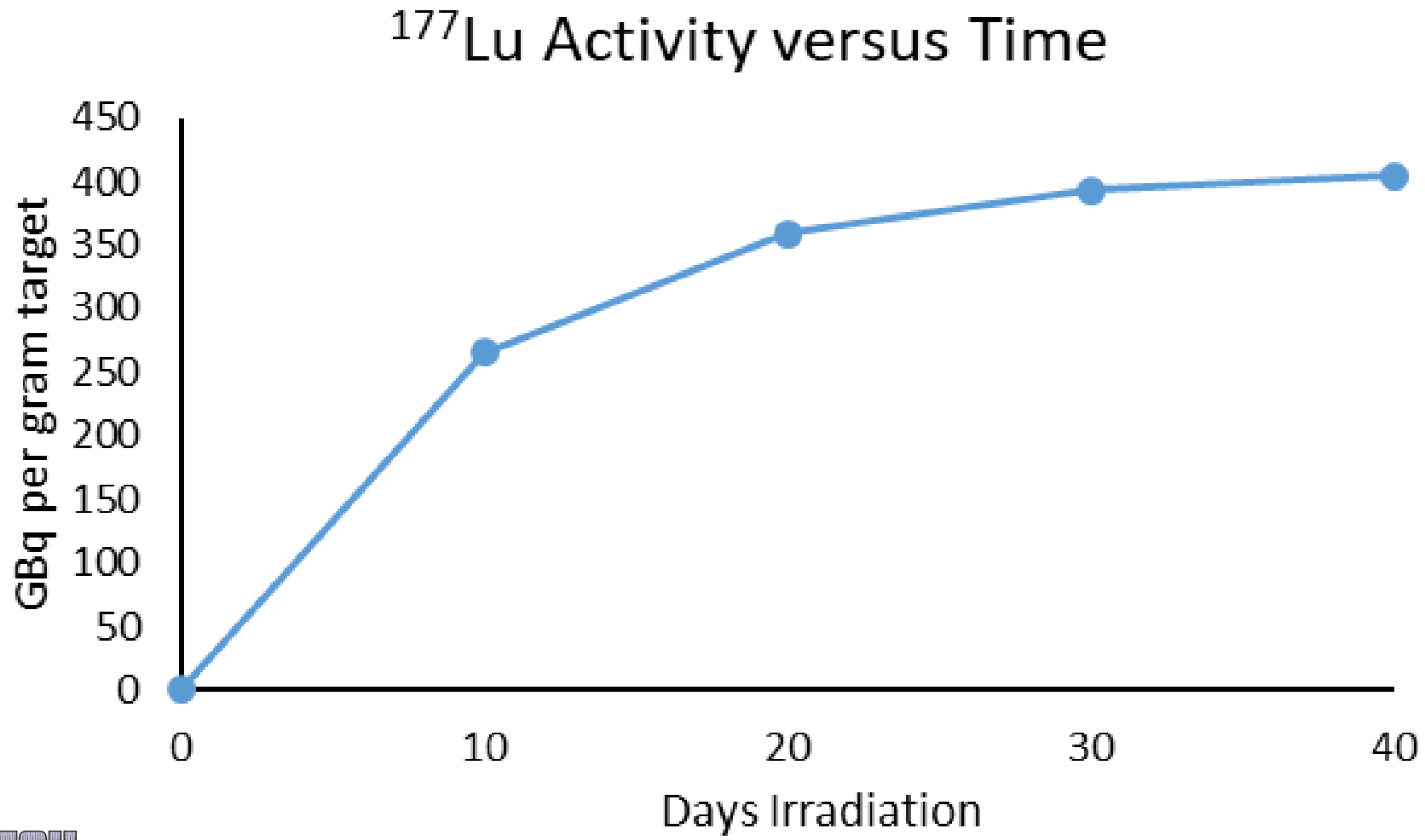
How?

- New solvents allow for new chemistries

Lutetium-177 Demand Grows

- ^{177}Lu-DOTATATE, approved in 2018 for neuroendocrine tumors (12,000 diagnoses per year)
- ^{177}Lu-PSMA-617 for prostate cancer was approved in March 2022, (268,000 diagnoses per year)
- Currently numerous clinical trials are progressing

Irradiated Target



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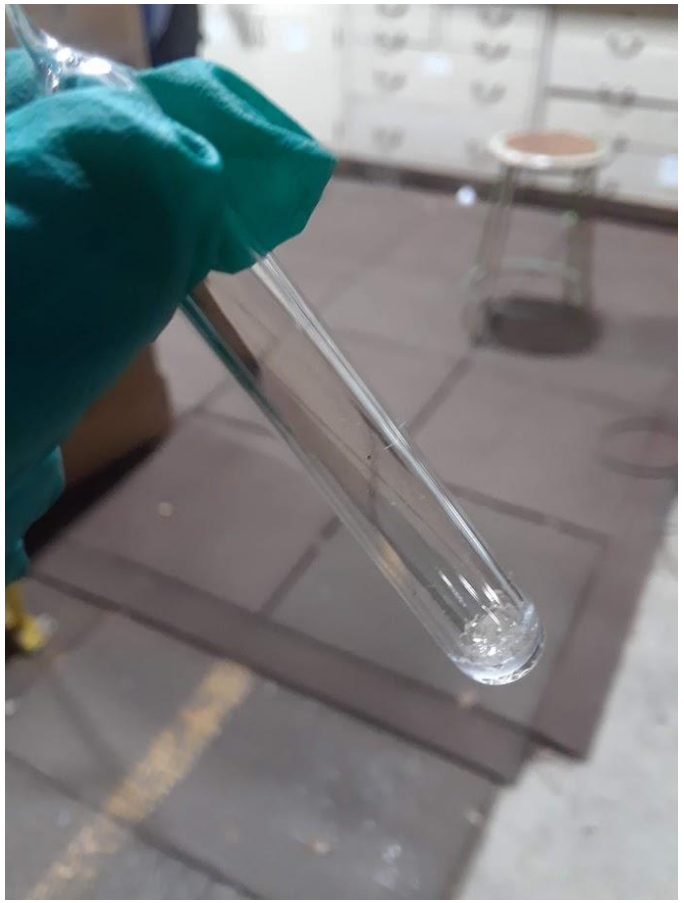
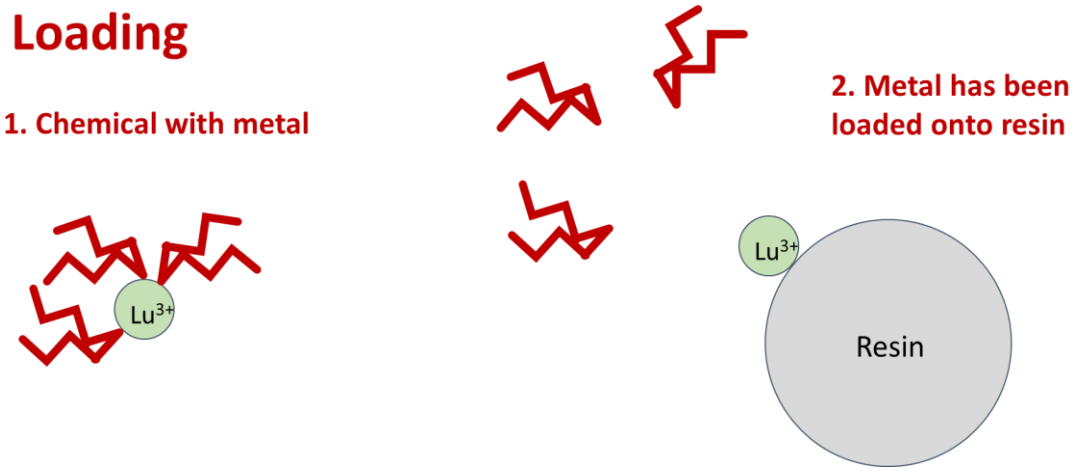
Three Irradiations this year, 2 of Ytterbium-176, and 1 of Lutetium 176

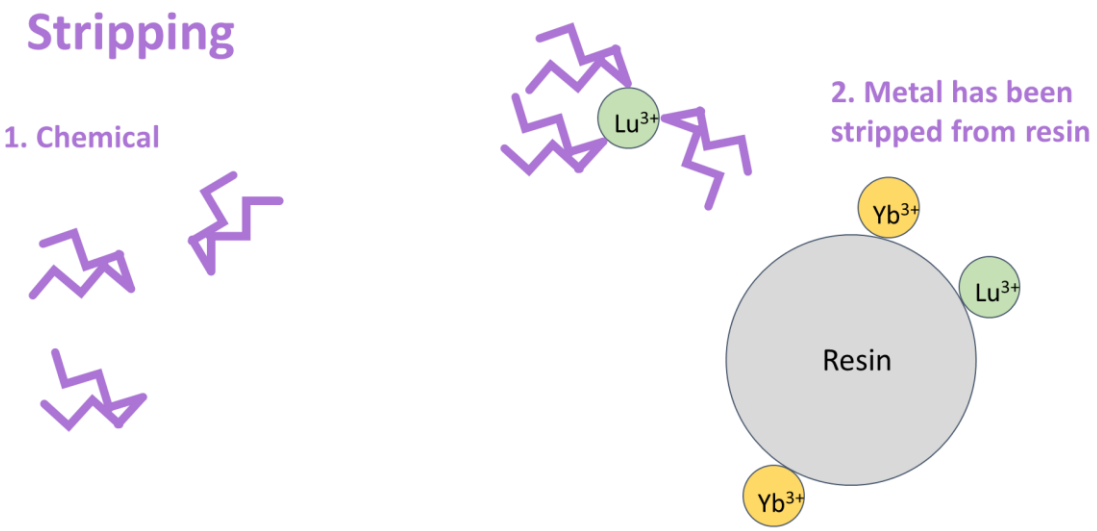


Ampoule with Yb 176

3 Ampoules Loaded into the Titanium Rabbit for Irradiation

Chromatography Purification Process





The metal – extractant complex is repeatedly loaded on to and stripped off of the resin as the mobile phase flows through the column.
Since Lutetium does not bind to the resin as strongly as the Ytterbium, the Lu elutes from the column before the Yb.

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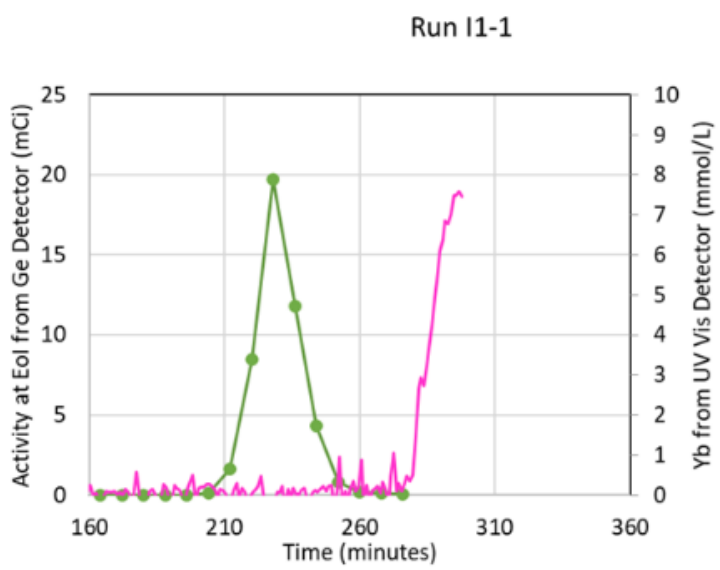
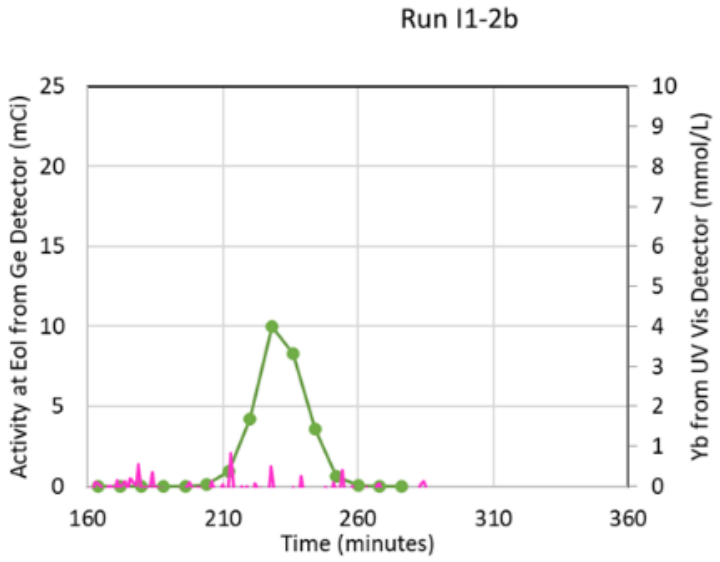
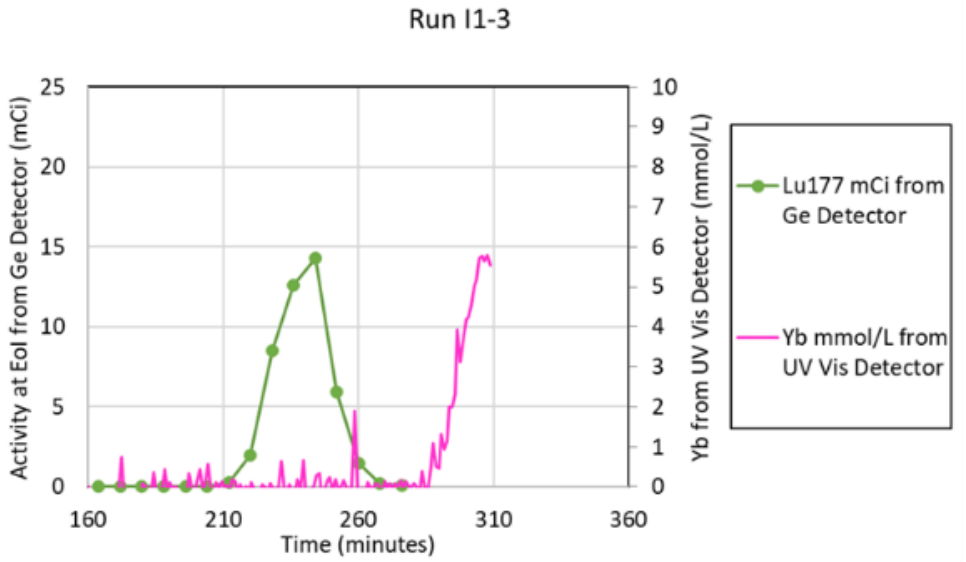
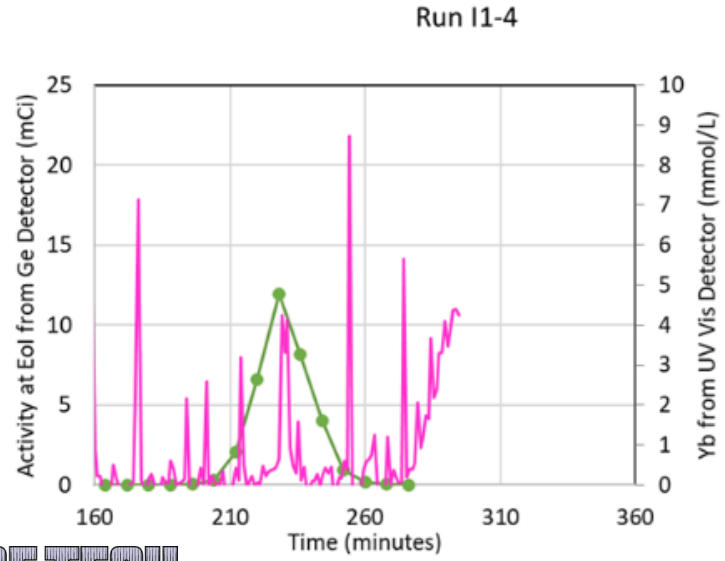
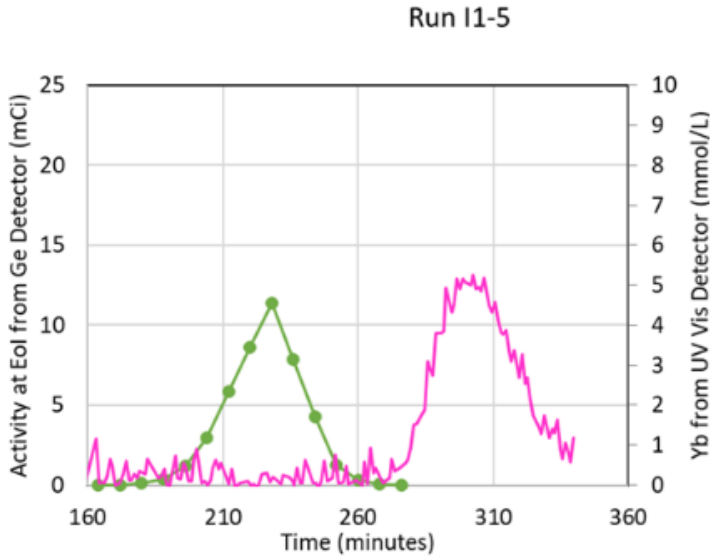
Irradiation 1, Lutetium Ytterbium Separation

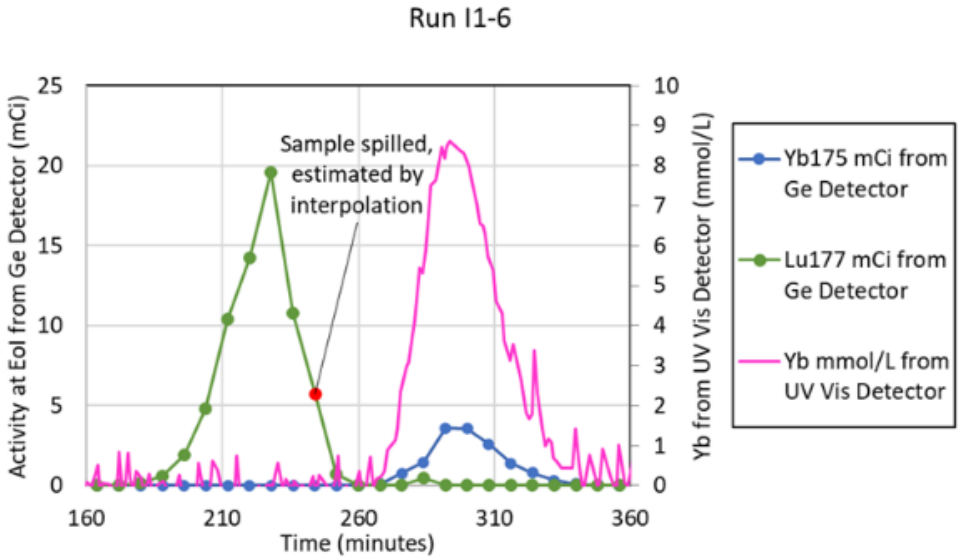












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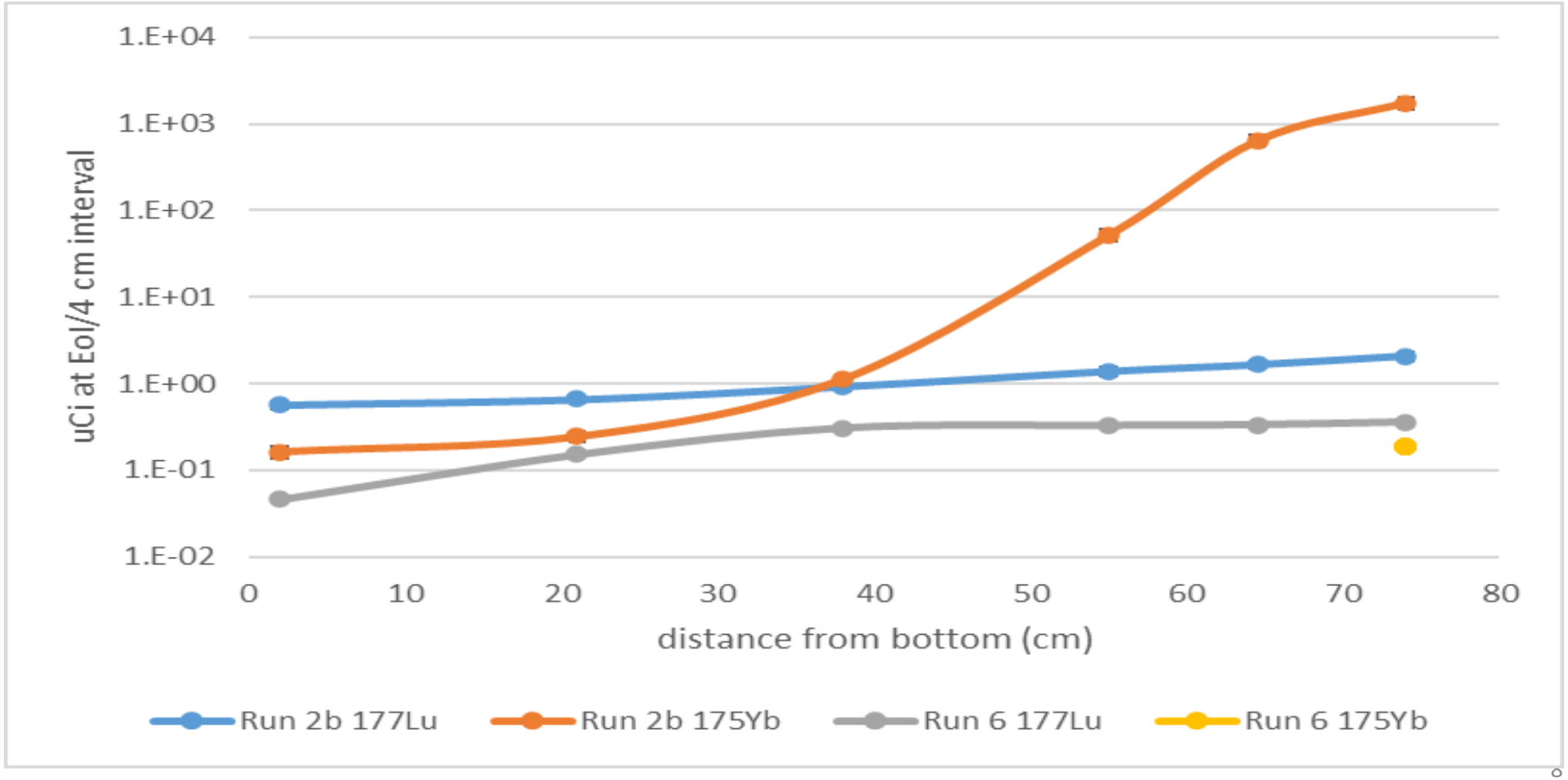
Lutetium remaining over the length of the column, Irradiation 1, Columns 2b and 6



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Lutetium Chemical and Radionuclidic Purity Spec for Irradiation 1

Element	Spec/Goal Value	Run I1-1	Run I1-2	Run I1-3	Run I1-4	Run I1-5	Run I1-6
^{175}Yb	≤0.07%	≤0.028%	≤0.021%	≤0.023%	≤0.020%	≤0.020%	≤0.021%
^{177}Lu	≥99.9%	≥99.972%	≥99.979%	≥99.977%	≥99.980%	≥99.980%	≥99.979%
Fe	≤0.5 µg/GBq	Could not be measured with the method, limit of quantification was greater than spec.					
Cu	≤1.0 µg/GBq	≤0.013	≤0.019	≤0.008	≤0.015	≤0.017	≤0.012
Zn	≤1.0 µg/GBq	≤0.036	≤0.036	≤0.036	≤0.036	≤0.036	≤0.036
Pb	≤0.5 µg/GBq	≤0.052	≤0.01	≤0.004	≤0.008	≤0.008	≤0.006
^{176}Yb	≤0.1 µg/GBq*	≤0.09	≤0.198	≤0.095	≤0.175	≤0.209	≤0.083

*spec at end of 9 day shelf life

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Irradiation 1 Results

The Good

- Lutetium and Ytterbium Separation matched cold material processing
- There was not Irreversible Adsorption
- Excellent Product Yield from the chromatography process
- Most purity specifications were met

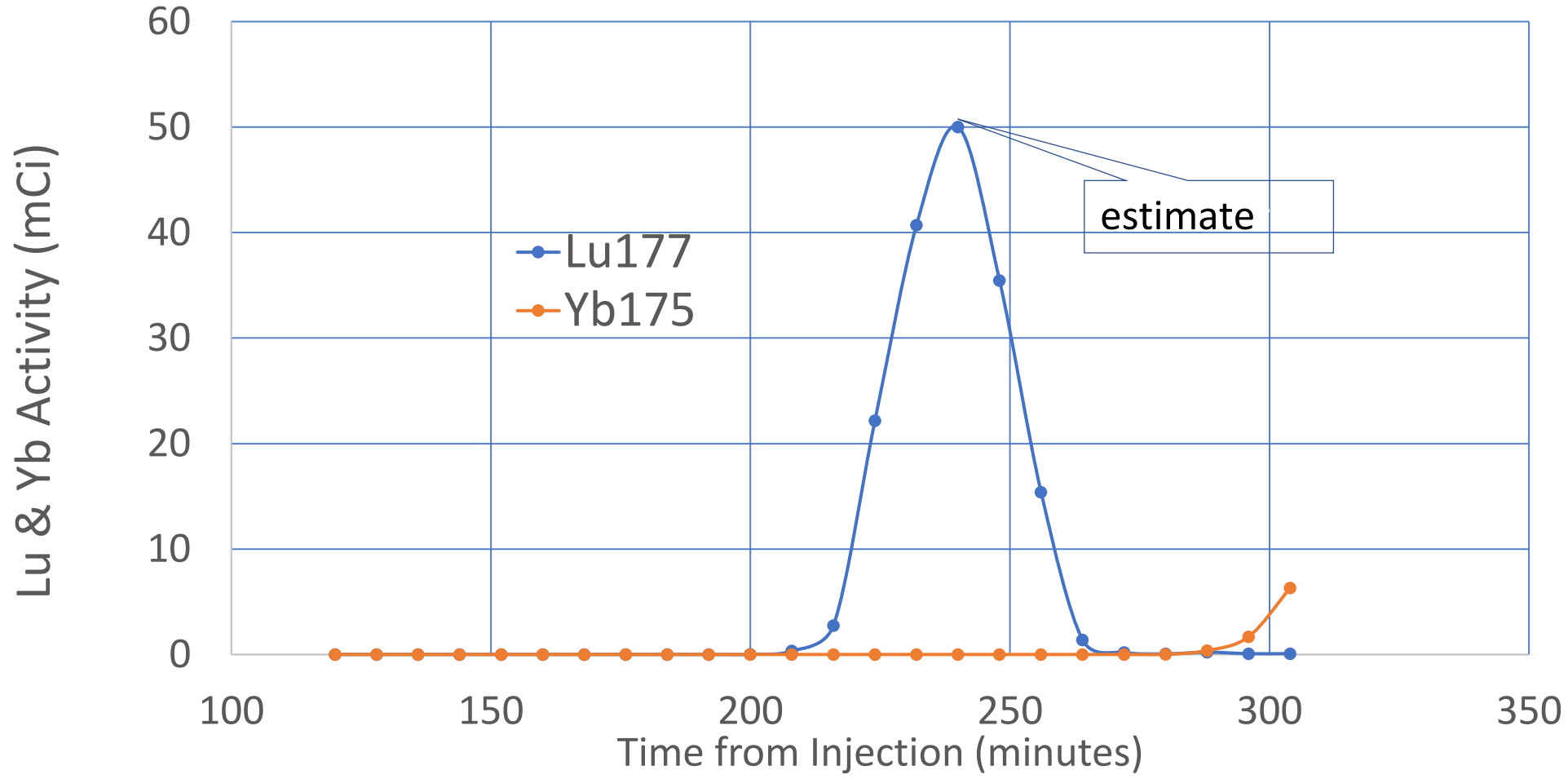
The Bad

- The Yb 176 moved in the ampoule prior to irradiation and was exposed to a lower flux than anticipated, resulting in about 600 mCi of Lu 177 produced, not the 1 Curie expected
- There was apparent degradation of processing materials exposed to radiation which resulted in less metal in the effluent than expected
- Limit of quantification was insufficient to demonstrate meeting all purity specifications

Irradiation 1.5

- Small quantity of Lu 176 was irradiated for testing various modifications to equipment and procedures, addressing issues in Irradiation 1
- Modified Ampoule
- Tested several preparation techniques and chemistries for preparing the target for injection
- Minimized the time from preparation to injection
- Additional automation added to minimize worker radiation exposure

Activity of Fractions Collected from Irradiation 2, Chromatography Test 3, Good Peak Shape and Excellent Lu – Yb Separation



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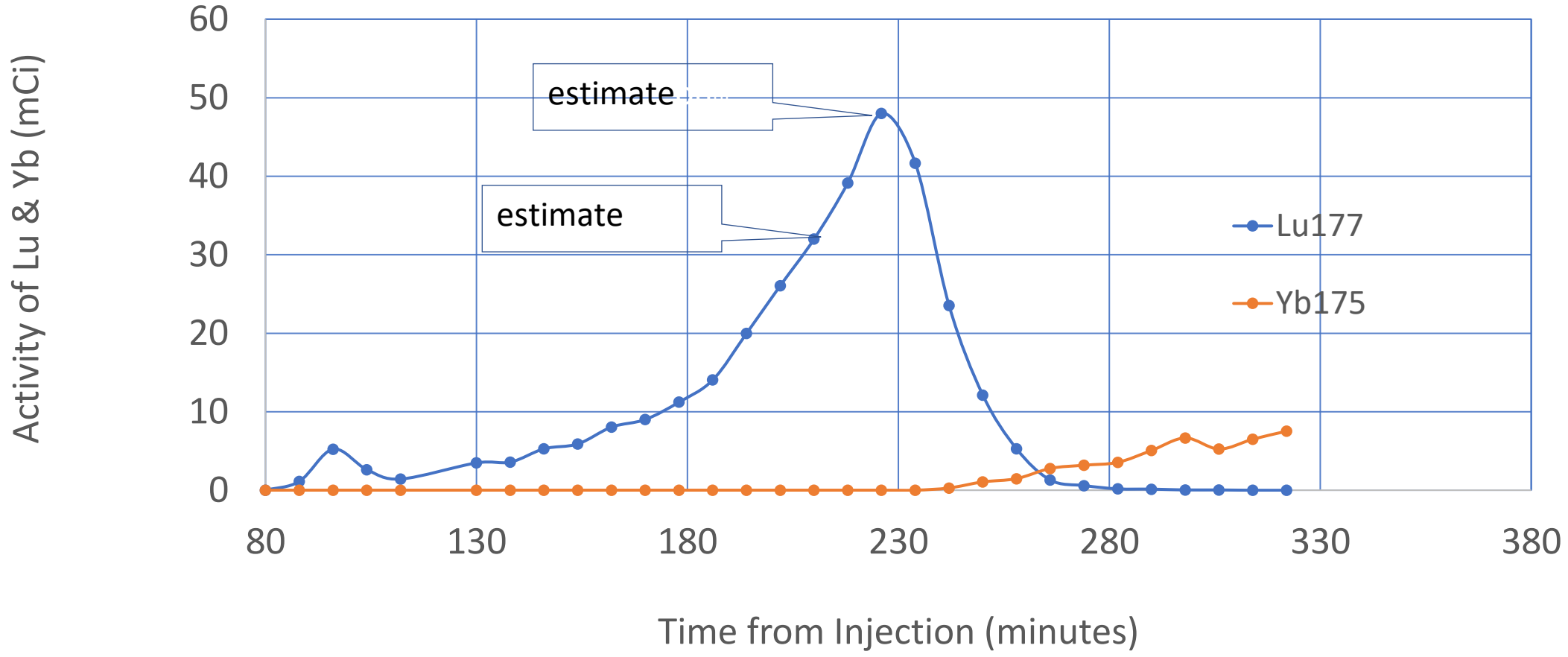
Activity of Fractions Collected from Irradiation 2, Chromatography Test 4, Column was Overloaded



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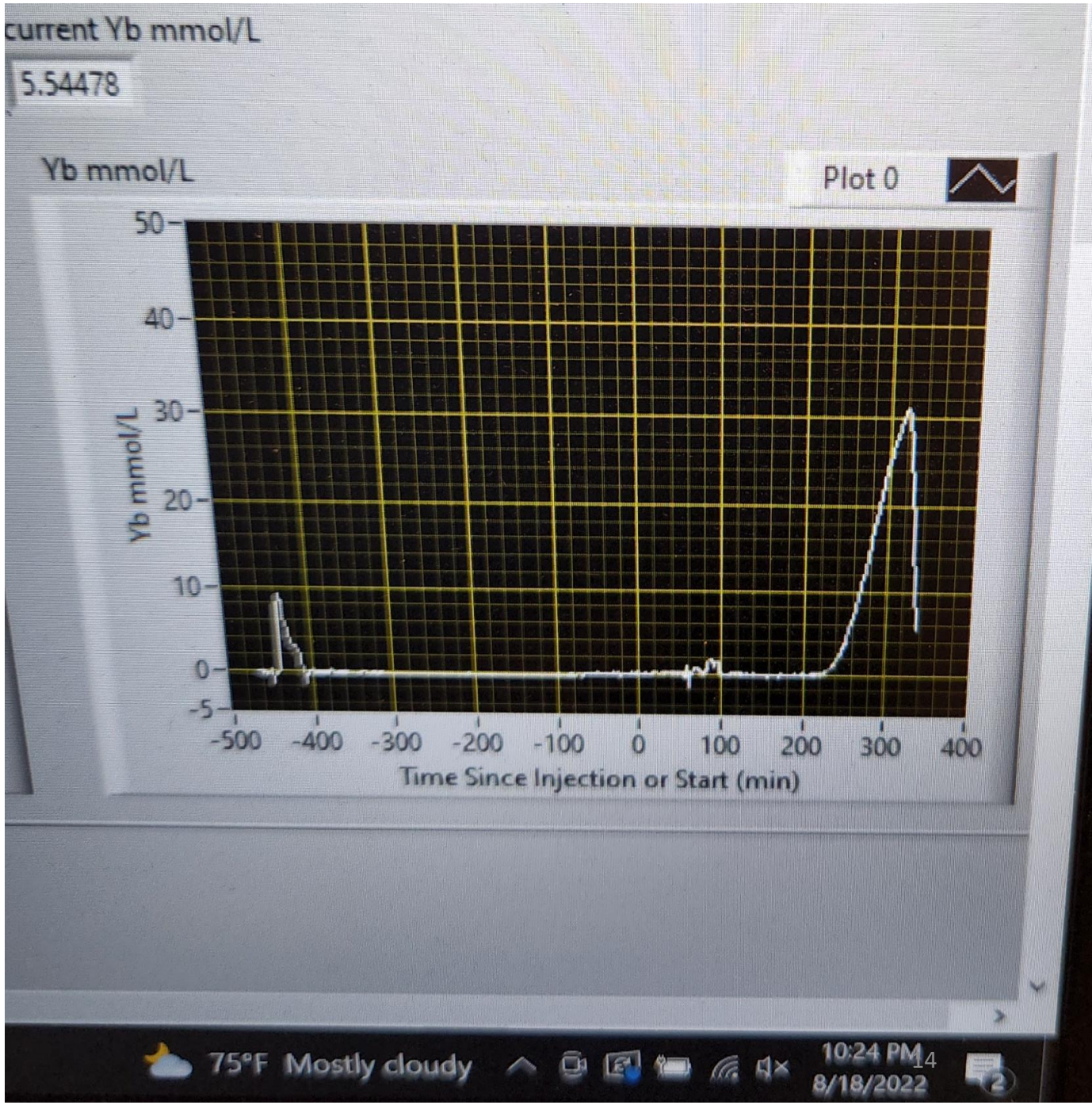
Irradiation 2, Chromatography Test 4, Ytterbium peak on UV-Vis, real time analysis of the mobile phase as it elutes from the column. Fronting of the peak indicates an overloaded column. Lutetium does not show up on UV-Vis.



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Conclusions

- The process developed with cold material, performed well with hot material after making a few modifications in the material preparation process.
- The product purity meets all specifications that we have been able to measure.
- The process capacity was not affected using hot material, with promise that it will easily scale to commercial capacity.

Thanks & Acknowledgement
DOE & the Team

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