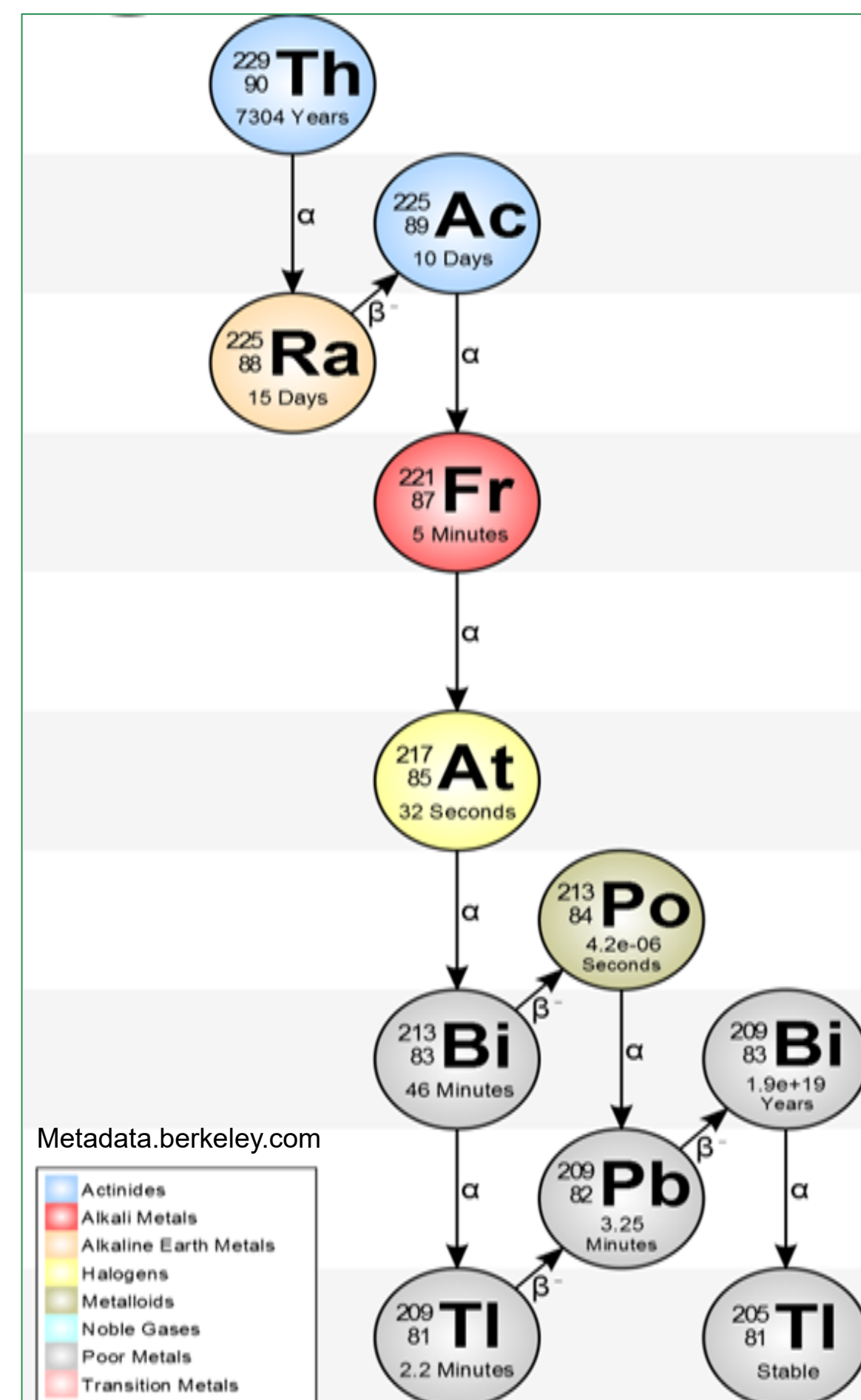


^{229}Th Generator Production of ^{225}Ac at Oak Ridge National Laboratory

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ORNL is a major producer of ^{225}Ac . In a total of 134 processing campaigns over 20 years, 10,000 mCi of ^{225}Ac in 1500 shipments has been dispensed for Targeted Alpha Therapy (TAT) research and clinical trials.

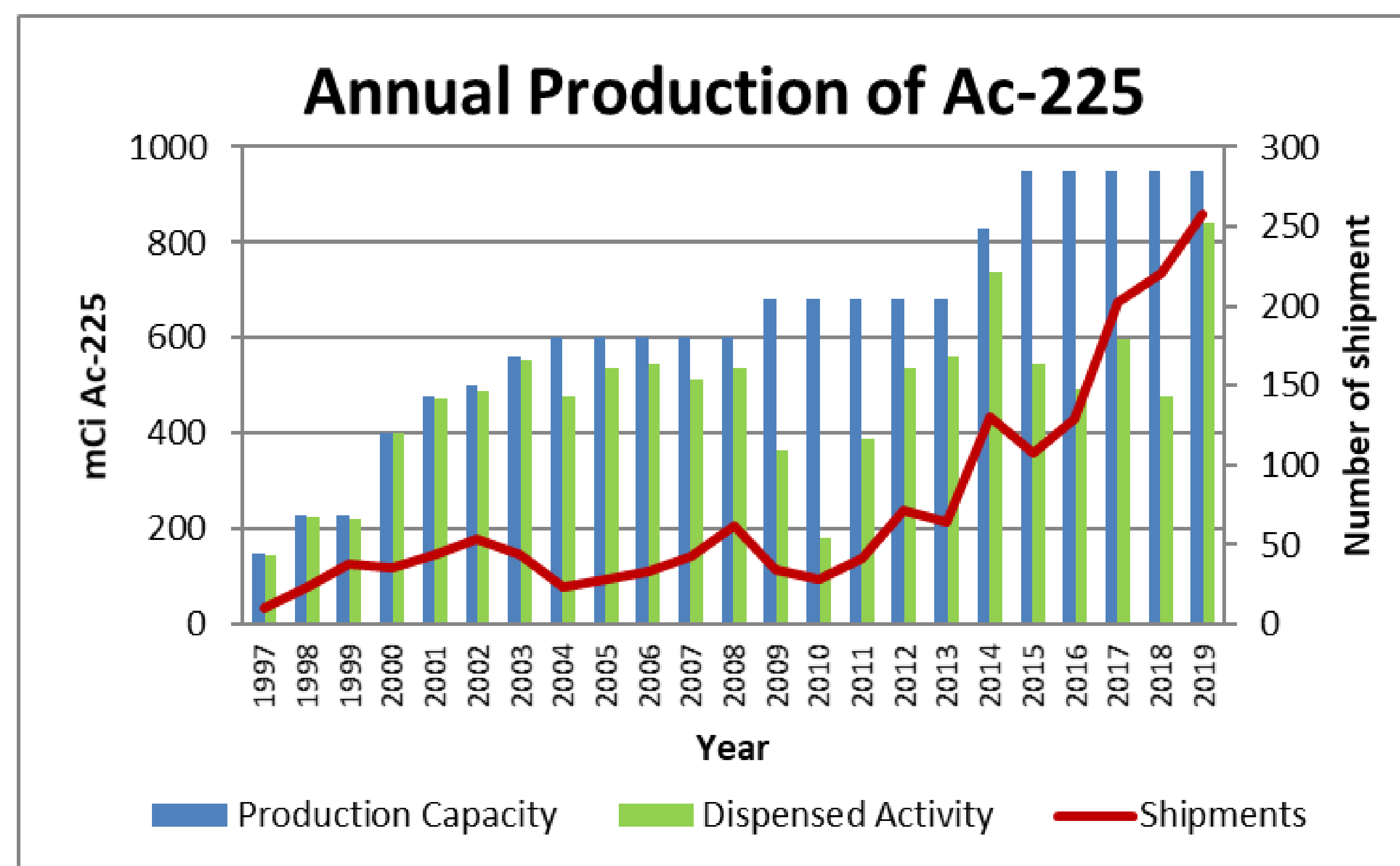
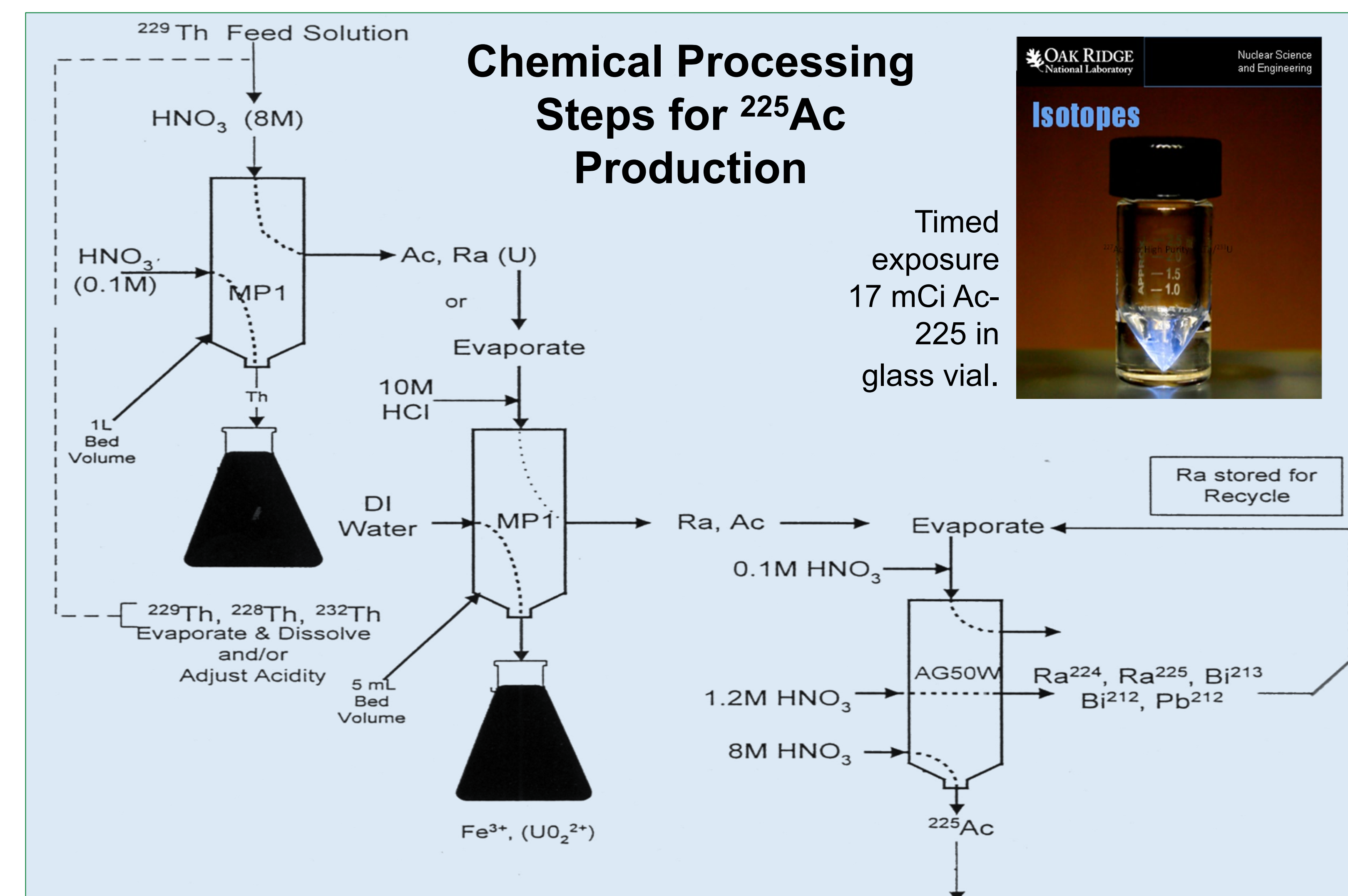


Radiochemical Engineering Development Center (REDC). REDC is a part of the High Flux Isotope Reactor (HFIR) Complex at ORNL.



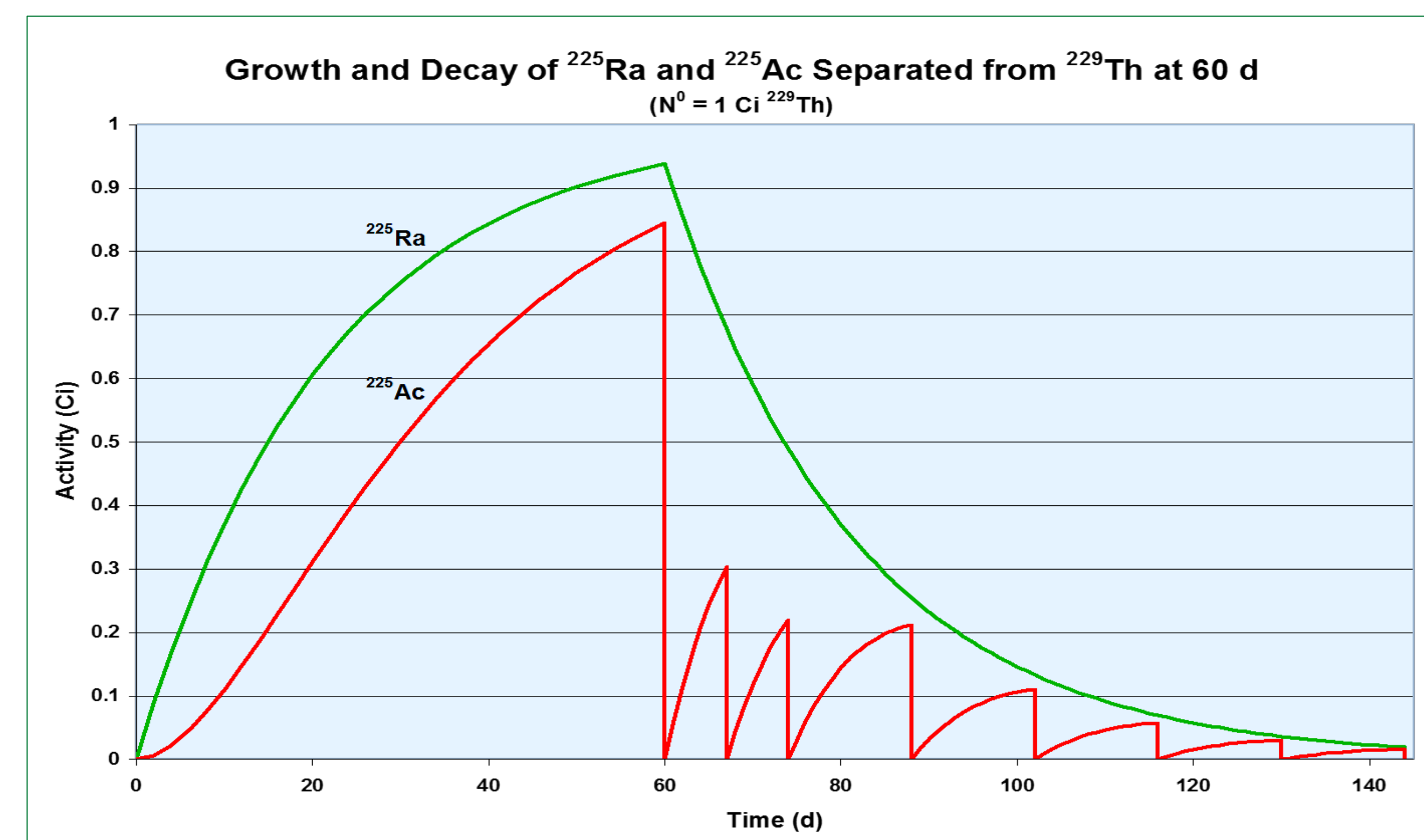
Anion exchange resin columns (MP1) in hot cell at REDC.

^{225}Ac is separated from a ^{229}Th cow, as shown below. The thorium feed solution is passed through two anion exchange MP1- HNO_3 columns to separate Ra and Ac from the parent Th. An MP1-HCl column removes Fe and other impurities. Finally, a cation exchange AG50x4 column is used to separate Ac from Ra.

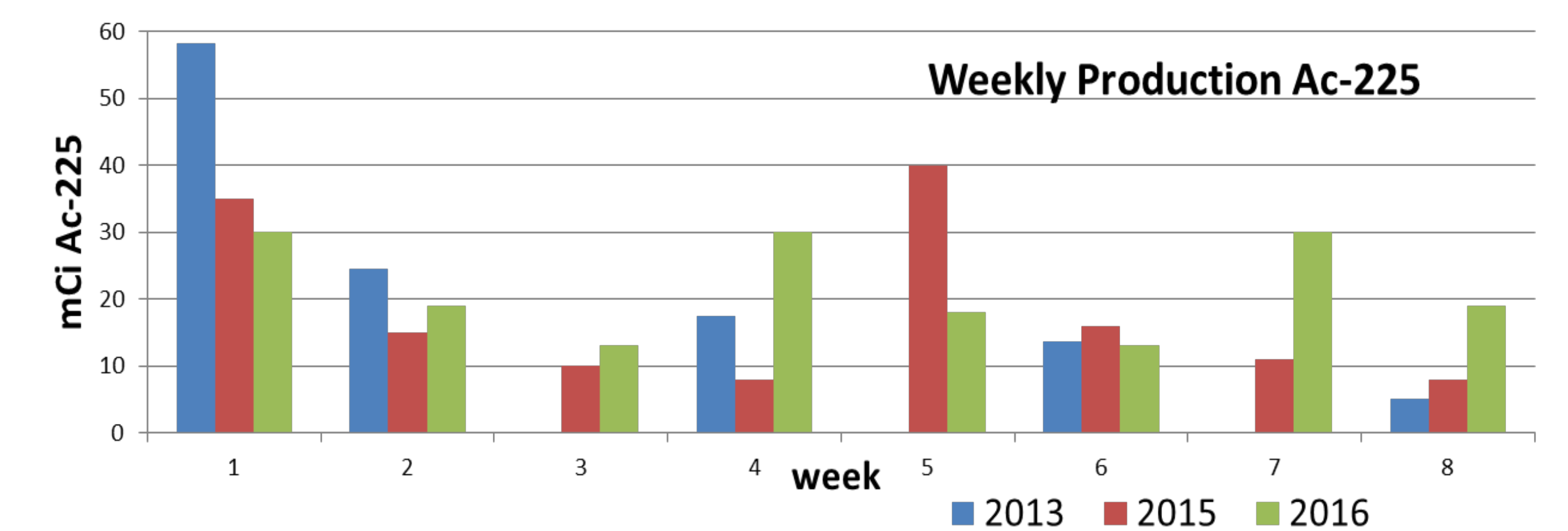


2019 projected based on actual shipment data from first quarter

The ^{225}Ac and ^{225}Ra are separated (milked) from the ^{229}Th parent (cow) approximately every 60 days. The chart above shows the percent ingrowth of the daughters at the time of milking. As the separated Ra decays (green line), the Ac is continually separated (red line) to provide additional material for dispensing.



DMF and CGMP for Ac-225 product is planned to be completed in 2020

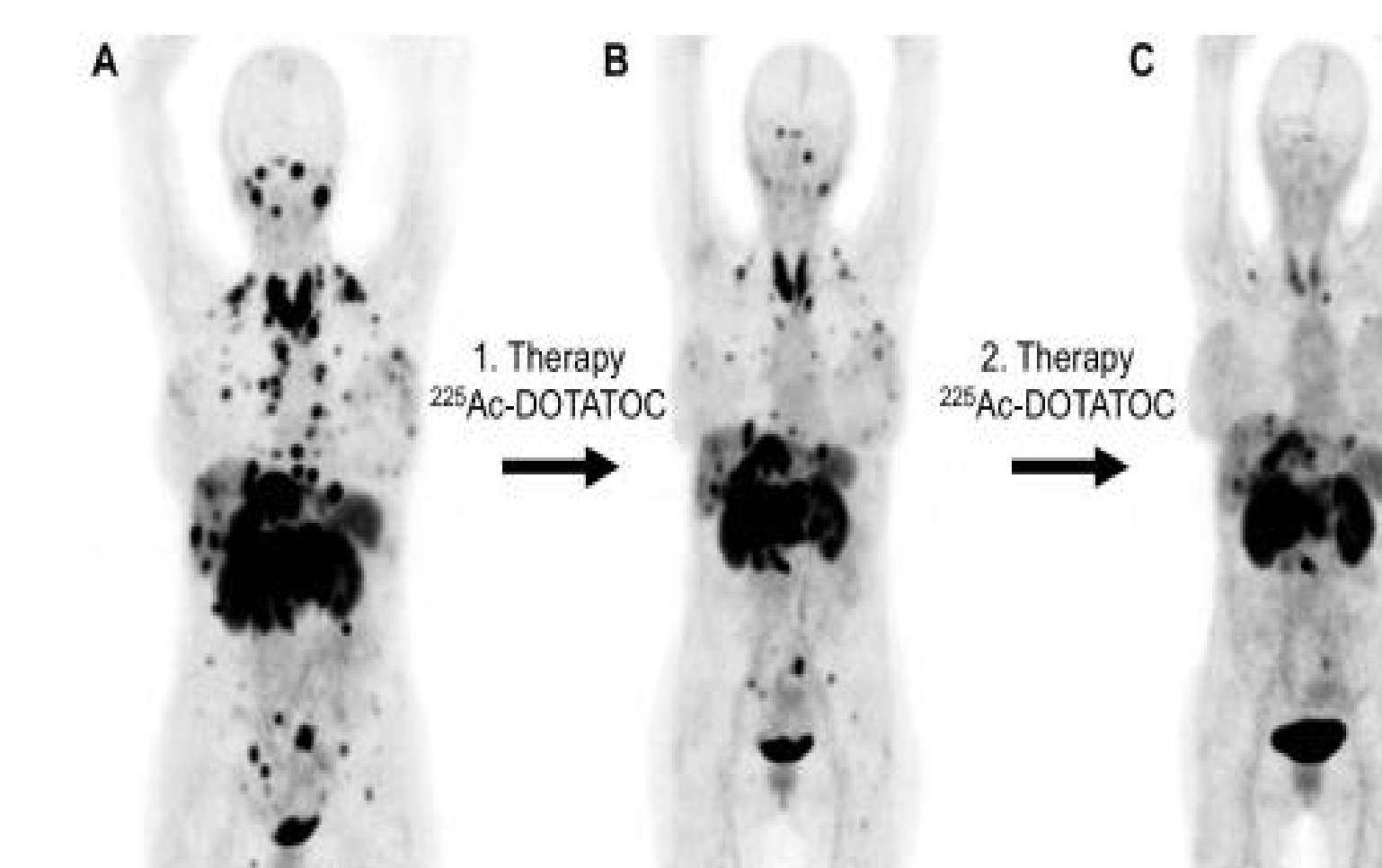


Initially, the total ^{229}Th cow was milked once every nine weeks which provided a large supply that decreased to a very small amount by the end of nine weeks. During 2014, the processing schedule was adjusted such that one-half of the ^{229}Th cow was milked every four weeks, which provides a slightly more balanced supply of Ac over time. In 2016, in order to provide an even more uniform weekly supply, the milking of one-half of the ^{229}Th cow was moved to every three weeks. With a little Ac hold-over from week one, this processing pattern can provide ~16 mCi per week for patient treatments and/or research. See chart above.

Radioisotopic purity

- 1 mCi ^{225}Ac = ~0.2 μg
- ^{225}Ra LOD < 0.005 μCi in 5 min γ -count/mCi ^{225}Ac ,
- ^{229}Th < 5×10^{-6} μCi /mCi ^{225}Ac

Mass Spectroscopy Data ($\mu\text{g}/\text{mCi}$ of ^{225}Ac)				
Element \ Year	2017	2012	2007	2003
Al	4.04	3.7	3.7	<4
Ca	1.77	<0.01	<0.005	288
Cr	8.5×10^{-2}	0.13	0.13	8
Fe	2.3×10^{-2}	0.12	0.12	4.5
Mg	0.115	0.01	7.80×10^{-3}	8
Mn	1.2×10^{-5}	6.1×10^{-4}	6.10×10^{-4}	0.7
^{229}Th	< 3×10^{-6}	2.3×10^{-5}	2.30×10^{-5}	6.50×10^{-3}
^{232}Th	7.9×10^{-6}	1.0×10^{-2}	6.50×10^{-7}	0.3
Zn	0.305			



68Ga-DOTATOC PET/CT images of a patient with a multi-resistant neuroendocrine tumor showing partial response after two treatment cycles with 16 MBq (1st cycle) and 42 MBq (2nd cycle) ^{225}Ac -DOTATOC.

An Overview of Targeted Alpha Therapy with ^{225}Ac and ^{213}Bi
 Author(s): Alfred Morgenstern*, Christos Apostolidis, Clemens Kratochwil, Mike Sathekge, Leszek Krolicki, Frank Bruchertseifer. Current Radiopharmaceuticals (2018) p.200-208