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The Need for Medical Radionuclides – A National Cancer Institute Perspective

1st Workshop on Isotope Federal Supply and Demand

January 11-12, 2012

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Medical Radionuclide Production: Types of Radionuclides

- Accelerator/cyclotron produced
  - DOE National Labs
  - Other Gov't labs (*e.g*. NIH)
  - Medical centers/academic sites
  - Private industry
- Reactor produced
  - DOE National Labs
  - Academic sites
- Natural produced/fission materials
  - DOE National Labs

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Isotope	Physical Form	Purity and/or specifications	Production method	Production capacity	Comments
^{211}At	H[^{211}At]At (sol)	> 99.5%	^{209}Bi(alpha,2n)^{211}At	5-10 mCi	dry distillation, taken up in MeOH, $CHCl_3$ or 0.01 N NaOH,
^{76}Br	NH_4[^{76}Br]Br	> 99.5%	^{75}As(^{3}He, 2n)^{76}Br	5-20 mCi	wet-distillation into ammonia, dried in delivery vial
^{64}Cu	[^{64}Cu]$CuCl_2$	> 99.5%, 9000 Ci/mmol	^{64}Ni(p,n)^{64}Cu	50-500 mCi	AG1-X8 resin separation, taken up in H_2O
$^{205/6}$Bi	[$^{205/6}$Bi]BiI_3	> 99.5%	^{205}Pb(p,n)^{205}Bi	2-5 mCi	target precipitation, AGMP-50 resin separation, eluted in 0.1 N HI
^{124}I	Na[^{124}I]I	> 99.5%	^{124}Te(p,n)^{124}I	2-5 mCi	dry distillation, taken up in 0.1 N NaOH
^{203}Pb	[^{203}Pb]$Pb(OAc)_2$	> 99.5%	^{203}Tl(d,2n)^{203}Pb	2-5 mCi	Pb^+-selective resin separation, dried, taken up in 0.1 N NH_4OAc
^{186}Re	Na[^{186}Re]ReO_4	> 99.5%	^{186}W(p,n)^{186}Re	1-2 mCi	MEK extraction, alumina column filtration, dried, taken up in saline
^{86}Y	[^{86}Y]$Y(NO_3)_3$	> 99.5%	^{86}Sr(p,n)^{86}Y	10-30 mCi	Sr^+-selective resin separation, dried, taken up in 0.1 N HNO_3
^{89}Zr	[^{89}Zr]Zr-oxalate	> 99.5%, 800 Ci/mmol	^{89}Y(p,n)^{89}Zr	10-30 mCi	hydroxamate resin separation, eluted in 1N oxalic acid

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- currently able to produce all the radionuclides on the list, except for ^{124}I and ^{186}Re which have not made for several years, but could be brought back into production, if needed.

- the CC does not currently have a mechanism to recover costs to provide radionuclides directly to external users. A mechanism to provide radionuclides directly to external users through a MOU and inter-agency transfer of funds has been discussed with the DoE. The DoE would formally provide the radionucldes to users.

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Research Isotopes Used at the NIH

^{211}At $^{205/6}$Bi ^{76}Br ^{64}Cu

^{177}Lu ^{203}Pb ^{212}Ra/^{212}Pb

^{86}Y ^{89}Zr

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Medical Radionuclide Production: Meetings and Reports

- Separated Isotopes: Vital Tools for Science & Medicine. A report of the National Research Council, 1982.
- Audit Report: Management of the Departments' Isotope Program. DOE/IG-0709. November 2005.
  - "The audit disclosed that the Department had not always provided researchers with the isotopes needed to conduct planned research. Much of this research was designed to identify breakthroughs in the diagnosis and treatment of various cancers and other life-threatening diseases."
- Advancing Nuclear Medicine Through Innovation. A report of the NRC/IOM, commissioned by the NIH and DOE, 2007.
  - "In spite of exciting possibilities, deteriorating infrastructure and loss of federal research support are jeopardizing the advancement of nuclear medicine. It is critical to revitalize the field to realize its potential."
  - "The lack of year-round uninterrupted production of medical radionuclides for research is discouraging the development and evaluation of new radiopharmaceuticals."

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The Challenge of Predicting Radioisotope Needs: The Radionuclide/Grant Merry-Go-Round

Successful grant funding allows for the purchase of additional radionuclides

Purchase of additional radionuclides makes additional production possible

Additional production assures supply and allows for successful grant funding

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Research Isotopes Prioritization - SNM

Isotope	Priority		Isotope	Priority	
^{225}Ac	1	(2)	^{124}I	2	
^{211}At	3	(1)	^{177}Lu	4	
^{213}Bi	2		^{212}Pb	2	
^{76}Br	3		^{188}Re	1	
^{77}Br	3		^{228}Th	3	
^{64}Cu	2		^{229}Th	3	(2)
^{67}Cu	2	(3)	^{86}Y	1	
^{166}Ho	4		^{89}Zr	1	

(1 = highest need, 2 = some need, 3 = little need, 4 = no need)

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Research Isotopes Prioritization - SNM

^{223}Ra	2
^{227}Th	3
^{212}Bi	2
^{188}W	2
^{186}Re	2
^{73}As	3
$^{95/96}Tc$	3
^{99}Tc	3
$^{122}Xe/^{122}I$	2
^{88}Y	3
^{109}Cd	3
^{177m}Sn	3

(1 = highest need, 2 = some need, 3 = little need, 4 = no need

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Research Isotopes Prioritization - SNM

“It's worth thinking about DOE's definition of a "low energy" cyclotron. Most researchers would consider biomedical cyclotrons (<~15 MeV) low energy, but the spreadsheet lists low energy as <30 MeV, which many people might consider medium energy. There are lots of 15 MeV machines around. There are many fewer 20-30 MeV machines.”

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RECOMMENDATIONS

1. In spite of adequate supplies of some radionuclides, we need to develop a national isotope policy and a long-term strategic plan to meet the needs of the medical research community.
2. Supplies of radionuclides for most, maybe all, research and clinical cancer imaging needs are currently being met internally or through DOE. However, many research radionuclides which could be used in the development of therapeutic radiopharmaceuticals are in inadequate supply.
3. For research radionuclides that are not available in sufficient quantity recommendations are:
   - Reprioritize the use of reactors to better meet the needs of the medical research community;
   - Establish a “consortium” of accelerators (cyclotrons) to schedule radionuclide production to meet the needs of the medical research community.
4. For research radionuclides made by the DOE a mechanism needs to be developed to assure investigators and funding agencies that these radionuclides will be available for research when needed.

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RECOMMENDATIONS (cont'd)

5. A long-term plan for assuring that research radionuclides, if used successfully in the development of pharmaceuticals, will be available as cGMP components for use in the commercially licensed products is recommended.
6. The DOE should work with the NCI (and other funding agencies) to advertise the availability of these radionuclides and to reinvigorate the use of these agents in medical research.
7. Consider revising the current DOE fissionable feedstock disposal policy to allow for the maintenance of some U-232 U-233 to feed the radionuclide production system.
8. The US needs to revisit the advisability of relying (largely or solely) on foreign sources of some research and clinical radioisotopes (*e.g.* Mo-99).