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FDA's Regulatory Role in Medical Isotope Production

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The Mo99/Tc99m Generator

- Developed in 1958 by the national labs.
- Came into wide spread medical use in the early 1960's.
- Mo99/Tc99m passes through column with "pure" Tc99m coming out
- Annual use is 30 million globally, 14 million domestically
- Represents ~ 80% of all nuclear medicine use
- **$^{235}U + n \rightarrow$ fission products + ^{99}Mo**
- **$^{99}Mo \rightarrow {}^{99m}Tc + 140$ keV γ**

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What's FDA's Role in this?

In 2007 the National Academy of Sciences (NAS) asked this question of FDA. There was confusion regarding FDA's regulatory requirements when switching from Highly Enriched Uranium (HEU) to Low Enriched Uranium (LEU) and other non-HEU methods for the manufacturing of medical isotopes.

Unless alternatives to HEU for medical isotope production could be found, drug shortage concerns would pressure the need for HEU.

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Medical Isotope Production Without Highly Enriched Uranium- 2009

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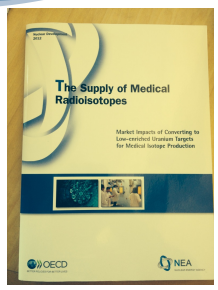

High Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR)
Organization of Economic Cooperation and Development-Nuclear Energy Agency (OECD-NEA)

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Regulation of Medical Radioisotopes

- Regulated exclusively by the Atomic Energy Commission (AEC) until 1975.
- When the AEC split into the NRC, and the Energy Research and Development Administration (ERDA), precursor to Department of Energy, drug authority passed to FDA.
- The licensed possession of the radioactive material remains an NRC statutory authority.

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Regulations, Research, Approval, and the Drug Master File (DMF)

- Research Phase for a drug involves the
  - Investigational New Drug Application (IND)
- NDA: New Drug Application
- sNDA: Supplement – changes to an NDA, (amendments describe IND changes).
- DMF- Drug Master File

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Reasons for a Drug Master File

- Maintain confidentiality of proprietary information.
- Permit review of information by reviewers at FDA to support applications submitted by more than one applicant, e.g. Company A and Company B may receive Mo99 from same Reactor C.

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Drug Master File

"A Drug Master File (DMF) is a submission to the Food and Drug Administration (FDA) that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs. The submission of a DMF is not required by law or FDA regulation. A DMF is submitted solely at the discretion of the holder."

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How does this apply in our situation?

For Mo-99, a drug master file (DMF) may be filed for how it is produced, including the composition of the target material, the irradiation process, and the chemical separation of the Mo99 from the irradiated uranium target material. This is considered proprietary information.

A DMF may be amended when this information changes, e.g. when converting target material from highly enriched uranium (HEU) to low enriched uranium (LEU). If the DMF is already part of an approved NDA, the change must be submitted as a supplement to the NDA (sNDA).

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