Perspectives on the Reliable Supply of Molybdenum-99

Cardinal Health
Nuclear Pharmacy Services

David Pellicciarini
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Logistics
Product
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Agenda

- Company Overview
- Supply Chain
- Perspectives

Speaker

David Pellicciarini
Vice President,
Pharmacy Safety, Practice and Technical Operations
Cardinal Health Nuclear Pharmacy Services
david.pellicciarini@cardinalhealth.com

Company Overview

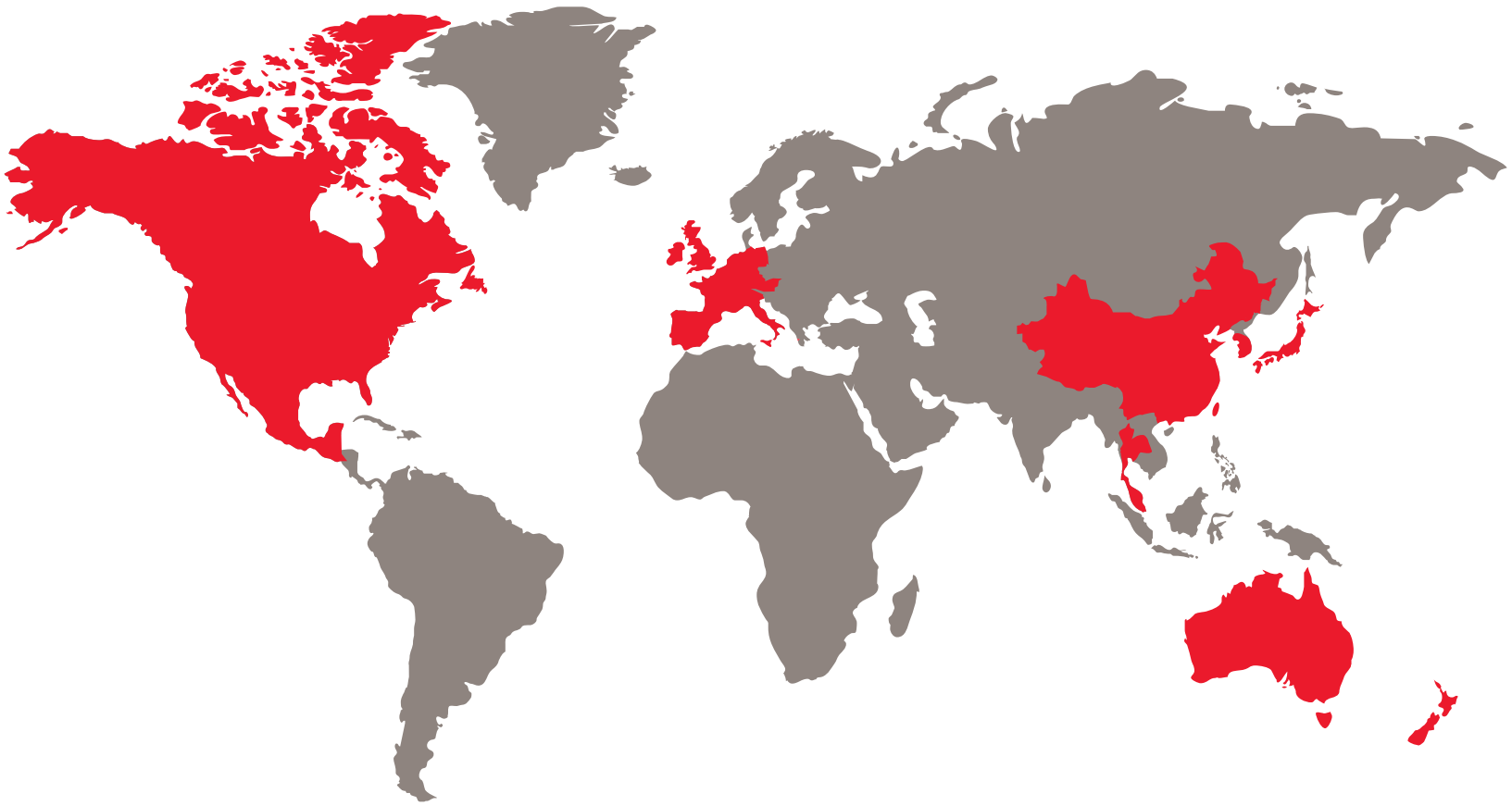
Who we are

Over
36,000
employees
worldwide

#26
on the
Fortune 500

$100B+
annual revenue

Where we are



Corporate HQ = Dublin, OH

Who we serve

Acute

Health systems, community hospitals and surgery centers

Retail

Chain and retail-independent pharmacies and other merchants

Physician Offices

Physician offices and ambulatory care centers

Manufacturer/ Supplier

Manufacturers and suppliers of medical products and pharmaceuticals

Payor

Government and third party national and regional insurers

Patient

Patients/ consumers in need of medical help or wellness support

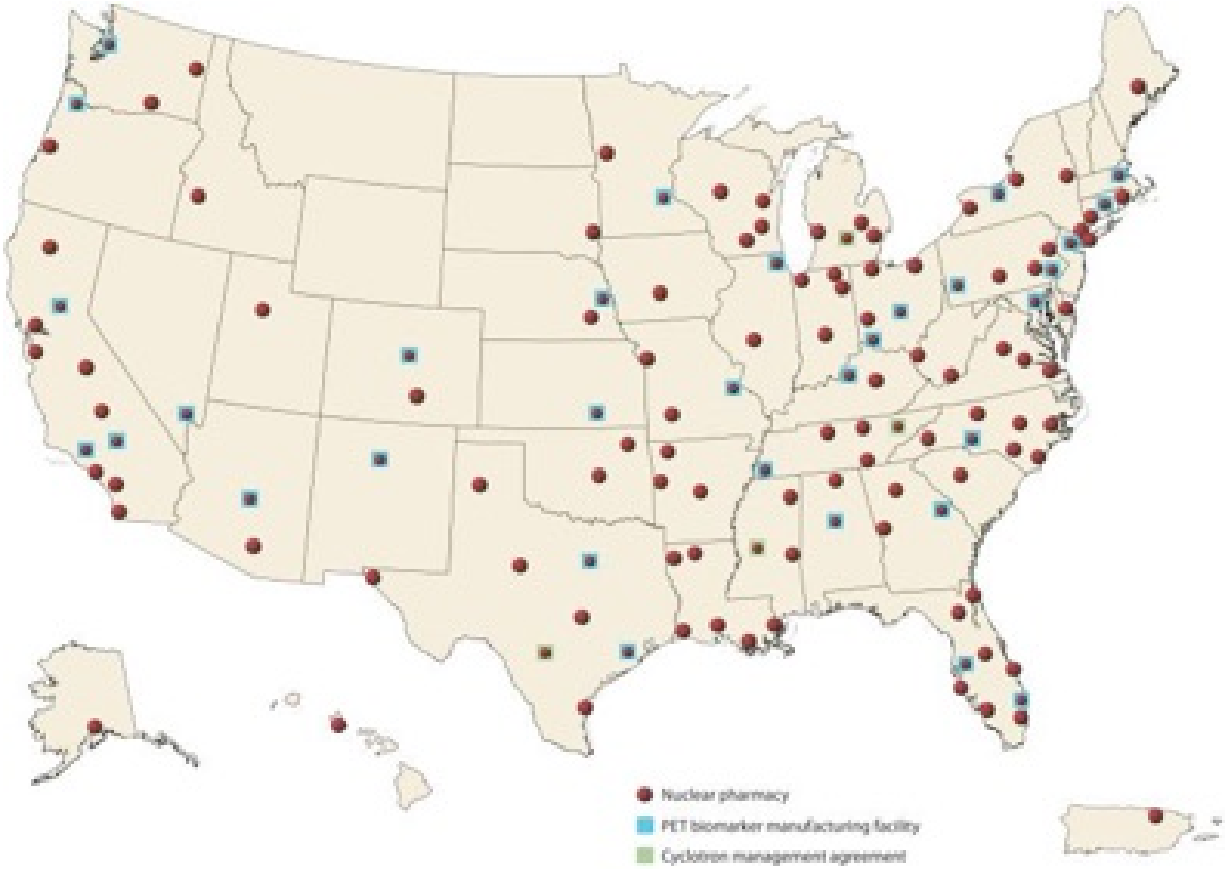
Nuclear Pharmacy Services Overview

Cardinal Health Nuclear Pharmacy Services

Nuclear Pharmacy Services produces, dispenses and delivers radiopharmaceuticals throughout the US

Capabilities

- 130 nuclear pharmacies
- 30 PET biomarker manufacturing sites
- Collaborate with industry, trade and patient advocacy groups
- Ancillary products and services

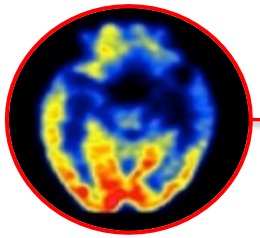


Business overview

We operate a network of nuclear pharmacies and positron emission tomography (PET) biomarker manufacturing facilities that dispense and deliver time-critical, patient-specific radiopharmaceuticals for diagnostic imaging and therapy.

Partner

Pharmaceutical Research



Support the development of novel pharmaceutical agents and biomarkers

Operations

PET biomarker manufacturing

30 facilities

Radiopharmaceutical compounding

130 pharmacies

Distribution

Able to reach 95% of U.S. hospitals within three hours

Patient

Acute care

Hospital imaging customers

Clinics

Cardiology and oncology clinics

To advance the diagnosis and treatment of disease through the use of radiopharmaceuticals

Isotopes typically handled by nuclear pharmacies:

Isotope	Half Life	Isotope	Half Life
Mo-99	66 h	F-18	110 m
Tc-99m	6 h	N-13	10 m
I-123	13 h	C-11	20 m
I-131	8 d	Ge-68	271 d
Xe-133	5 d	Ga-68	68 m
In-111	2.8 d	Ra-223	11 d
Tl-201	3 d	Sm-153	46 h
Ga-67	3.3 d	Others	vary

PET

Tc-99m based radiopharmaceuticals

Mo-99 / Tc-99m

- $NaTcO_4$
- MDP
- DTPA
- Exametazine
- Mebrofenin
- Bicisate
- Disofenin
- MAA
- Mertiatide
- Oxidronate
- Pyrophosphate
- Sestamibi
- Succimer
- Sulfur colloid
- Tetrofosmin
- Tilmanocept
- […]

Supply Chain

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Typical Day at a Nuclear Pharmacy

- Around midnight
  - First run staff arrive
- Early AM hours
  - Elute generators, prepare kits
  - Several dispensing and distribution runs
- ~7-8AM
  - Typical time for first patient diagnostic scans
- Late AM / early PM
  - Stat doses; add-on doses
- Afternoon
  - Order receipt, set-up for next day

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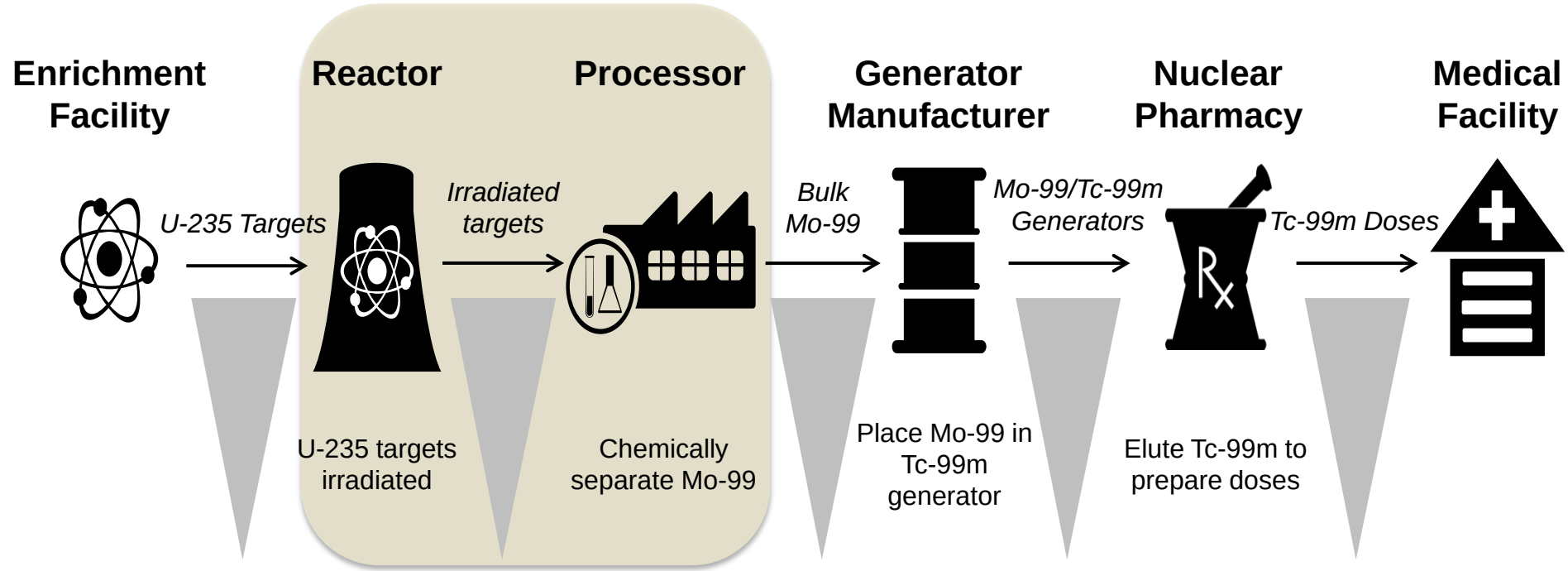
Current US Mo-99 Supply Chain



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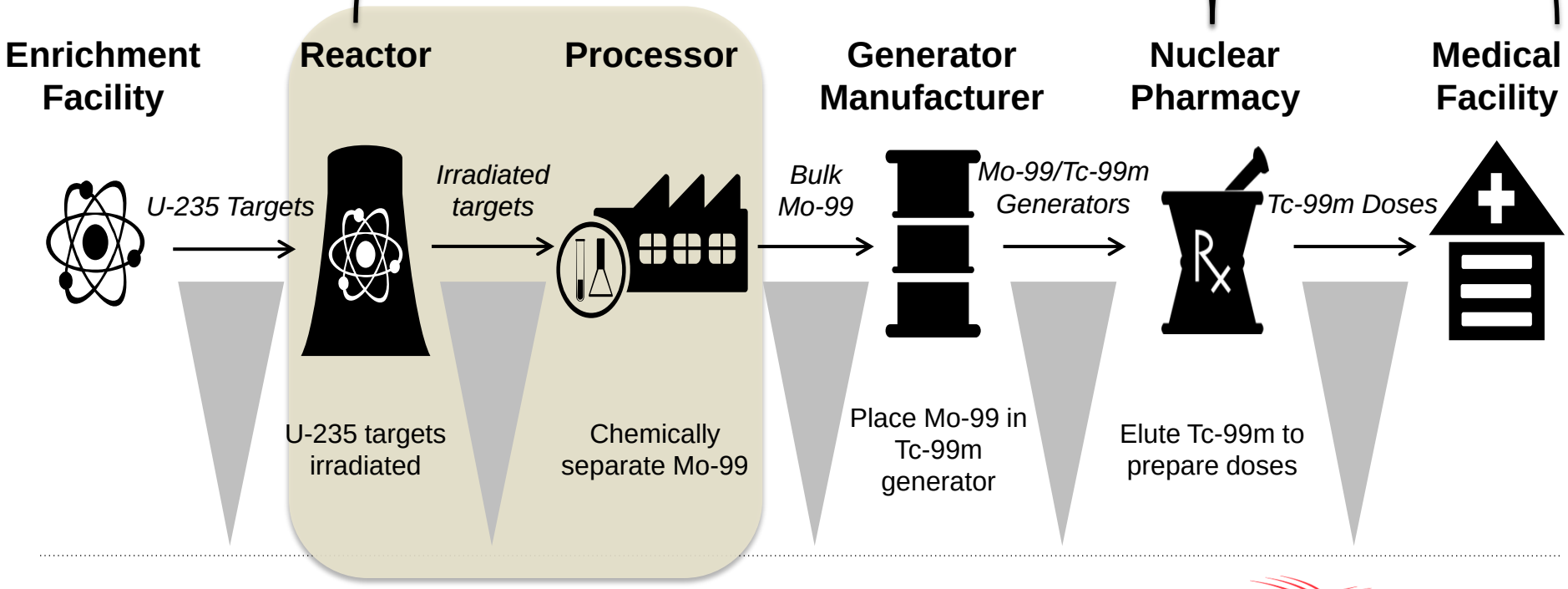
Current US Mo-99 Supply Chain

Mo-99 -- 66h half life
12h delay = 12% product lost
24h delay = 22% product lost

Tc-99m -- 6h half life
12h delay = !



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Impact of Mo-99 Supply Chain Problems

- It is estimated there are about 18 million nuclear medicine procedures per year in the US, 80% of which use Tc-99m (SNMMI Sep 2015)
  - 18 million per year x 0.8 / 365 d/y ≈ 40,000 per day

- For <u>every day</u> without Mo-99, approximately 40,000 patients in the US would not receive their prescribed diagnostic imaging procedure

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Perspectives

Perspectives

- Supply chain stability is critical to patient care
- Disruptions to the Mo-99 supply chain…
  - …directly impact patient care
  - …directly impact the modality
- Radiopharmaceutical dispensing is the opposite of durable good distribution
- Nuclear pharmacies attempt to mitigate impacts of supply chain disruptions, but cannot completely overcome an interruption in supply of Mo-99
  - In the (very) short run you can increase materials efficiencies.
  - But then you run out of runway.
  - Triage.

Perspectives

- Global coordination and awareness by AIPES and OECD can help mitigate disruptions

- Based on AIPES and OECD projections, there are still tight weeks, even with all of the reactor and processor coordination
  - Annual view is “ok,” but with some vulnerability; things look a little different at the week-to-week view.
  - What happens when things are tight and something unexpected occurs? This is where having the 35% reserve capacity mentioned by OECD would help.
  - Communication of possible problems ahead of time is extremely helpful.

- NRU contingency

Perspectives

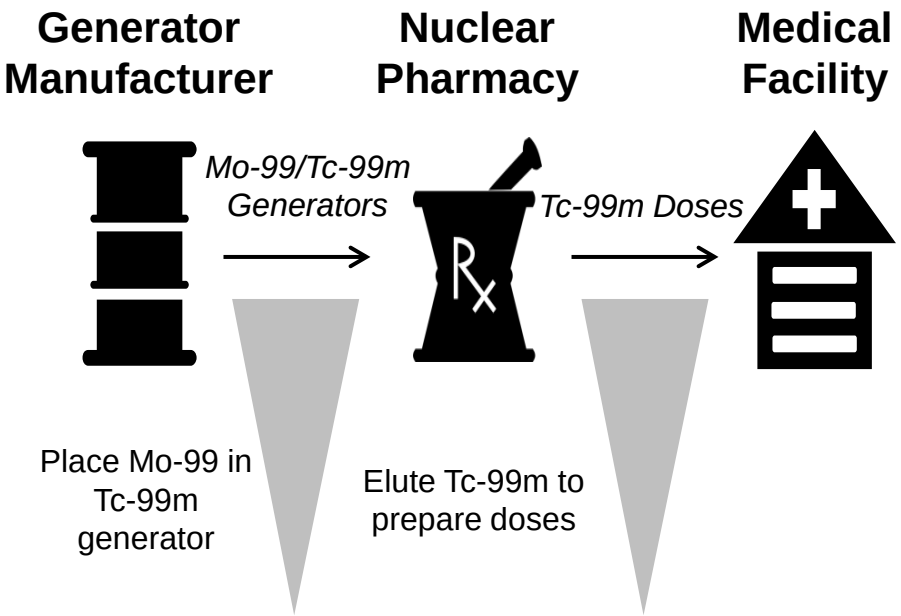
- AMIPA (2012) directed the DOE “to evaluate and support projects for the production in the United States, without the use of highly enriched uranium, of significant quantities of molybdenum-99 for medical uses.”

- The transition from HEU to LEU sources of Mo-99 is in support of non-proliferation initiatives, which we all support.

This transition needs to be very carefully managed to reduce the likelihood of a supply interruption or shortage.

Perspectives

- Customers are eligible for a $10 reimbursement for use of LEU Tc-99m
- Consideration should be given to increasing the amount based on inflation and other factors



Perspectives

- In addition to non-HEU sources, AMIPA (2012) also directed the DOE “to evaluate and support projects for the production in the United States…”

- US production offers
  - Increased efficiency due to improved logistics
  - Reduced risk due to shorter logistics
  - Reduced risk due to international factors

- Continued US government support for domestic Mo-99 sources

Perspectives

- AMIPA addresses Mo-99 production
- In nuclear medicine, there are other reactor-produced radioisotopes, such as I-131 and Xe-133, in use. For example:
  - I-131 has both therapeutic and diagnostic indications
  - Xe-133 is a diagnostic imaging agent
- Supply chain instability can impact these products as well

Thank you.

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