Perspectives on the Reliable Supply of Molybdenum-99

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Cardinal Health
Nuclear & Precision Health Solutions

CardinalHealth
Essential to care™

Speaker

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Agenda

- Introduction and Company Overview
- Nuclear Pharmacy Operations
- US Supply Chain for Mo-99/Tc-99m Radiopharmaceuticals
- Perspectives on Reliable Supply
- Conclusion

Company Overview

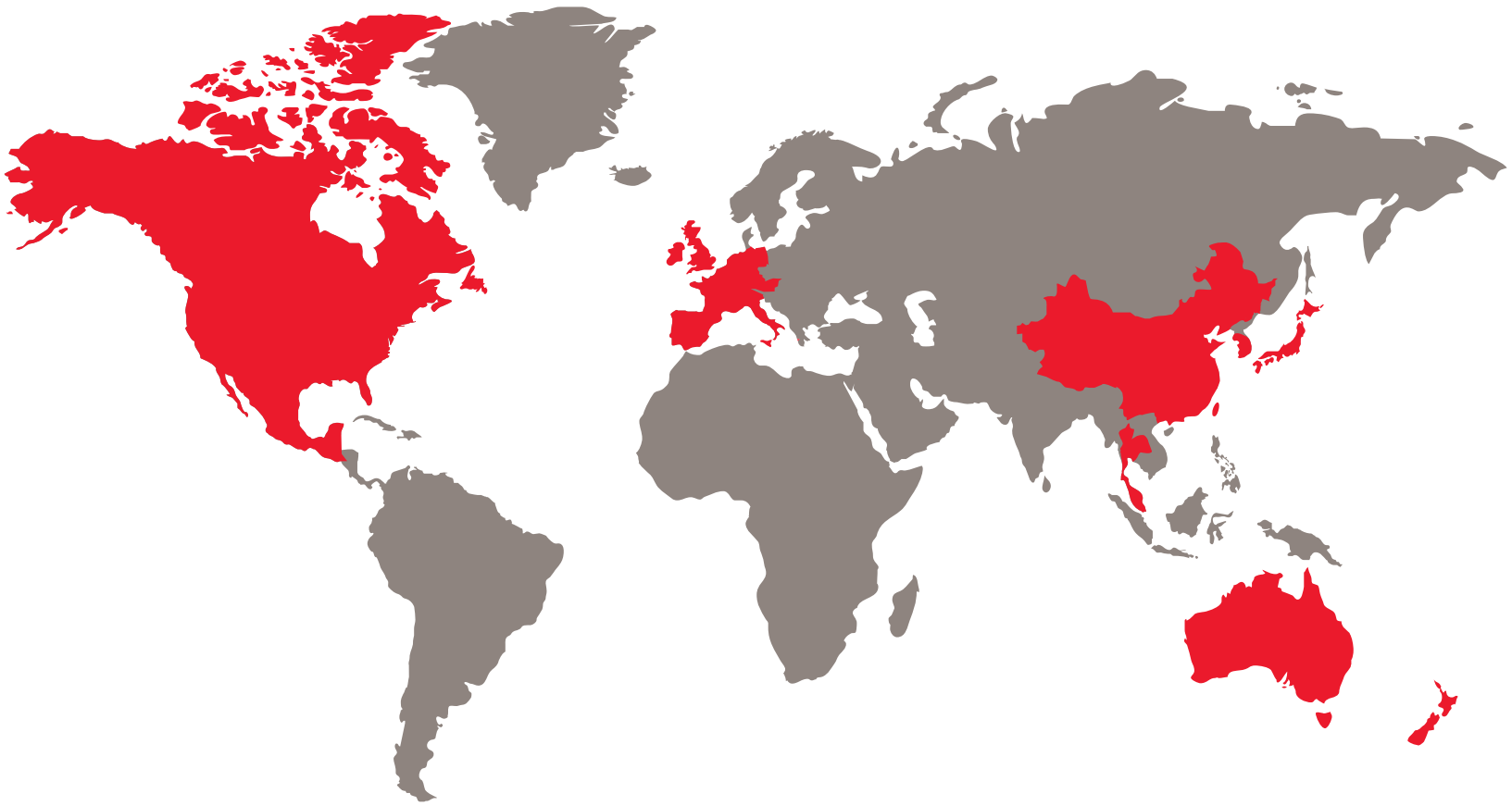
Who we are

Over
36,000
employees
worldwide

#15
on the
Fortune 500

$100B+
annual revenue

Where we are



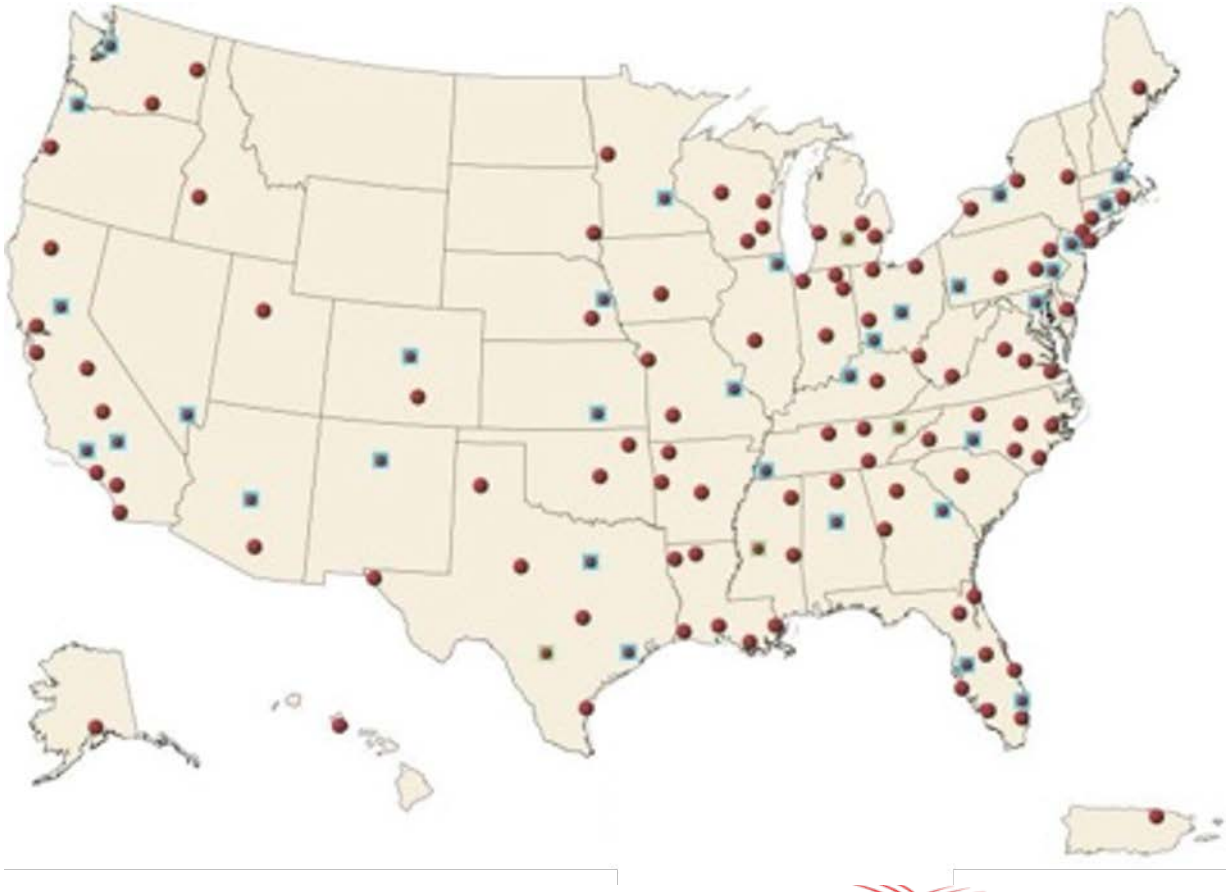
Corporate HQ = Dublin, OH

Nuclear & Precision Health Solutions Overview

Cardinal Health
Nuclear & Precision Health Solutions

NPHS produces, dispenses and delivers radiopharmaceuticals throughout the US

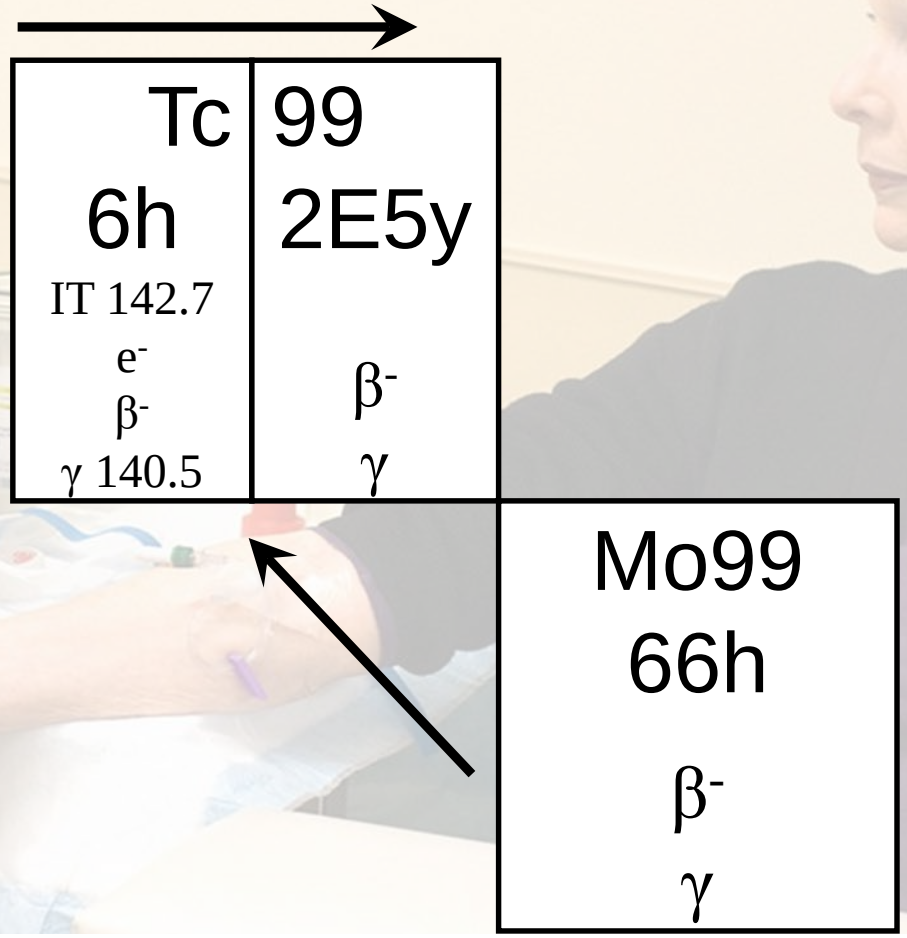
- 130 nuclear pharmacies
- 30 PET biomarker manufacturing sites
- Collaborate with industry, trade and patient advocacy groups
- Ancillary products and services



CardinalHealth™

Why are we here?

To provide the highest quality health care to our patients.



Use of Mo-99 / Tc-99m in the US

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

18 million per year x 0.8 / 255 d/y ≈ 56,000 per day

Nuclear Pharmacy Operations

What is a nuclear pharmacy?

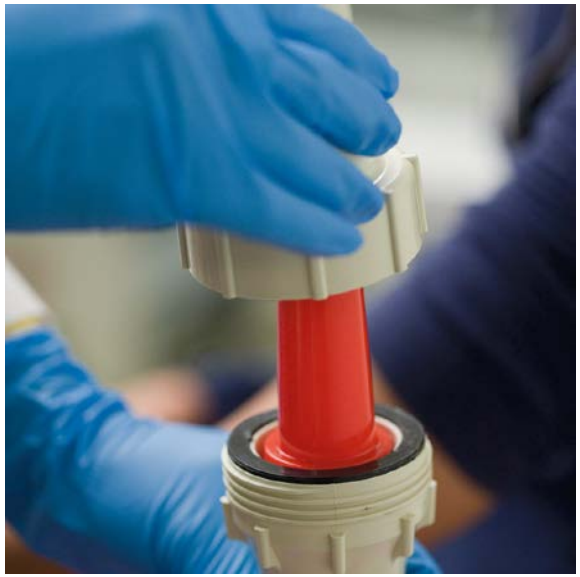
- Nuclear pharmacies prepare and dispense radioactive drugs for human (and sometimes animal) use.
- Nuclear pharmacies employ licensed pharmacists and pharmacy technicians:
  - Must meet both US Nuclear Regulatory Commission requirements and State Board of Pharmacy requirements
- Support often provided by other professionals, such as health physicists.

What is a nuclear pharmacy?

Nuclear pharmacies prepare radioactive drugs

- Most often by combining a radioisotope with a chemical compound to form a radiopharmaceutical
- In the case of Mo-99/Tc-99m generators:
  - Can dispense $NaTcO_4$ directly
  - Most often combine Tc-99m with a radiopharmaceutical kit (“cold kit”)

What is a nuclear pharmacy?



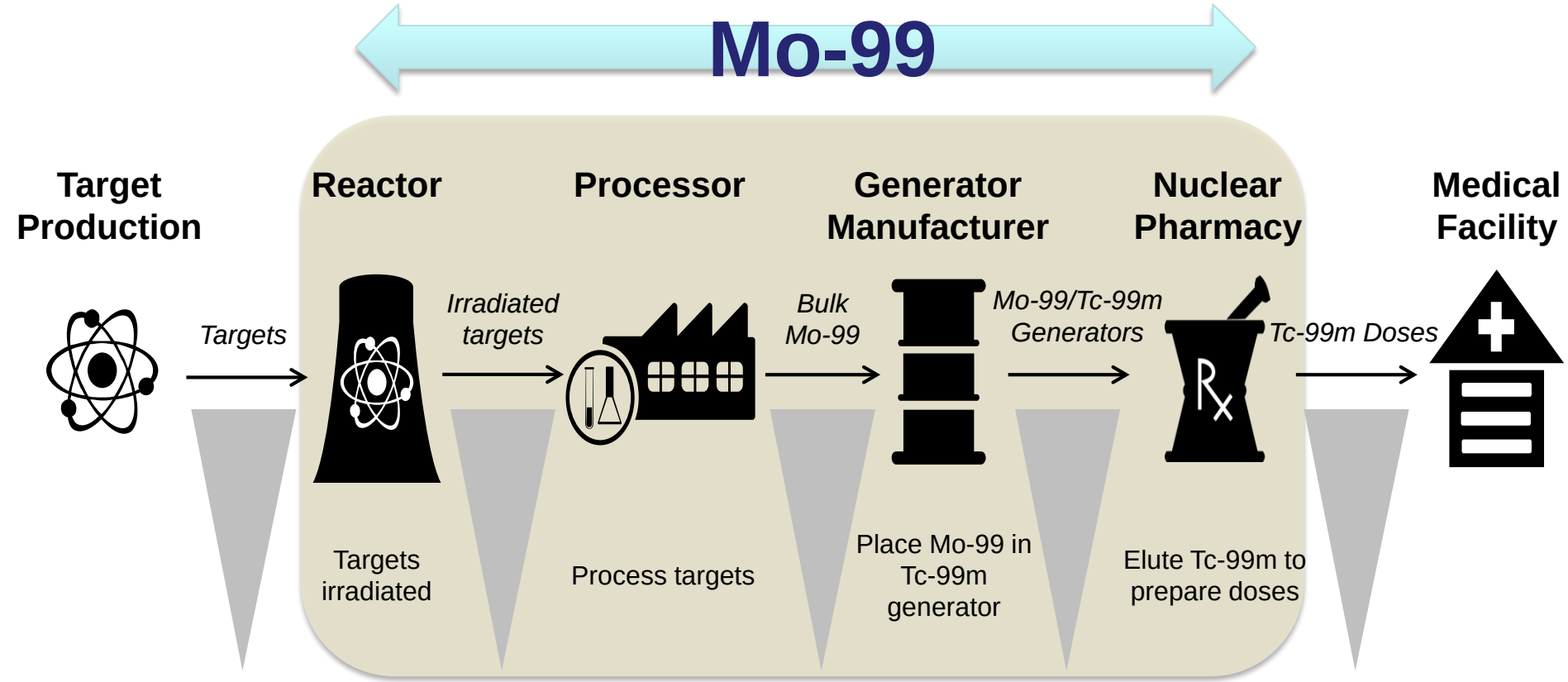
Shipped to a hospital or imaging facility

Typical Day at a Nuclear Pharmacy

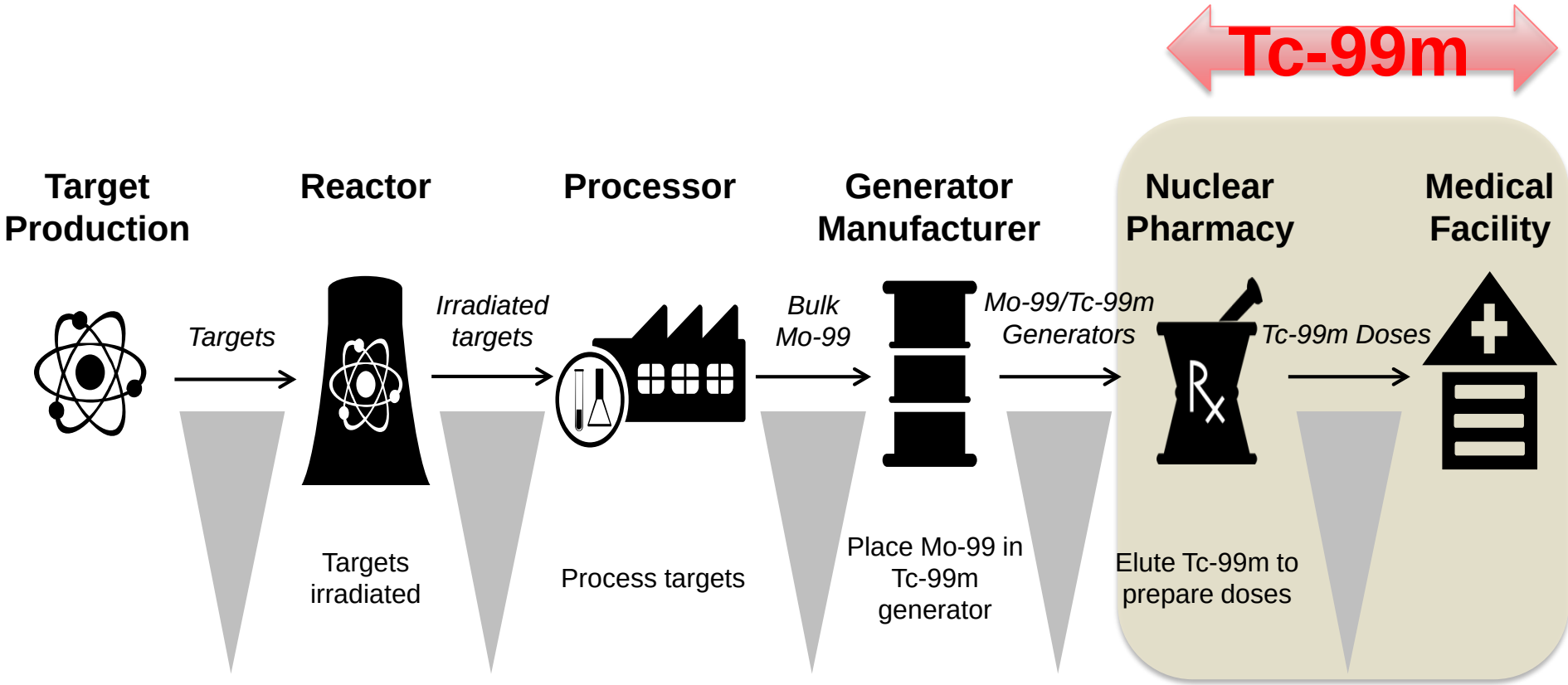
- Around midnight
  - First run staff arrive
- Early AM hours
  - Elute Mo-99/Tc-99m generators, prepare kits
  - Several dispensing and distribution runs
- ~7-8AM
  - Typical time for first patient diagnostic scans
- Late AM / early PM
  - Stat doses; add-on doses
- Afternoon
  - Order receipt, set-up for next day

US Supply Chain

Mo-99 Supply Chain



Tc-99m Supply Chain

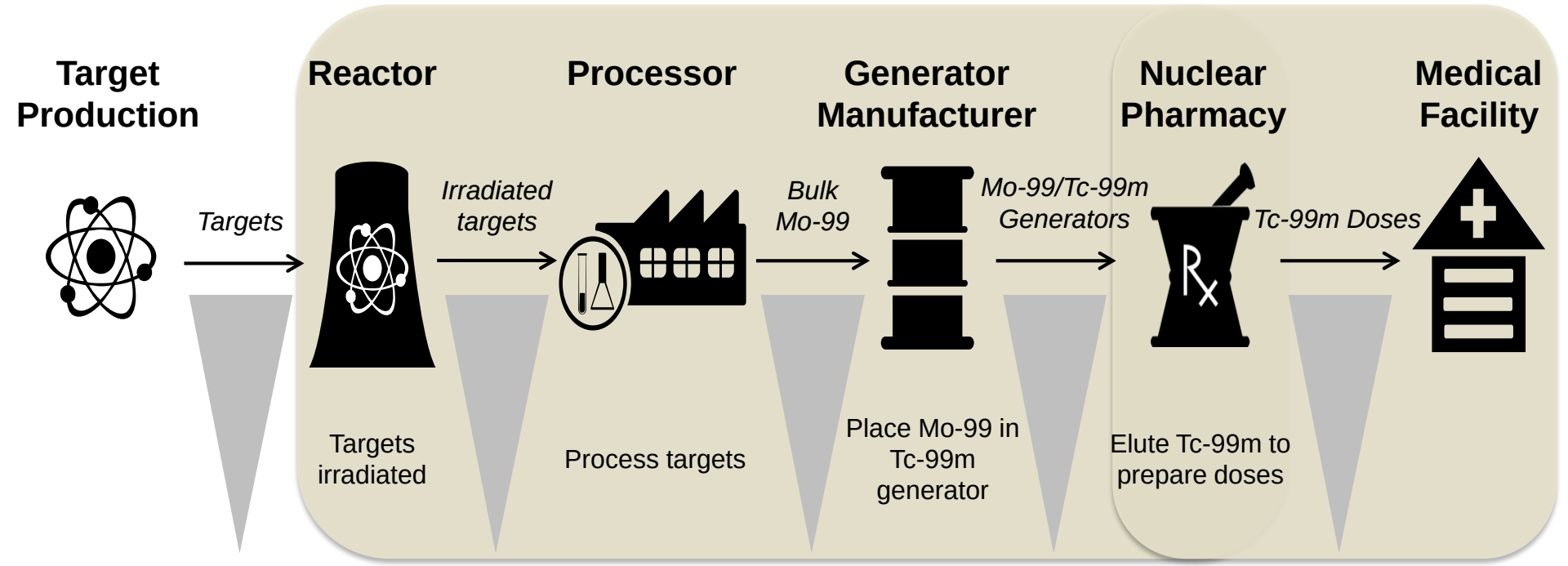


Mo-99/Tc-99m Supply Chain

66h half life:
12h delay = 12% product lost
24h delay = 22% product lost

6h half life
12h delay = _____

Mo-99 **Tc-99m**



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

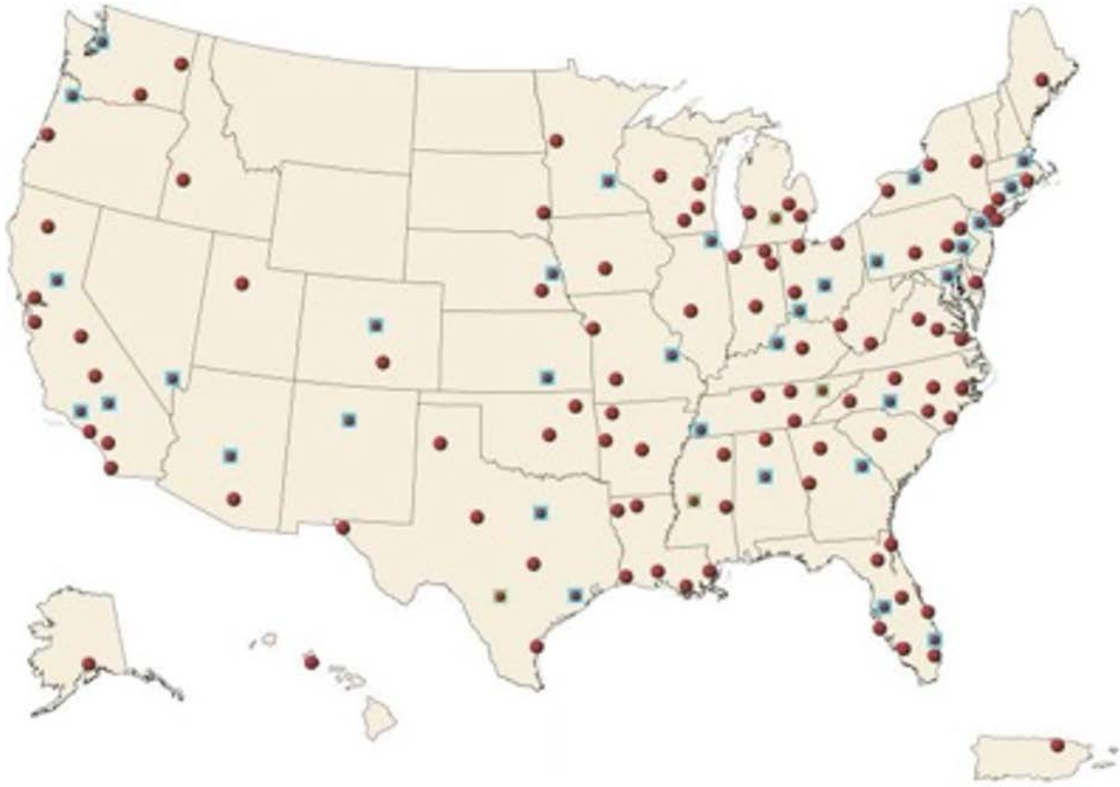
Tc-99m based radiopharmaceuticals

Mo-99 / Tc-99m

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

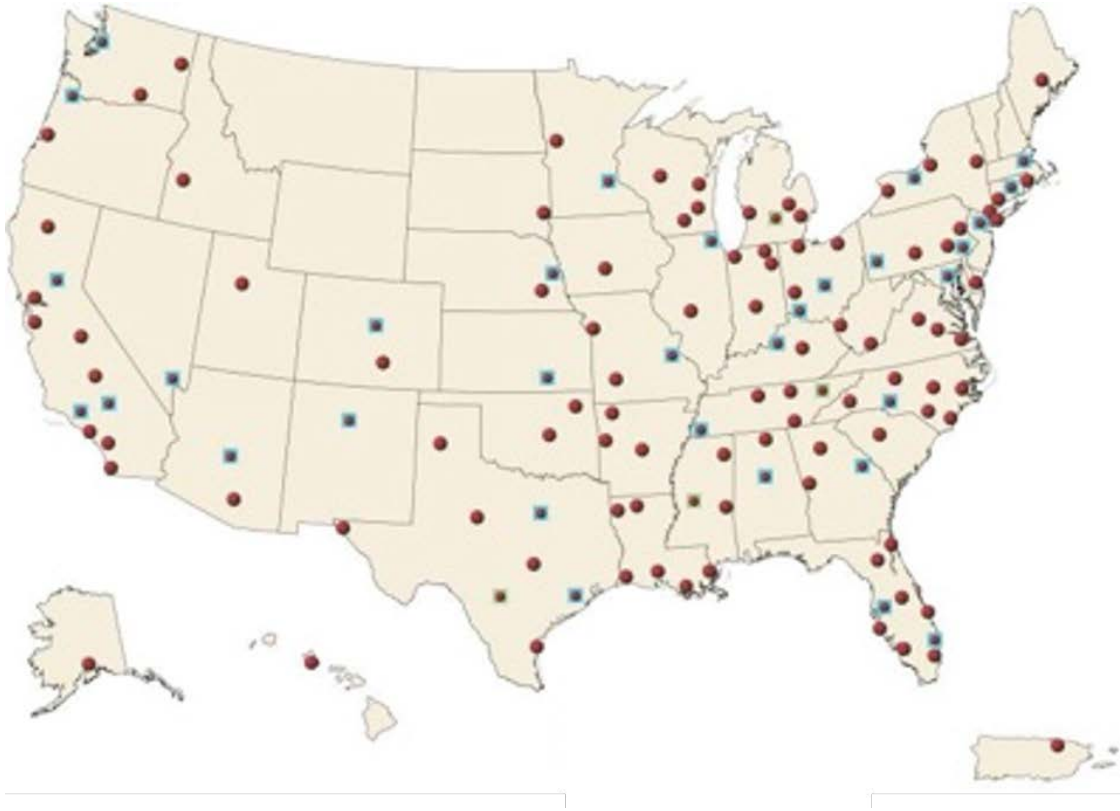
Supply Chain Disruptions

- Supply chain stability is critical to patient care
- Close communication and coordination with vendors, before and during any disruptions
- Contingency planning



Supply Chain Disruptions

- Disruptions to the Mo-99 supply chain…
  - …directly impact patient care
  - …directly impact the modality
- Consequences
  - Strain on nuclear pharmacies
  - Strain on hospitals and outpatient facilities
  - Missed doses to patients
  - A reduction in the quality of medical care in the US



Perspectives

"Availability and stability of supply of Tc-99m is critical to public health."

FDA, Mo-99 Topical Meeting, Sep 24, 2018

Perspectives

- Supply chain stability is critical to patient care and to the modality
- The supply of Mo-99/Tc-99m generators to nuclear pharmacies in the US has had several interruptions over the past year
- This was and is further exacerbated by
  - A lack of domestic Mo-99 supply
  - Inadequate outage reserve capacity

Perspectives

- Patient care in the US is being impacted based on overseas producers going off line.
- This not only impacts patient care, but it impacts overall trust and confidence in the modality.
- Are physicians starting to leave nuclear medicine?

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 Mo-99 is in support of non-proliferation initiatives, which we all support.

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

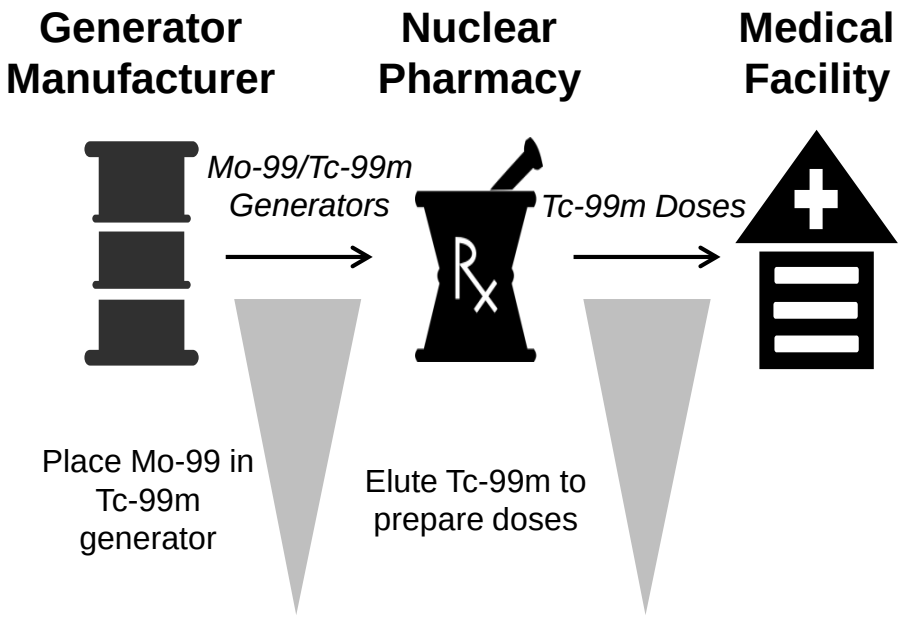
Perspectives

- AMIPA (2012): "…production in the United States…"
- US-based production offers
  - Increased efficiency due to improved logistics
  - Reduced risk due to shorter logistics
  - Reduced risk due to international factors
- We urge continued support for domestic Mo-99 sources and for adequate outage reserve capacity

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

- AMIPA addresses Mo-99 production, but nuclear medicine also uses other reactor-produced radioisotopes, such as I-131 and Xe-133.
  - I-131 has both therapeutic and diagnostic indications. Recent reports of shortages in certain international markets.
  - Xe-133 is a diagnostic imaging agent
- Supply chain instability can impact these products as well

Perspectives

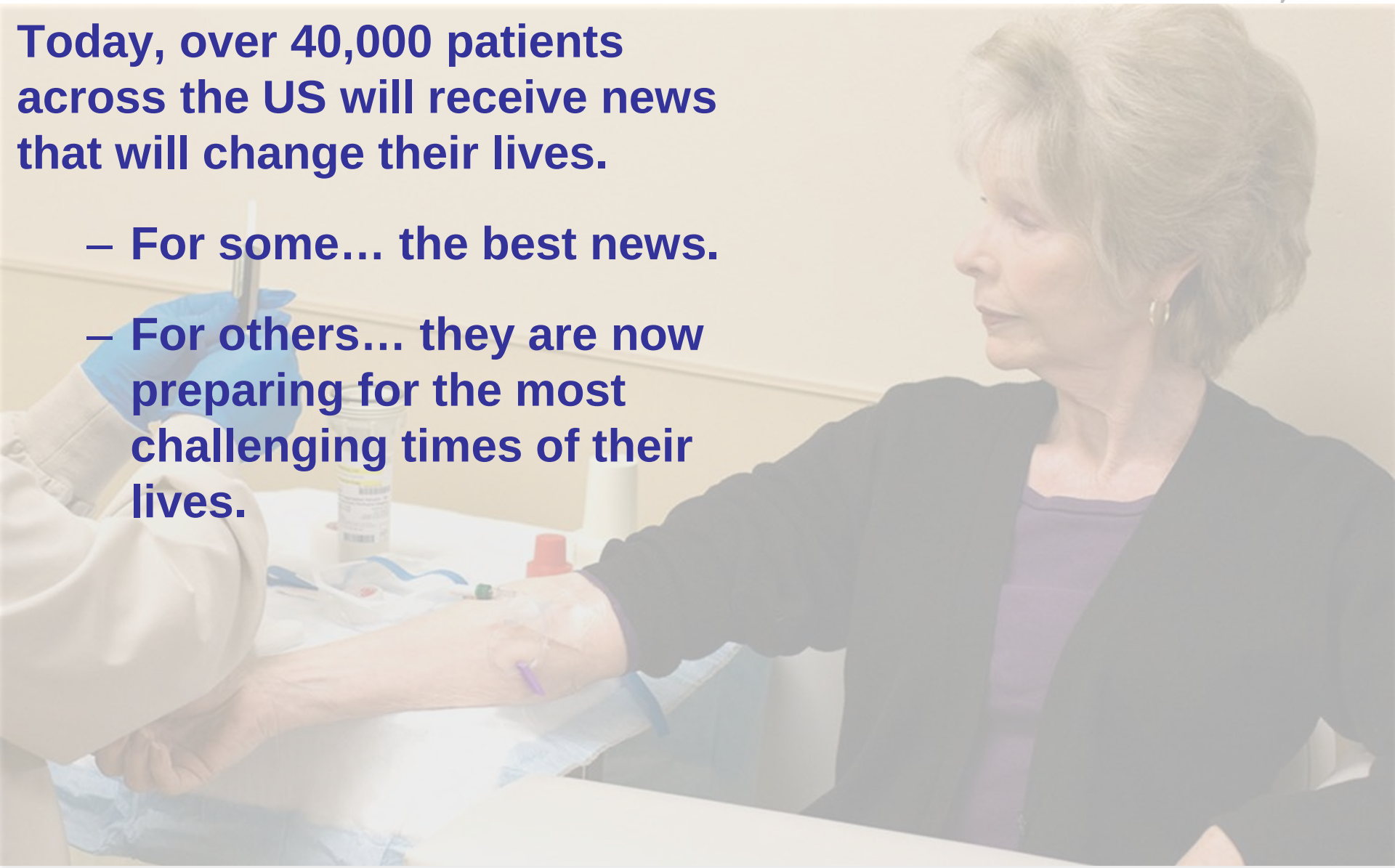
Good progress on HEU to LEU conversions...

…but there is more work to be done on supply chain stability.

Conclusion

Today, over 40,000 patients across the US will receive news that will change their lives.

- **For some… the best news.**
- **For others… they are now preparing for the most challenging times of their lives.**



Thank you.