

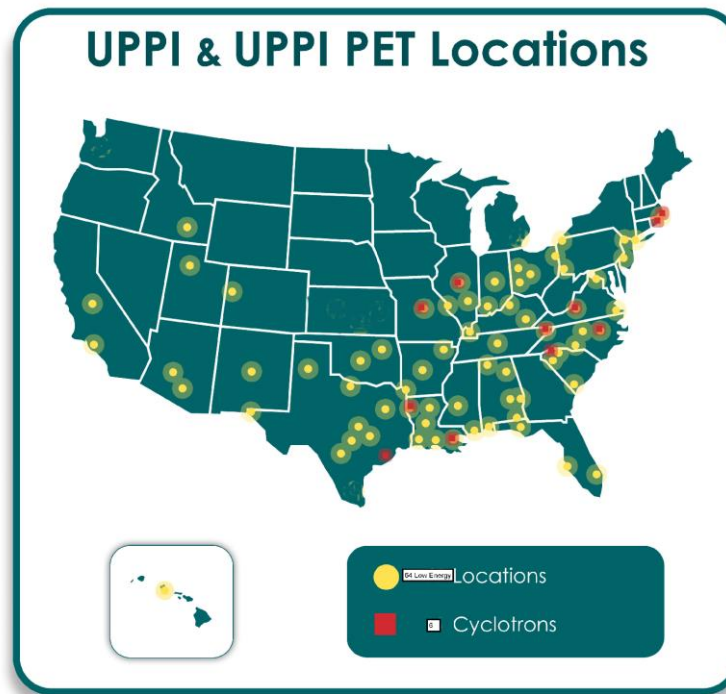
U.S. Mo-99 Supply Status – Industry Perspectives

**NNSA Mo-99 Stakeholder Meeting
Agenda**

November 4, 2021



About UPPI



- UPPI is an alliance of small business and university owned nuclear pharmacies.
- Formed in 1998, with low energy and high energy nuclear pharmacies.
- UPPI represents 8,000 of the 50,000 unit doses dispensed every day in the U.S.

UPPI LEU Walk

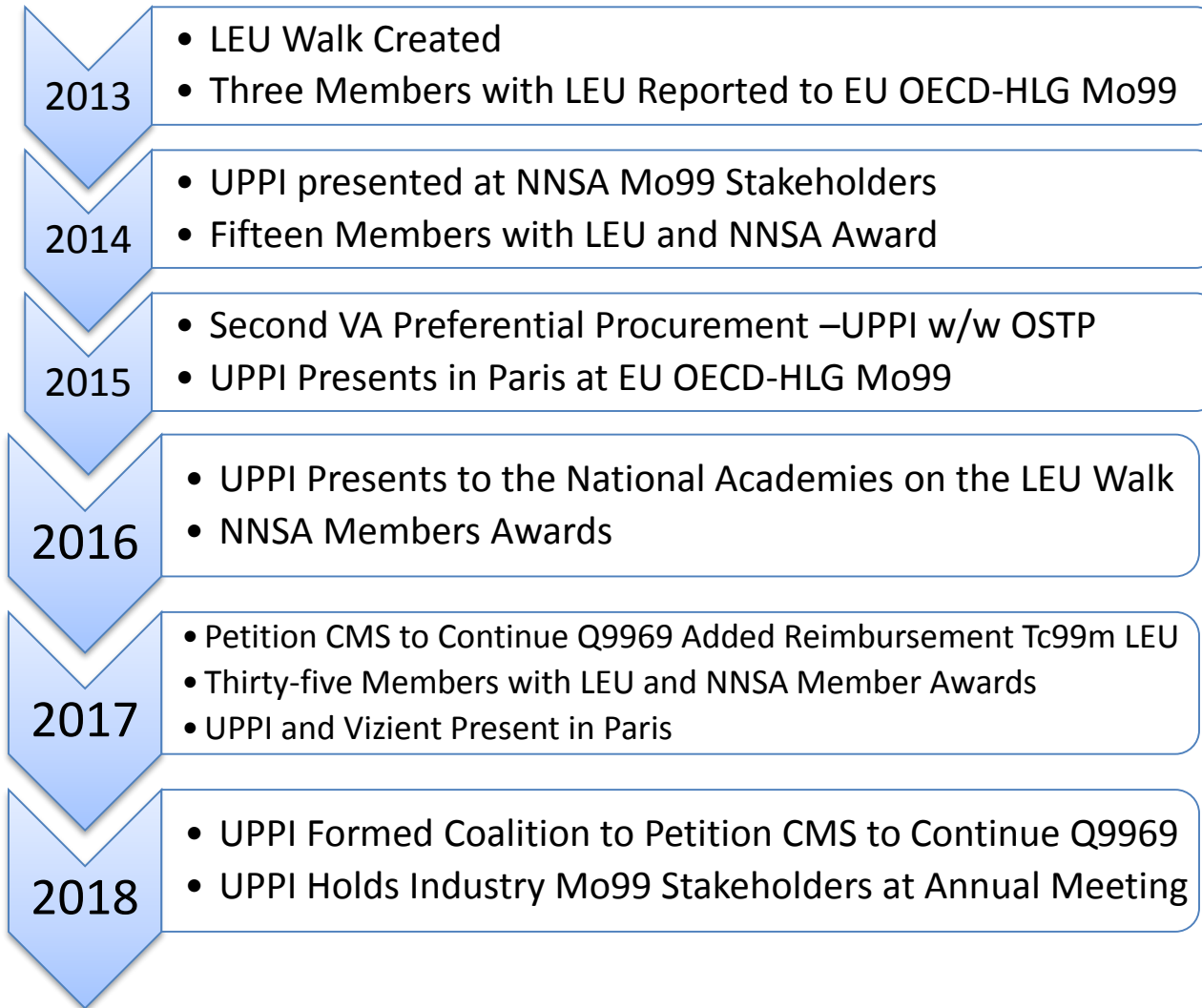
UPPI Branded Mo99 LEU Walk: 2013 - 2017



4

UPPI members adopted the conversion of highly enriched uranium to low enriched uranium Mo99 generators, UPPI LEU Walk, leading the transition when the supply was very limited.

UPPI Advocacy and Branding LEU Walk



UPPI Advocacy and Branding LEU Walk

2019

- UPPI presents at NNSA Mo99 Stakeholder Meeting
- CMS continues Q9969

2020

- UPPI pens letter in favor of extending HEU target shipments to help IRE complete LEU conversion
- CMS continues Q9969

2021

- CMS continues Q9969
- UPPI joins Patients for a Safer Nuclear Medicine Coalition

2021

- UPPI pens letter to CNSC in favor of licensing BWXT Mo99
- UPPI participates on NRC Regulatory Information Conference: Mo99

2021

- UPPI panelist on NNSA M3 Mo99 Stakeholders Meeting
- UPPI contributes to IAEA TECHDOC Mo99 and UPPI Model

Views of the Current Market for Mo-99

- Mo-99 production, processing, generator fills and delivery to UPPI radiopharmacies held up very well during the COVID-19 lockdown.
- Credit for supply resilience was due to the industry's resolution of prior Mo-99 production shortages several years ago.
- Mo-99 supply improved with NorthStar Medical Radioisotopes cMo-99 approval that increased the curies for distribution to radiopharmacies.
- When nuclear imaging increased post-lockdown, the Mo-99 supply equaled that of the return-to-preCovid demand.
- Xenon 133 for ventilation studies has not recovered from the initial moratorium on lung studies in some areas of the country.

Development/Changes to the Current Supply Chain

DEUTSCHE OPTIK

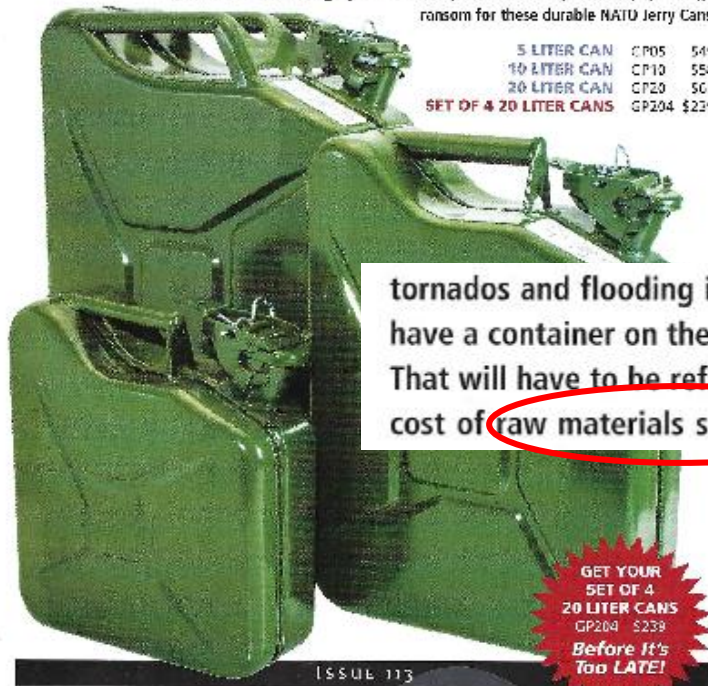
FALL - WINTER ★ 2021

DON'T WAIT UNTIL IT IS TOO LATE!

We just want to issue an availability warning. When the Colonial Pipeline hack occurred the sales of Jerry Cans went berserk! We sold every single can, regardless of size, within three days! (So did every other supplier). They were supposed to last us until late Fall. Now, with Hurricane Ida, and the ensuing tornados and flooding in PA, NJ, and New York, we are getting deluged with orders once again. We have a container on the water, arriving mid-October, but there's a hitch: the cost of shipping tripled! That will have to be reflected in the prices, obviously. Furthermore, the future prices look bleak. The cost of raw materials soared 27%, and that'll make 'em even more pricey on the next go-around!

Therefore, we encourage you to stock up NOW, before you must pay a king's ransom for these durable NATO Jerry Cans.

5 LITER CAN	CP05	549
10 LITER CAN	CP10	558
20 LITER CAN	CP20	505
SET OF 4 20 LITER CANS	GP204	\$239



GET YOUR
SET OF 4
20 LITER CANS
GP204 \$239
Before It's
Too LATE!

An example of the global pandemic pressures on products. The same effects flowdown in the radiopharmacy space.

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Supply Chain Challenges: Listing of Tc-99m Labeled Products

- Tc-99m methylene diphosphonate
- Tc-99m macro aggregates of albumin
- Tc-99m pyrophosphates
- Tc-99m mebrofenin
- Tc-99m human serum albumin
- Tc-99m sulfur colloid
- Tc-99m exametazime
- Tc-99m tetrofosmin
- Tc-99m Cardiolite/sestamibi
- Tc-99m dimercaptosuccinic acid
- Tc-99m mertiatide
- Tc-99m Oxidronate
- Tc-99m Diethylenetriamine pentaacetate
- Tc-99m bicisate
- Bone imaging
- Lung imaging
- Bone/blood pool imaging
- Biliary imaging
- Blood pool imaging
- Liver, sentinel node imaging
- Brain and infection imaging
- Heart imaging
- Heart imaging
- Renal imaging
- Renal imaging
- Bone imaging
- Renal/lung imaging
- Brain imaging

Supply Chain Challenges: Tc-99m Labeled Products Experiencing Out-of-Stock in 2021 (labeled in red)

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Developments/Changes in the Broader Market: Nuclear Medicine Imaging

- Believe downward market pressure on Tc-99m product prices over the next several years due to pandemic cost increases.
- Out of Stock shortages of cold kits to label Tc-99m creates gaps with patients lost to non-nuclear modalities.
- Manufacturing/production problems:
 - API shortages
 - Parts to repair vendor's production line
- COVID-19 protocols impact on staffing at production facilities.
- Stock shortages leads to price increases and hospital structures will push back –reason: pandemic effects all services in the care setting.

Developments/Changes in the Broader Market

The Report was updated on 2/21/20 to include revised economic analysis about production increases and supply restoration after a shortage. See the [FDA Archive for the original Report](#).

Drug Shortages:

Root Causes and Potential Solutions

2019



U.S. Food and Drug
Administration



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Developments/Changes in the Broader Market

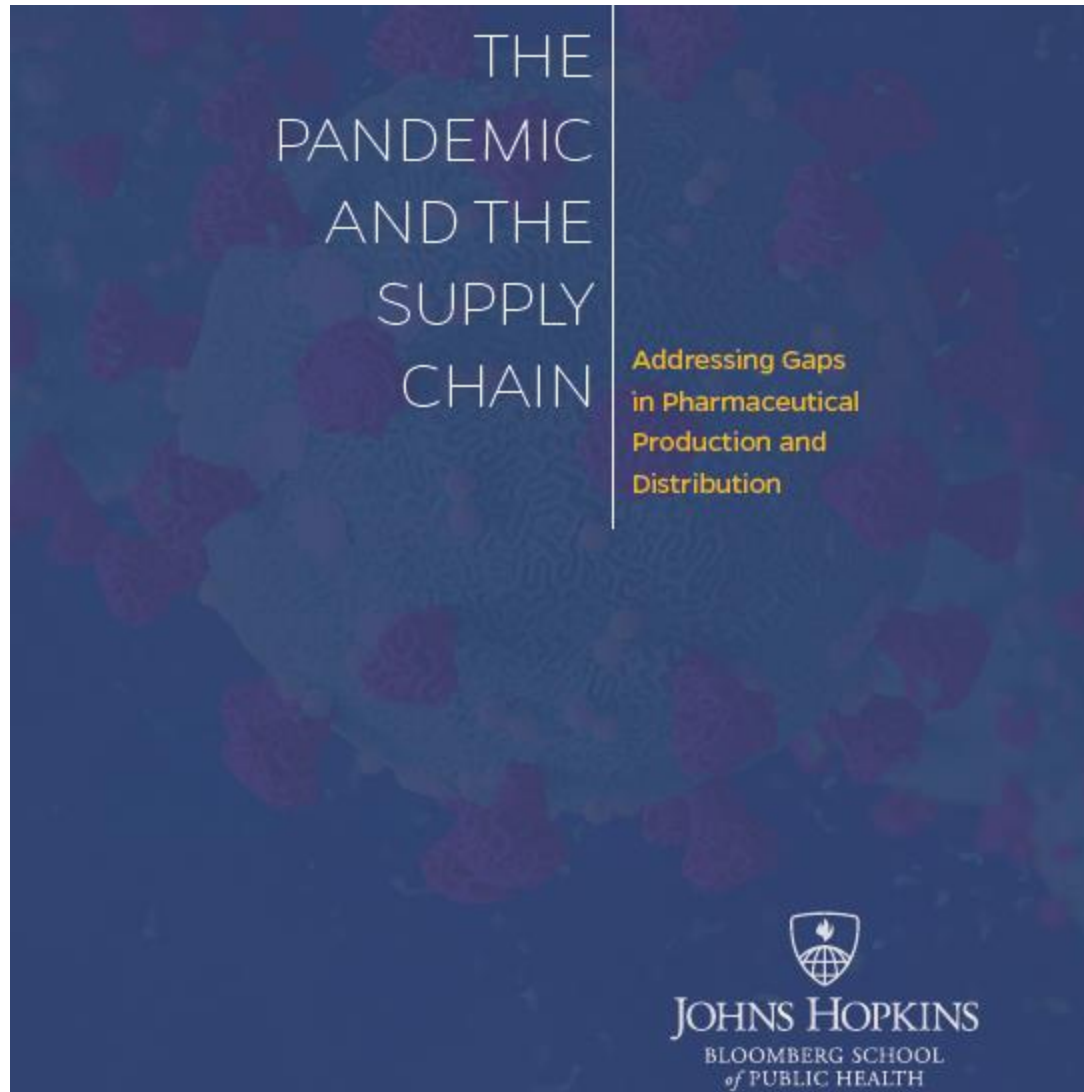
From the FDA 2019 report:

“Drug shortages persist... prices rise after a supply disruption...”

- Lack of incentive to produce less profitable drugs.
- Product life cycle matured on the drugs.
- Market fails to recover after the supply disruption.

One noteworthy recommendation: Better characterization of the shortage between the public sector (FDA) and the private sector (manufacturer).

Developments/Changes in the Broader Market



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Developments/Changes in the Broader Market

From the Johns Hopkins *Pandemic and the Supply Chain* white paper:

- Recognized disruption to Active Pharmaceutical Ingredient (API) and finished pharmaceutical product manufacture.
- Cited lock-downs led to shortage of raw materials.
- Group purchasing organizations mobilized in 2019-2021 for drug shortages (non-nuclear products) for critical medications.
- White House issued Executive Order (EO) that allowed US International Development Finance Corporation to invest in domestic production.
- EO parallels NNSA actions taken years ago to mitigate supply disruption of Mo-99.



Drug Shortage: Causes, Impact, and Mitigation Strategies

Sundus Shukar^{1,2,3,4}, Fatima Zahoor^{5,6}, Khezhar Hayat^{1,2,3,4,7}, Amna Saeed^{1,2,3,4},
Ali Hassan Gillani^{1,2,3,4}, Sumaira Omer^{1,2,3,4}, Shuchen Hu^{1,2,3,4}, Zaheer-Ud-Din Babar⁸,
Yu Fang^{1,2,3,4} and Caijun Yang^{1,2,3,4*}

¹Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmacy, Xi'an Jiaotong University, Xi'an, China, ²Center for Drug Safety and Policy Research, Xian Jiaotong University, Xi'an, China, ³Shaanxi Centre for Health Reform and Development Research, Xi'an, China, ⁴Research Institute for Drug Safety and Monitoring, Institute of Pharmaceutical Science and Technology, China's Western Technological Innovation Harbor, Xi'an, China, ⁵Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan, ⁶Yusra Institute of Pharmaceutical Sciences, Islamabad, Pakistan, ⁷Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan, ⁸Department of Pharmacy, School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom

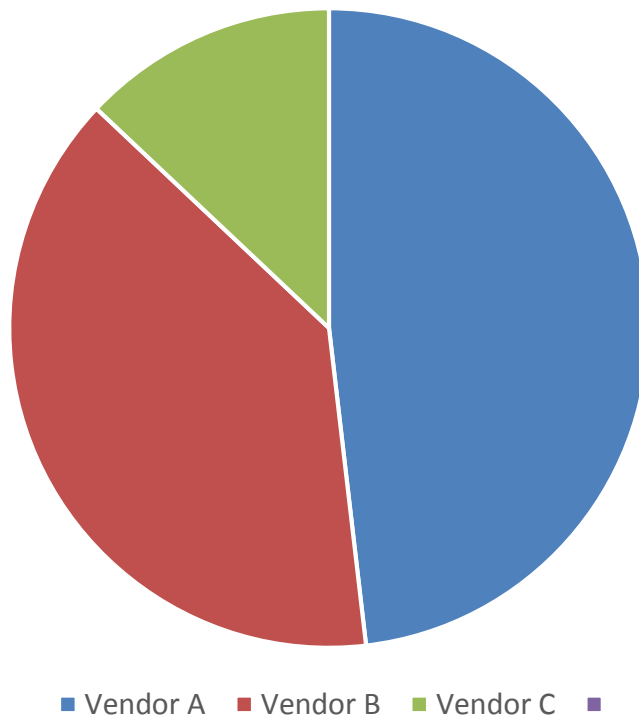
*“All types of drugs, such as essential life-saving drugs, oncology medicines, antimicrobial drugs, analgesics, opioids, cardiovascular drugs, **radiopharmaceutical**, and parenteral products, are liable to the shortage.”*

Developments/Changes in the Broader Market

- How demand is affected:
 - Unavailability of raw materials,
 - Logistic problems,
 - Business problems –**products in life cycle decay,**
 - Demand issues of **just-in-time inventory,**
 - Increased demand for product in **shortage shifts to other suppliers stressing market coverage,**
 - COVID-19 led to unpredictable demand patterns for the manufacturers.

Emergence of Domestic Production of Mo-99: Generator Supply Chain Today

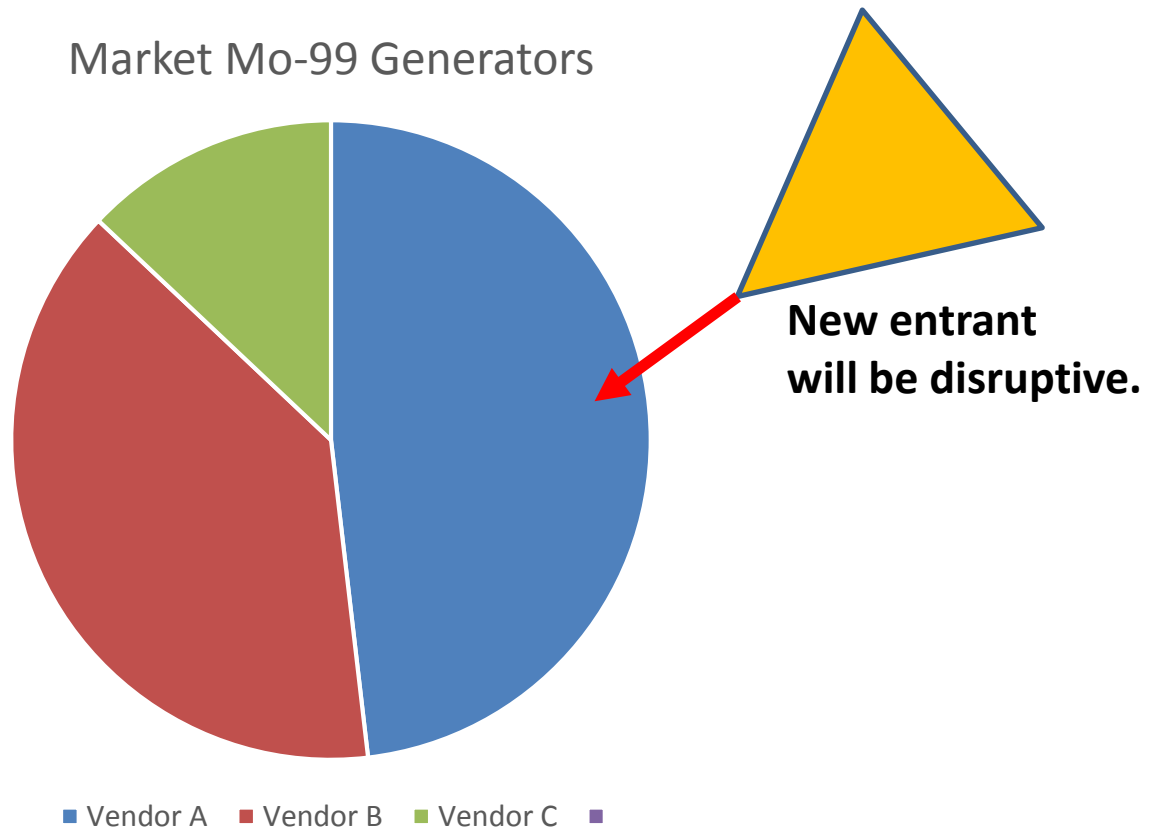
Market Mo-99 Generators



Please note: the size of market share is demonstrative only.

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Emergence of Domestic Production of Mo-99: Generator Supply Chain Tomorrow



Please note: the size of market share is demonstrative only.

U.S. Mo-99 Supply Status – Industry
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Emergence of Domestic Production of Mo-99

- New Mo-99 Generator entrants will want market share and will seek radiopharmacy partners.
- Potential new entrants lead to current suppliers positioning to secure or improve its market share.
- Radiopharmacy must balance Mo-99 requirements with essential imaging products that are **sole source** to one supplier.
- Initial disruption will settle down.

Mo99 Supply: Future in Nuclear Imaging

- Expect new Tc-99m labeled doses to grow the diagnostic imaging market:
 - When an FDA approved product reaches the market for:
 - Prostate cancer imaging
 - NSCLC –lung cancer imaging
 - Colon cancer imaging
 - Breast cancer imaging
 - What technology is possible for the new labeled products?
 - FAPI
 - Nanoparticles

Thank You

