Status and challenges of the IRE LEU conversion program

Valery Host
Mo-99 Topical Meeting 2018, Knoxville, TN

Excellence dedicated to nuclear medicine, healthcare and environment
Institute for Radioelements

- 200 employees

- Missions
  - Contribute to public health
    - First producer of fission I-131
    - Major producer of Mo-99 for Europe
    - Xe-133 producer
  - Environmental protection
One of the most reliable source for the supply of radioisotopes

25%

of the world demand of $^{99}$Mo and $^{131}$I

- Outstanding performances (QoS, release, dosimetry...)
- without any single day of interruption,
From diagnosis to therapeutics

DIAGNOSTIC

INNOVATIVE
SIMPLE
SUSTAINABLE

Solutions for development, production, end-use of RADIOPHARMACEUTICALS

- $^{68}$Ge/$^{68}$Ga generator
- $^{188}$W/$^{188}$Re generator

THERAPY
Institute for Radioelements

Continuous investments for innovation, modernization and safety improvements

LEU conversion project
IRE LEU conversion challenges

- Safety improvements required
  - Chemical process modifications
  - Production equipment modifications
  - Production environment updates: hot cells and ancillaries

- Post Fukushima stress tests

- 3 processes to convert
  - Mo-99
  - I-131
  - Xe-133

- Product validation not under direct IRE control
Process development

LEU conversion impacts

- Target design
- Target specifications
- Dissolution
- U filtration
- $^{99}$Mo - $^{131}$I separation step
- $^{99}$Mo purification
- $^{131}$I purification

Improved safety
LEU conversion achievements

Transport container

Hot cells

Waste management

Safety improvements

Irradiation

Ire LEU

Target manufacturing

Customers

Processing
IRE conversion achievements

- Hotcells refurbishment
- Process development
- Cold commissioning
- > 200 irradiated targets processing

- 2012: Target specifications and manufacturability
- 2013: Approval of target transport container
- 2014: BR2 Qualification
- 2015: LVR15 Qualification
- 2016:
- 2017: Safety approval
- 2018:
Hot commissioning

- Provide safety demonstration of active LEU process
- Ramp-up
  - Increase progressively the batch size
  - Processing of irradiated targets up to full scale
  - Preparing pharmaceutical file modifications with customers
- Pharmaceutical validation
  - Full scale runs
  - Regulatory file modifications
- Obtain GMP certificates and validation by customers
Hot commissioning: status

- Ramp-up phase
  - 1:3 full scale achieved
- > 200 irradiated targets processed
- Production of pharmacopeia specifications compliant LEU Mo-99
- Sample of Xe-133 sent to customer
Hot run feedback

- **R&D full scale tests**
  - R&D in GMP production environment
  - People management

- **3 HEU production a week**
  - Preserve Mo-99 supply

- **Weekly LEU run**
  - According to irradiation position availability
Hot run feedback

- Higher impact of highly active targets
  - Good results from preliminary tests, not repeated at higher activity

- Variable fission product recovery with I-131 present in unwanted fractions

  - Safety issue

- Task force implemented with additional resources
  - Project management strengthened
  - Additional resources for R&D, Production departments, data analyst
  - Support of National Labs
Hot run feedback

- Modifying operating and chemical conditions
  - Dedicated task force - Peer reviews with National labs
  - R&D tests

- Production of small quantities of hydrogen confirmed
Hydrogen issue and status

- **ATEX explosion risk assessment**
  - Routine and incidental conditions assessed
    - New equipment and SOP
    - Segregate hydrogen containing streams
    - Prevent introduction of oxygen

- **Hot tests resumed with modified operating and chemical conditions**
  - Mo-99 and Xe-133 recovery at target
  - Still working on iodine management
  - Probable origin of iodine losses identified
Test planning

- Design of experiments has been reviewed
  - Systematic approach
  - List of actions for iodine management discussed
    - chemicals and other physical parameters are being tested
    - Additional R&D lab work

- Hot R&D tests on going
  - Without impacting HEU supply

- Validation
  - Will start as soon as tests finalized
Planning

Mo-99 ; Xe-133 timeline

Hot commissioning

Validation & Approvals

HEU Phase out

I-131 timeline
Conclusions

• Important milestones have been achieved:
  • Mo-99 and Xe-133 recovery at target
  • Hydrogen risk under control
  • Production of LEU Mo-99 meeting quality criteria
  • Xe-133 sample production

☐ Process safety remains is our highest priority

→ No compromises on safety and security of supply
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