Status and challenges of the IRE LEU conversion program

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Mo-99 Topical Meeting 2018, Knoxville, TN

IRE Elit
Environment & Lifescience Technology

Excellence dedicated to nuclear medicine, healthcare and environment

Institute for Radioelements

- **200** employees

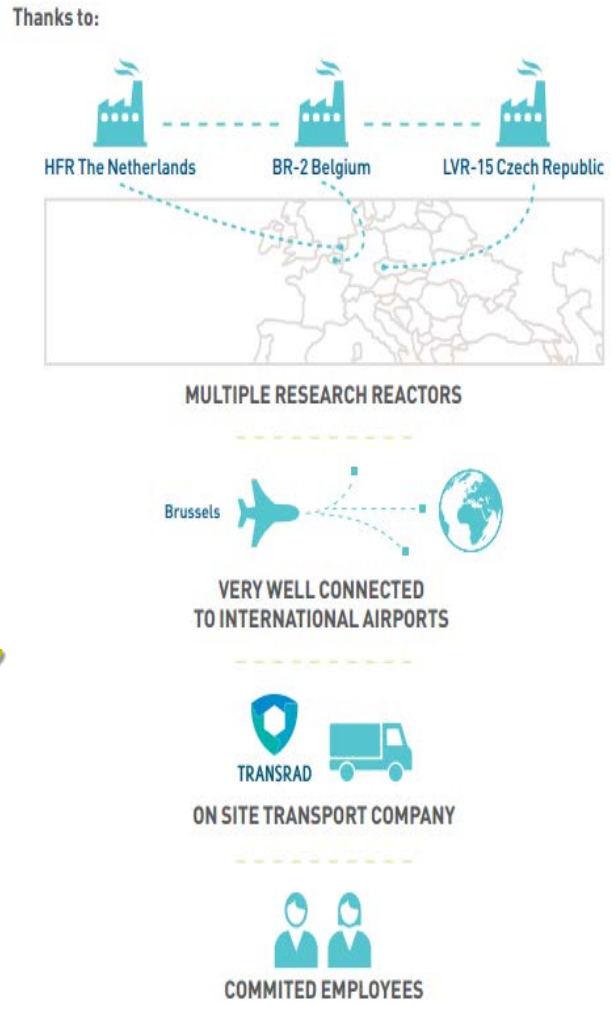
- Missions
  - ➢ ***Contribute to public health***
    - ✓ First producer of fission I-131
    - ✓ Major producer of Mo-99 for Europe
    - ✓ Xe-133 producer
  - ➢ ***Environmental protection***

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 **THERAPY**

IRE Elit
Environment & Lifescience Technology

INNOVATIVE
SIMPLE
SUSTAINABLE

Solutions for **development, production, end-use** of
RADIOPHARMACEUTICALS

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

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

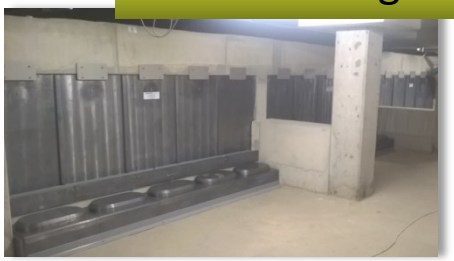
Improved safety

LEU conversion achievements

Transport container

Hot cells

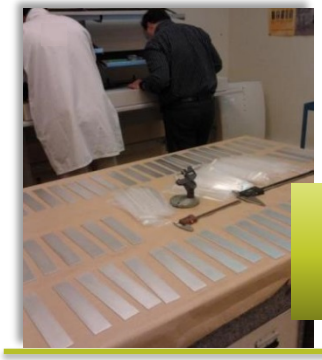
Waste management



Irradiation

IRE LEU

Safety improvements

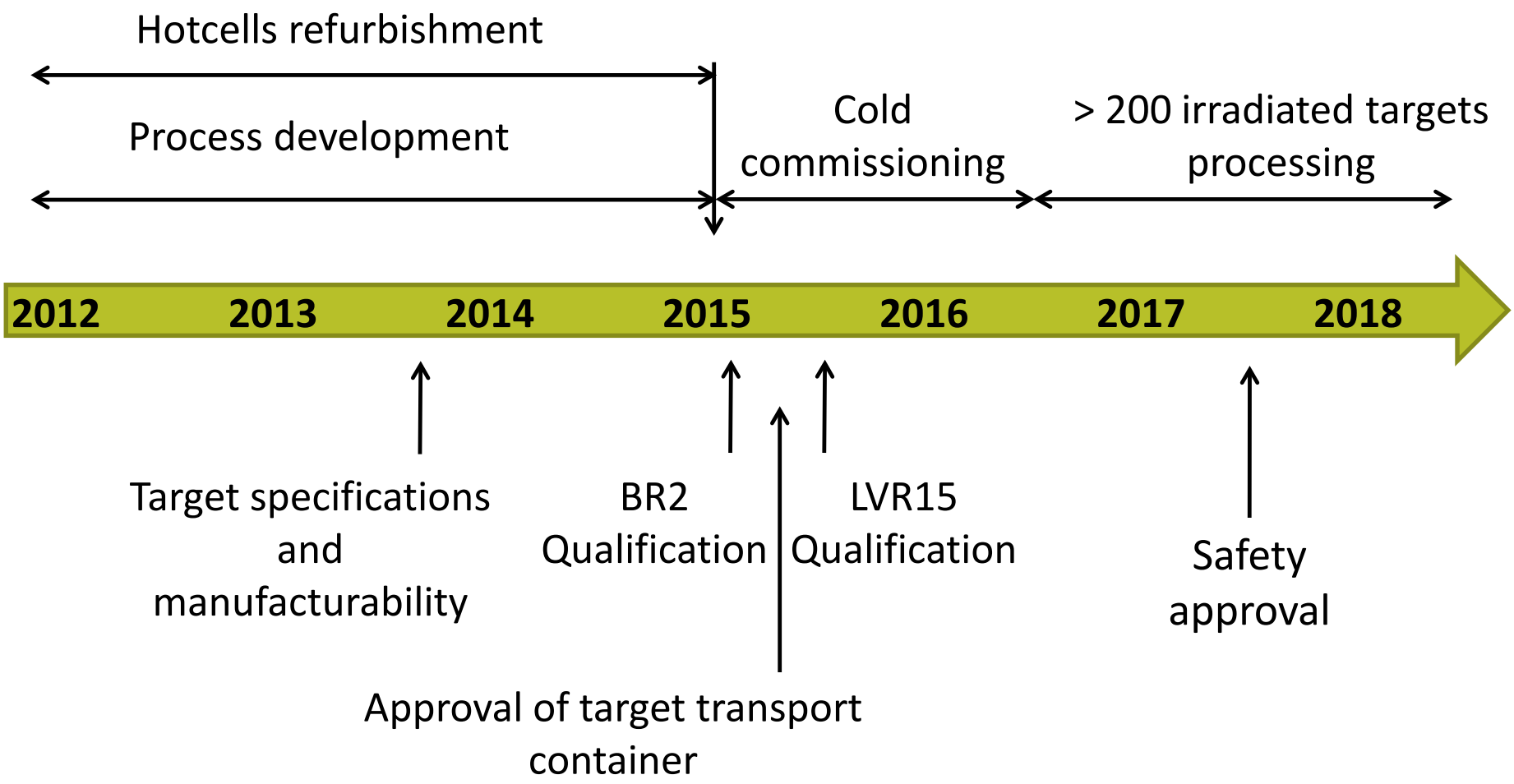


Target manufacturing

Customers

Processing

IRE conversion achievements



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

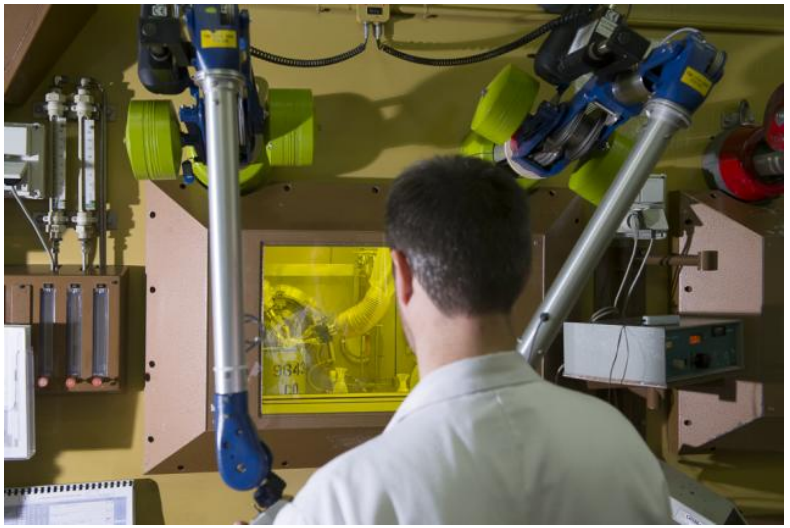
- Pharmaceutical validation
  - Full scale runs
  - Regulatory file modifications

- Obtain GMP certificates and validation by customers

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Hot commissioning : status



- Ramp-up phase
  - ➢ 1:3 full scale achieved
- > 200 irradiated targets processed
- Production of pharmacopea 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

Hot commissioning

Validation & Approvals

HEU Phase out

Mo-99 ; Xe-133 timeline

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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