# E-beam Technology Industrial Deployment-

## Regulatory Framework and Quality Control Measures for Food Irradiation and Medical Device Sterilization

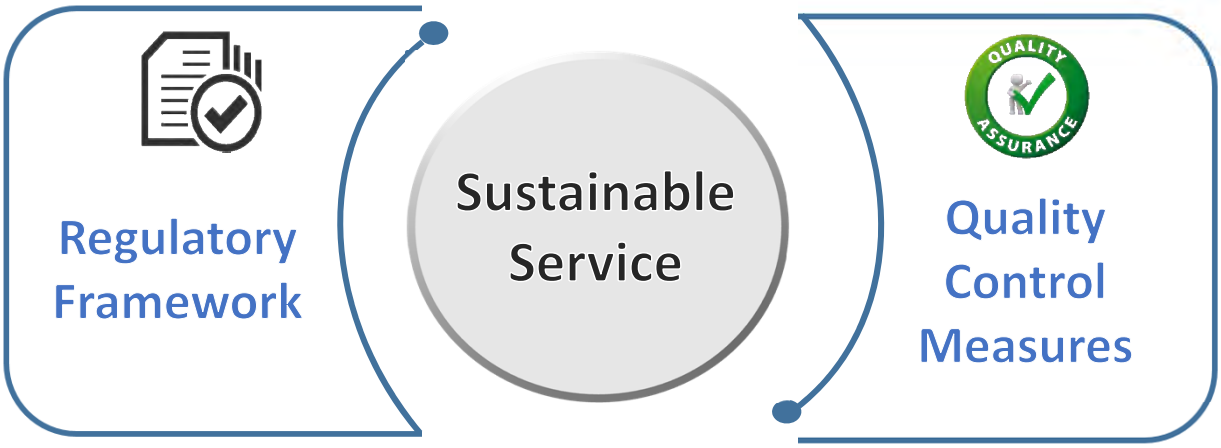
**V.C. Petwal,**
**Industrial Accelerators Division, RRCAT, Indore**
vikash@rrcat.gov.in

**"Commited to take DAE technologies to commons for wellbeing"**

## Outline

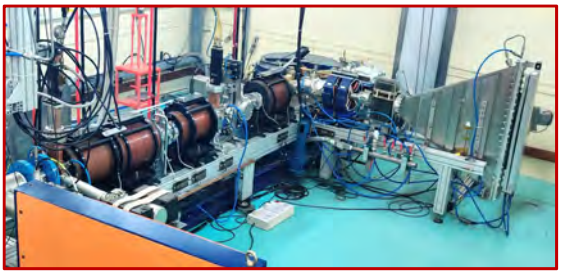
- ✓ **Indian E- beam technology (10 MeV Linac based) and its industrial deployment**
- ✓ **Overview of E-beam facility and E-beam processing**
- ✓ **Regulatory framework for E-beam processing (food & medical devices)**
- ✓ **Licensing requirements and procedures**
  - ❖ **License for safe operation**
    - ***AERB "Type Approval" qualification (IQ, OQ)***
    - ***AERB License for operation***
  - ❖ **License for commercial irradiation**
    - ***Quality management system (QMS) : MDR-2017***
    - ***ISO 9001 & ISO 13485***
    - ***CDSCO/SLA license for MD sterilization***
- ✓ **E-beam sterilization & quality control: ISO 11137**
  - **Process qualification and validation**
  - **Product/ process specification**
  - **Process control and integrity**
  - **Product release and customer feedback**
- ✓ **Conclusion**

## E-beam Technology: Emerging radiation processing service in India




## Industrial deployment of RRCAT E-linacs

Linac-1 and Linac-2 (10 MeV,6 kW) deployed at ARPF



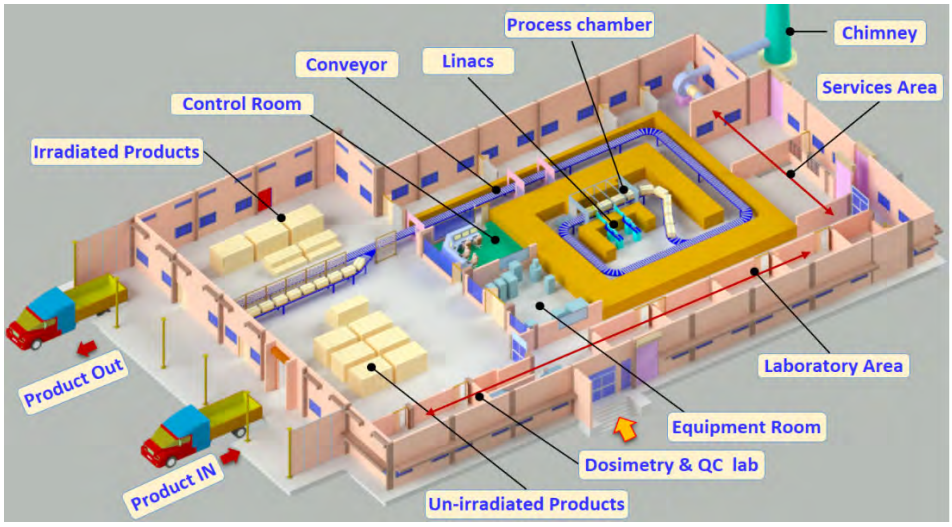
Endurance testing of Linac-3 at 10 MeV, 10 kW RRCAT


10 MeV, 10 kW Linac deployed at M/s MSSPL Bangalore

Linac-4 on test bench at RRCAT, 10 MeV, 15 kW

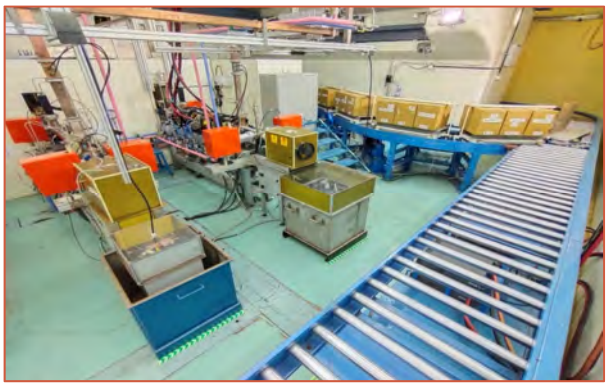
## E-Beam Facility at RRCAT, Indore

**The firs E-beam facility (ARPF) in the country: providing commercial sterilization service to regulated medical devices**




**Designed , developed and operated by RRCAT**

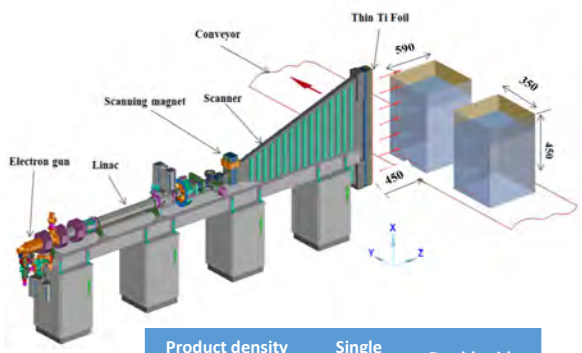
## Salient features



| | |
|---|---|
| Radiation source | 10 MeV, 6 kW RRCAT electron Linac |
| Regulatory licenses | Plant operation: AERB, MD sterilization: CDSCO-FDA |
| QMS | MDR 2017 |
| QMS accreditation | ISO 9001 and ISO 13485 for e-beam sterilization as per ISO 11137-1 |

| | |
|---|---|
| QMS surveillance audit | CDSCO Notified body CE auditing |
| Processing capacity | 200 kg per hour (for a minimum dose of 25 kGy) |
| Box dimension | 590 x 430 x 340 mm (Typical) |
| Beam availability | 100% |

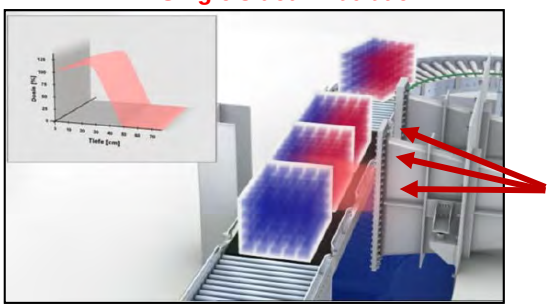
# E-beam Technology



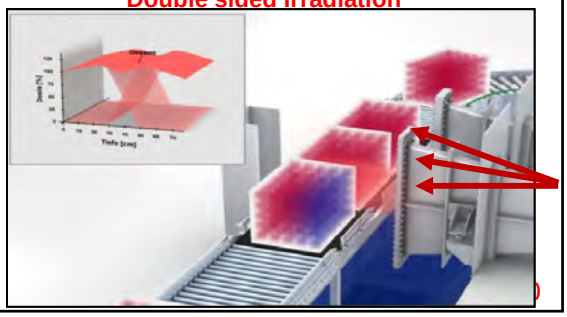

| Product density (g/cc) | Single side | Double side |
|---|---|---|
| 1 | 3.5 cm | 8 cm |
| 0.5 | 7 cm | 16 cm |
| 0.4 | 9 cm | 20 cm |
| 0.3 | 12 cm | 26 cm |
| 0.2 | 18 cm | 42 cm |
| 0.15 | 23 cm | 55 cm |

**Useful penetration depth**

**Single sided Irradiation**



**Double sided Irradiation**



# Regulatory Framework for radiation processing of food and medical products

- ✓ **Regulation ensures the safety, reliability, and quality of the process/service**
- ✓ **Regulation together with Quality Control ensures that product/service comply the requirement of standards and thus create public acceptance and trust.**

## Regulatory framework for radiation processing of food

1. **Radiation processing of food items under Atomic Energy (Radiation Processing of Food & Allied Products) Rules, 2012 - Class wise**
2. **Food Safety and Standards (Packaging and Labeling)Amendment Regulations, 2016**
3. **AERB Safety Code No. AERB/RF-RPF/SC-1 (Rev.1) Radiation Processing Facilities**

### Salient features

**Type of the radiation sources permitted**

a) **Gamma radiation;**
b) **Electron beams from a machine operated at or below ten million electron volts;**
c) **#X-rays generated from a machine operated at or below seven and half million electron volts;**

**# with *Tantalum or Gold as X-ray target material (USFDA)***

**Plant operation**

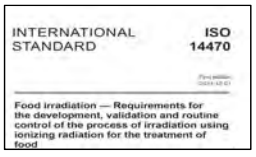
**By competent qualified personnel for operation , quality control and safety**

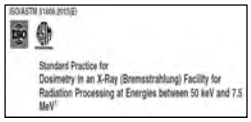
**Training as recognizes by Atomic Energy regulatory board**

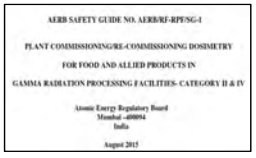
**Labeling**

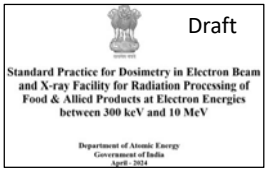
**Mandatory to label the product processed by radiation with RADURA symbol**





## Classes of Food Products and Dose Limits: GoI Atomic Energy Rules 2012

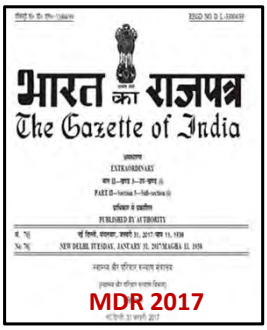
| Class | Food | Purpose | Dose Limit (kGray) | |
|---|---|---|---|---|
| | | | Min. | Max. |
| Class 1 | Bulbs, stem and root tubers and rhizomes | Inhibit sprouting | 0.02 | 0.2 |
| Class 2 | Fresh fruits and vegetables (other than Class I) | Delay ripening | 0.2 | 1.0 |
| | | Insect disinfestation | 0.2 | 1.0 |
| | | Shelf-life extension | 1.0 | 2.5 |
| | | Quarantine application | 0.1 | 1.0 |
| Class 3 | Cercal and their milled products, pulses and their milled products, nuts, oil seeds, dried fruits and their products | Insect disinfestation | 0.25 | 1.0 |
| | | Reduction of microbial load | 1.5 | 5.0 |
| Class 4 | Fish, aquaculture, seafood and their products (fresh or frozen) and crustaceans | Elimination of pathogenic microorganisms | 1.0 | 7.0 |
| | | Shelf-life extension | 1.0 | 3.0 |
| | | Control of human parasites | 0.3 | 2.0 |
| Class 5 | Meat and meat products including poultry (fresh and frozen) and eggs | Elimination of pathogenic microorganisms | 1.0 | 7.0 |
| | | Shelf-life extension | 1.0 | 3.0 |
| | | Control of human parasites | 0.3 | 2.0 |
| Class 6 | Dry vegetables, seasonings, spices, condiments, dry herbs and their products, tea and plant products | Microbial decontamination | 6.0 | 14.0 |
| | | Insect disinfestation | 0.3 | 1.0 |
| Class 7 | Dried foods of animal origin and their products | Insect disinfestation | 0.3 | 1.0 |
| | | Control of molds | 1.0 | 3.0 |
| | | Elimination of pathogenic microorganisms | 2.0 | 7.0 |
| Class 8 | Ethnic foods, military rations, space foods, ready-tocat, ready-to-cook/minimally processed foods | Quarantine application | 0.25 | 1 |
| | | Reduction of microorganisms | 2 | 10 |
| | | Sterilization | 5 | 25 |

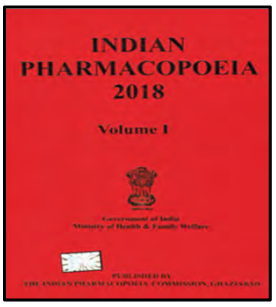
## Regulatory Framework for E-beam Sterilization of Medical Devices

1. **ISO-11137: 2010**
   **Sterilization of health care products Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices.**
2. **Medical Devices Rules (MDR-2017) GoI**
3. **Indian Pharmacopeia, Volume-1, 2018**
4. **ISO 13485: 2016**
   **Medical devices — Quality management systems — Requirements for regulatory purposes**
5. **AERB Guide No. AERB/SG/IS-5 and AERB/RF/SG/G-3**

**IAEA RTS No. 4**
Guidelines for the Development, Validation and Routine Control of Industrial radiation processing

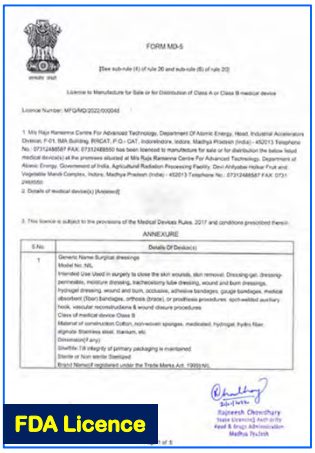
**IAEA Report**
Trends in Radiation sterilization of health care products


# Regulatory Licenses and ISO Certifications


AERB License for plant operation



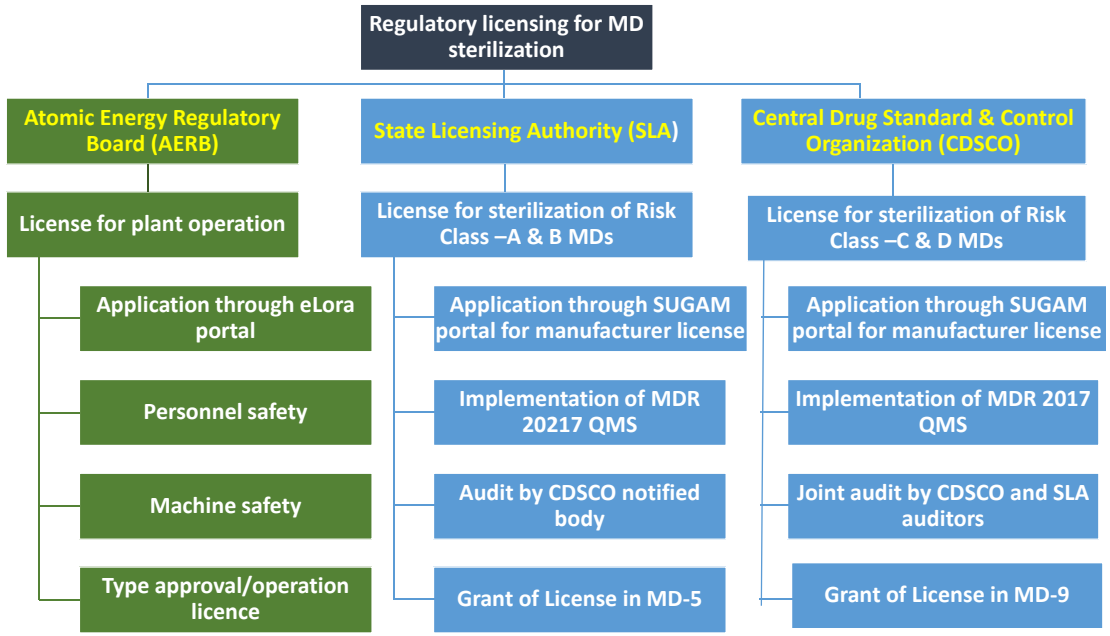

FDA (M P. State) License for sterilization of Risk Class-A & B Medical devices

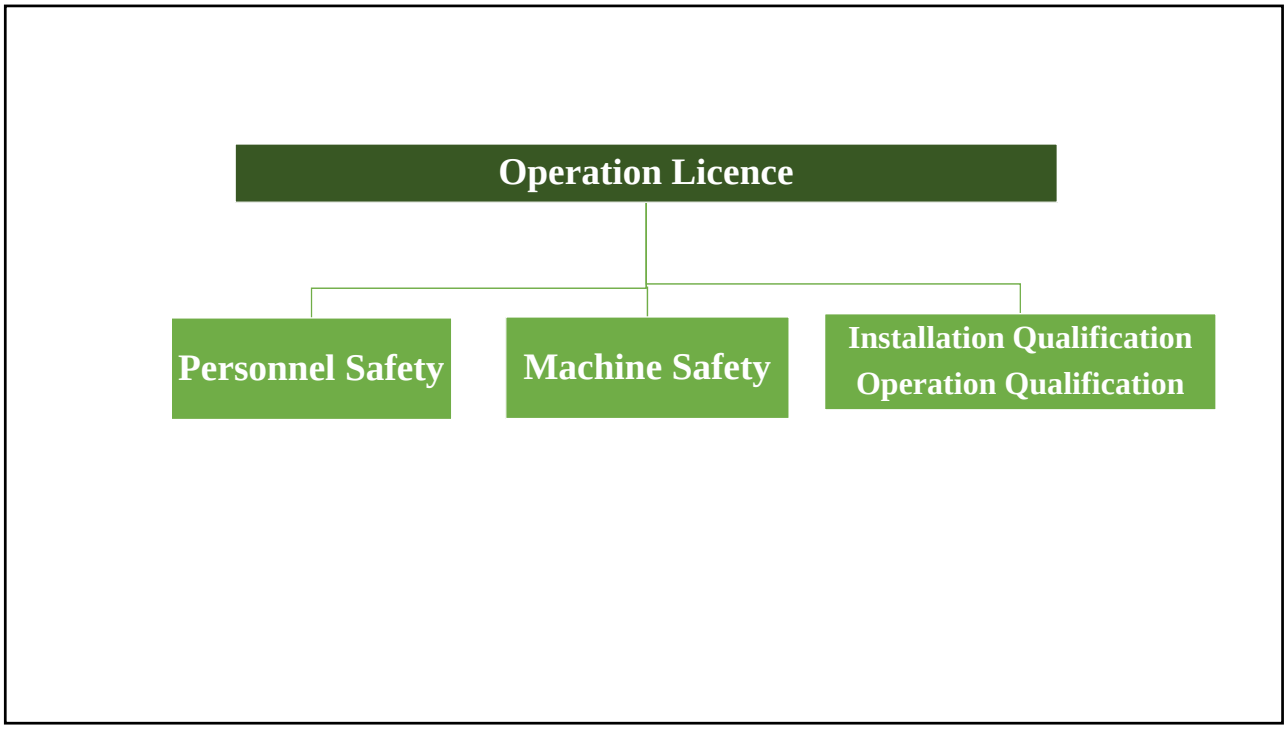


**Medical devices covered under the license**

1) Surgical dressing
2) Catheters (Gastroenterological)
3) Catheters (Urological procedures)
4) Catheters (Cardio-vascular use)
5) Catheters (Respiratory procedures)
6) Catheters (Gynecological procedures)
7) Catheters (Neurological procedures)
8) Catheters (ENT & ophthalmological)
9) Catheters (Orthodontic procedures)
10) Transfusion set
11) Syringes
12) Needles
13) Cannula
14) Scalp Vein Set
15) Dermatological devices

# Regulatory Licensing for E-Beam Sterilization of Medical Devices






## Safety & Interlock System

**Two category of interlocks implemented for Fail Safe operation**

**Working personnel safety and interlock system**

1. Search & secure systems
2. Emergency switches and pull rope
3. Door interlock, Door delay Interlock
4. Exhaust blower ON interlock
5. Air flow interlock
6. Beam dump at designated place
7. Machine ON status interlock
8. High radiation in accelerator vault
9. Surveillance and PA System
10. Audio visual warning system
11. Ozone extraction system
12. Fire detection, alarm and fighting system
13. Emergency plan, Mock drill, health check-up

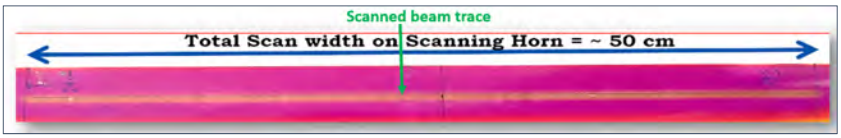
**Machine safety & interlock system**

1. Accelerating structure vacuum interlock
2. Cooling water flow interlocks
3. Cooling water temperature interlocks
4. Microwave system interlocks
5. Waveguide pressure interlock
6. Klystron vacuum ion pump interlock
7. Scanning magnet minimum current
8. Interlock for over voltage/current in power supplies
9. Beam dump temperature interlock
10. Collimator ON/OFF interlock
11. Product jam interlock

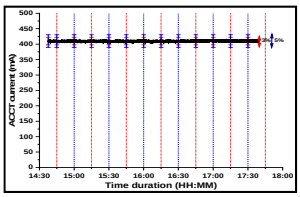
## Installation, Operation Qualification and Type Approval

- IQ is carried out to obtain documented evidence that the irradiation equipment and any ancillary items have been supplied and installed in accordance with their specifications (Testing of Safety Interlock systems, beam parameters)
- OQ is carried out in dummy products before machine is used for processing of actual products, Its characterization with respect to the range of operating parameters and operational stability is determined

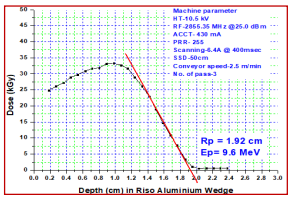
### Type approval testing



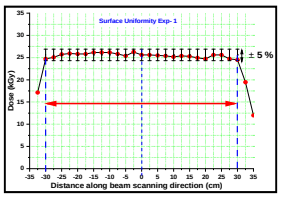

**Beam current measurement**



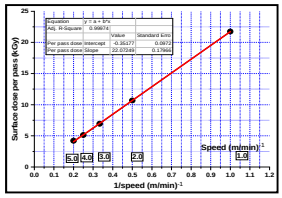

**Beam energy determination**



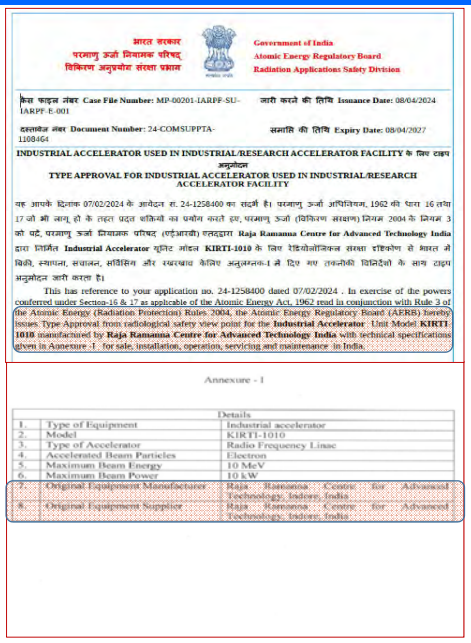

**Scan uniformity measurement**




**Conveyor speed Vs Dose**




## Type Approval certification (KIRTI-1010) with license for operation



भारत सरकार
परमाणु ऊर्जा नियामक परिषद
विकिरण अनुप्रयोग संरक्षा प्रभाग

Government of India
Atomic Energy Regulatory Board
Radiation Applications Safety Division

केस फाइल नंबर Case File Number: MP-00201-IARPF-SU-IARPF-E-001
जारी करने की तिथि Issuance Date: 08/04/2024
दस्तावेज नंबर Document Number: 24-COMSUPPTA-1108464
समाप्ति की तिथि Expiry Date: 08/04/2027

INDUSTRIAL ACCELERATOR USED IN INDUSTRIAL/RESEARCH ACCELERATOR FACILITY के लिए टाइप अनुमोदन
TYPE APPROVAL FOR INDUSTRIAL ACCELERATOR USED IN INDUSTRIAL/RESEARCH ACCELERATOR FACILITY

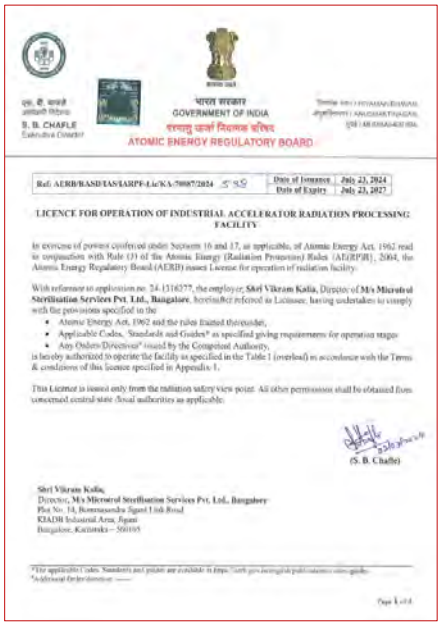
यह आपके दिनांक 07/02/2024 के आवेदन सं. 24-1258400 का संदर्भ है। परमाणु ऊर्जा अधिनियम, 1962 की धारा 16 तथा 17 जो भी लागू हो के तहत प्रदत्त शक्तियों का प्रयोग करते हुए, परमाणु ऊर्जा (विकिरण संरक्षण) नियम 2004 के नियम 3 को पढ़ें, परमाणु ऊर्जा नियामक परिषद (एईआरबी) एतद्वारा **Raja Ramanna Centre for Advanced Technology India** द्वारा निर्मित **Industrial Accelerator** यूनिट मॉडल **KIRTI-1010** के लिए रेडियोलॉजिकल संरक्षा दृष्टिकोण से भारत में बिक्री, स्थापना, संचालन, सर्विसिंग और रखरखाव के लिए नए तकनीकी विनिर्देशों के साथ टाइप अनुमोदन जारी करता है।

This has reference to your application no. 24-1258400 dated 07/02/2024 . In exercise of the powers conferred under Section-16 & 17 as applicable of the Atomic Energy Act, 1962 read in conjunction with Rule 3 of the Atomic Energy (Radiation Protection) Rules 2004, the Atomic Energy Regulatory Board (AERB) hereby issues Type Approval from radiological safety view point for the **Industrial Accelerator** Unit Model **KIRTI-1010** manufactured by **Raja Ramanna Centre for Advanced Technology India** with technical specifications given in Annexure -I for sale, installation, operation, servicing and maintenance in India.

Annexure - I

| Details | |
|---|---|
| 1. Type of Equipment | Industrial accelerator |
| 2. Model | KIRTI-1010 |
| 3. Type of Accelerator | Radio Frequency Linac |
| 4. Accelerated Beam Particles | Electron |
| 5. Maximum Beam Energy | 10 MeV |
| 6. Maximum Beam Power | 10 kW |
| 7. Original Equipment Manufacturer | Raja Ramanna Centre for Advanced Technology, Indore, India |
| 8. Original Equipment Supplier | Raja Ramanna Centre for Advanced Technology, Indore, India |

**Type approval certificate –KIRTI-1010**



भारत सरकार
GOVERNMENT OF INDIA
परमाणु ऊर्जा नियामक परिषद
ATOMIC ENERGY REGULATORY BOARD

Ref: AERB/RASD/IAS/IARPF-Lic/KA-70087/2024
Date of Issuance: July 23, 2024
Date of Expiry: July 23, 2027

LICENCE FOR OPERATION OF INDUSTRIAL ACCELERATOR RADIATION PROCESSING FACILITY

In exercise of powers conferred under Sections 16 and 17, as applicable, of Atomic Energy Act, 1962 read in conjunction with Rule (3) of the Atomic Energy (Radiation Protection) Rules (AERPR), 2004, the Atomic Energy Regulatory Board (AERB) issues License for operation of radiation facility.

With reference to application no. 24-1316277, the employer, **Shri Vikram Kalia**, Director of **M/s Microtrol Sterilisation Services Pvt. Ltd., Bangalore**, hereinafter referred to Licensee, having undertaken to comply with the provisions specified in the

- Atomic Energy Act, 1962 and the rules framed thereunder,
- Applicable Codes, Standards and Guides* as specified giving requirements for operation stage.
- Any Orders/Directives* issued by the Competent Authority,

is hereby authorized to operate the facility as specified in the Table 1 (overleaf) in accordance with the Terms & conditions of this licence specified in Appendix-1.

This Licence is issued only from the radiation safety view point. All other permissions shall be obtained from concerned central/state /local authorities as applicable.

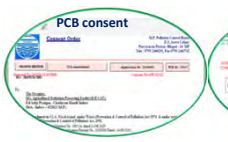
(S. B. Chafle)

Shri Vikram Kalia,
Director, M/s Microtrol Sterilisation Services Pvt. Ltd., Bangalore
Plot No. 18, Bommasandra Jigani Link Road
KIADB Industrial Area, Jigani
Bangalore, Karnataka – 560105

**License for Operation of KIRTI-1010 at MSSPL, Bangalore**

# Sterilization Process Qualification, Validation and Quality Control

## Medical Device Sterilization Protocol being Followed at ARPF

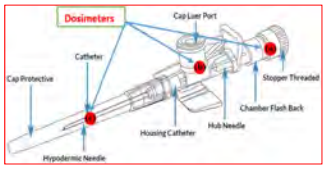




**Stage-1 Regulatory Approvals**

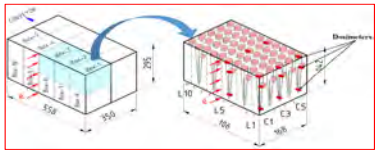
Establish QMS as per MDR-2017 and ISO
Regulatory Audits
Regulatory Licences and accreditations

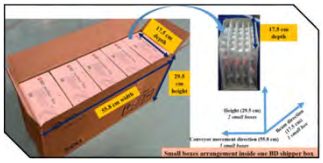





**Stage-2 Process Design**

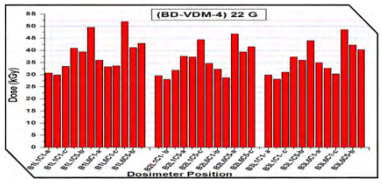
Vendor audit, Dose establishment, MAD
Process load optimization,
process parameter optimization

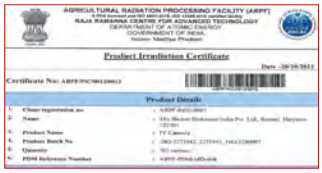




**Stage-3 Process Qualification and validation**

3-D dose mapping study,
Process integrity analysis,
Process validation by sterility testing

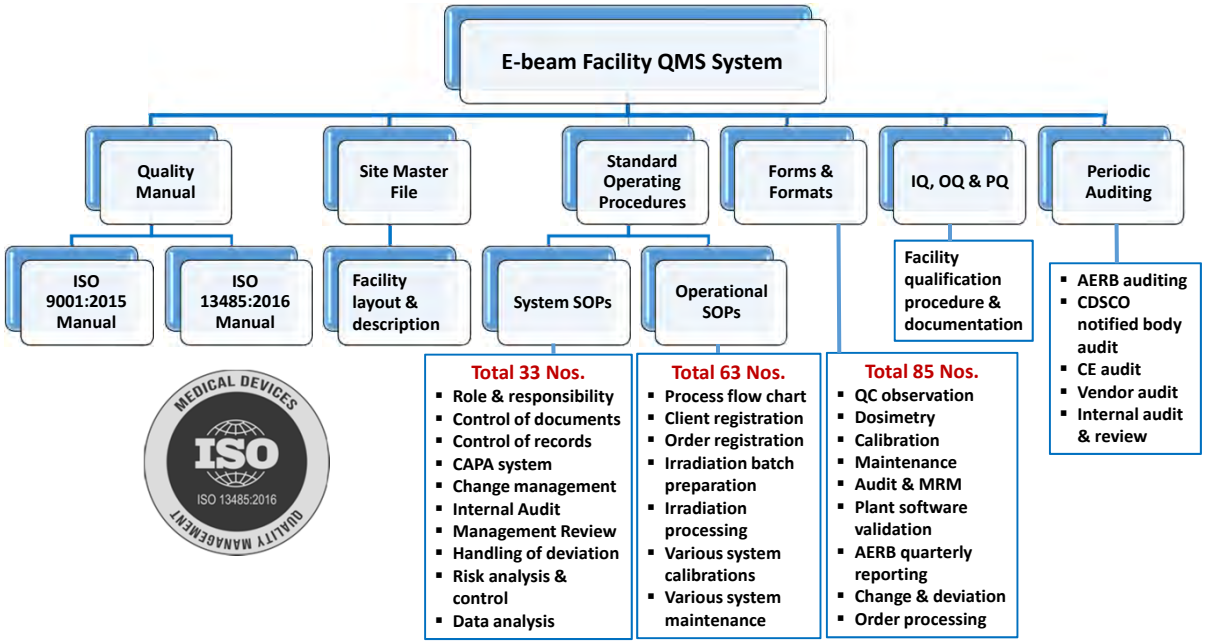



**Stage-4 commercial irradiation and acceptance**

Irradiation service agreement
Customer feedback,
Public acceptance, service continued

# Quality Management System




# Sterilization process development (PQ dosimetry)

| Dosimetry Box No | $D_{min}$ Dose (kGy) | $D_{max}$ Dose (kGy) | $D_{ref}$ Dose (kGy) |
|---|---|---|---|
| PQ-1 | 25.8 | 34.0 | 35.0 |
| PQ -2 | 26.6 | 34.3 | 35.1 |
| PQ -3 | 29.4 | 40.4 | 36.4 |
| PQ -4 | 26.2 | 33.3 | 34.6 |
| PQ -5 | 26.4 | 33.9 | 34.6 |
| PQ -6 | 26.4 | 34.3 | 36.0 |
| PQ -7 | 27.4 | 35.0 | 34.7 |
| PQ -8 | 27.1 | 37.4 | 34.9 |
| Average dose | 26.9 | 35.3 | 35.2 |
| S.D. ± | 1.1 | 2.4 | 0.7 |
| C. V. (%) | 4.2 | 6.8 | 1.9 |

- ✓ Identify $D_{min}$ and $D_{max}$ position
- ✓ Establish relation between reference position dose and $D_{min}$ & $D_{max}$ dose
- ✓ Set operating parameters to deliver the required dose with 95% confidence level

## Sterilization process validation

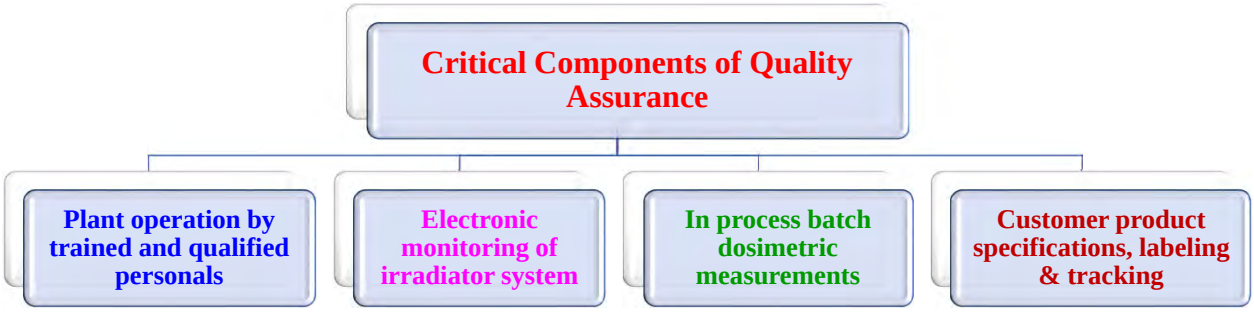

ACCUPREC RESEARCH LABS PVT. LTD.
Ultimate solution...
RESEARCH REDEFINE
CERTIFICATE OF ANALYSIS


Standard
TEST REPORT

**Third Party Sterility Testing at NABL Certified Labs**

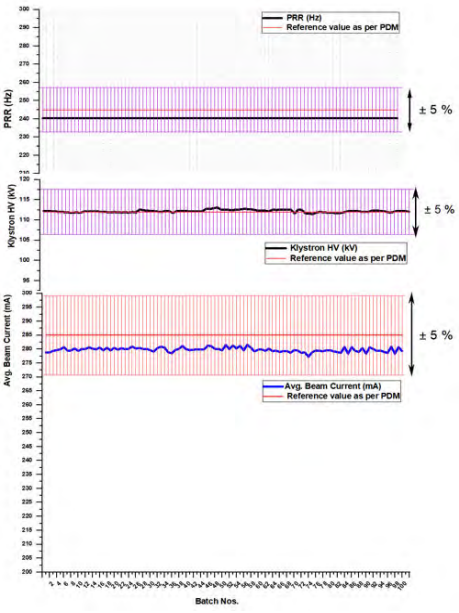
## Quality Assurance at ARPF: Regular operation

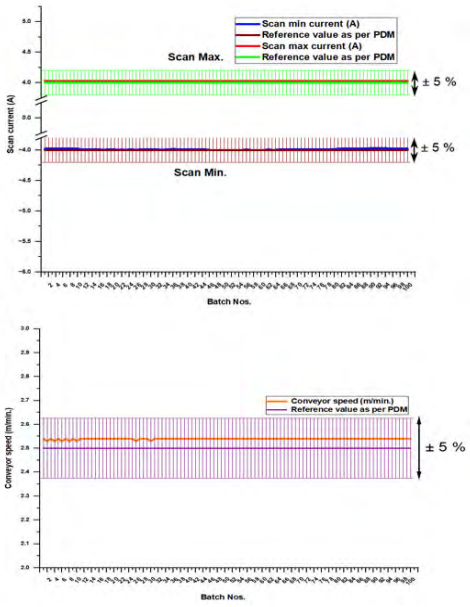
**QA measures to ensure that the irradiation process is in state of control to meet customer requirement**



## Process Control: Online Electronic Monitoring of Irradiator System

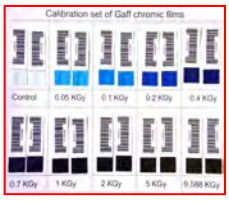
**Monitoring of critical process parameters of 100 Batches processed Indicates that the irradiation process is in state of control.**

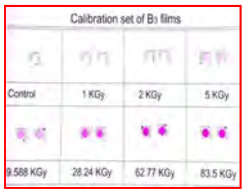



## Process Control: Dosimetry

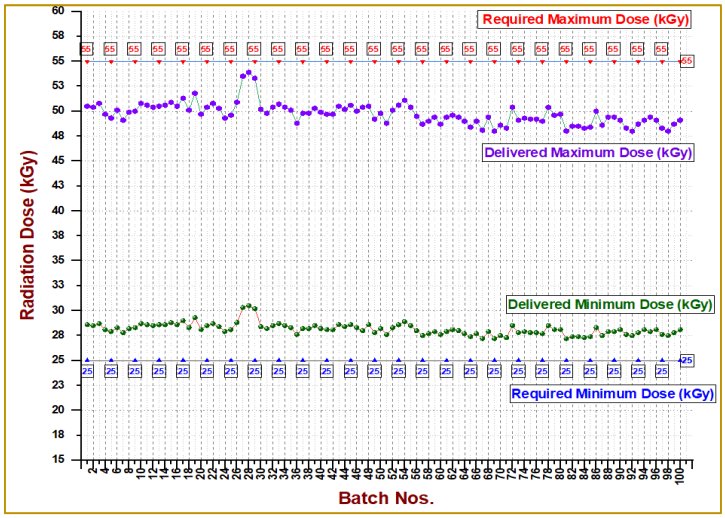
**Dosimetry data monitoring after processing of each batch of medical devices indicates that the Irradiation Process is in the state of control.**




Radiochromic Film Dosimetry System

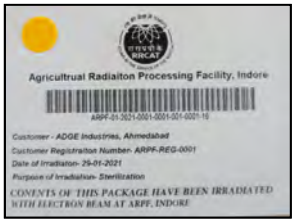
EPR Dosimetry System




**Dosimetry data of 100 batches processed**

## Process Control: Customer product specification

- Customer registration, order registration
- Generation of unique dose mapping number for a product
- QC checks: for incoming material, Batch preparation
- Product tracking during irradiation and after irradiation
- Generation of unique bar-code for each irradiated box.
- Product processing IN and OUT time logging.
- Dosimetry data recording and logging
- Generation of "Product Irradiation Certificate" and product release related documents



Certificate of Irradiation to release product

## Irradiation Agreement for commercial sterilization service

**Becton Dickinson, Haryana**

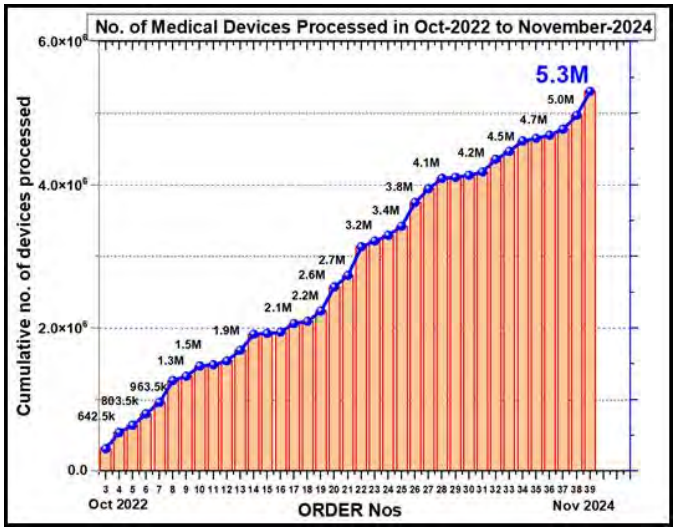




**Product box labelling**


**Triveni Polymers, Haryana**


## Medical device sterilization (Progressive Growth)




BD

**Letter of Acknowledgement for**

**Electron Beam Sterilization Services Received from RRCAT**

This letter is to acknowledge the high quality electron beam medical device sterilization services provided by Raja Ramanna Centre for Advanced Technology (RRCAT), Department of Atomic Energy, GoI for 1.78 million IV Venflon™ cannula in conformance with applicable regulatory standards and in alignment with the MoU signed in July 2022 between BD India and RRCAT.

Prior to availing the radiation processing services, the E-beam facility was critically audited by expert teams from our regulatory, QA&QC, production, logistics & supply chain management department as well by CE auditors and found the facility in compliance with ISO 13485, MDR-2017 and CE regulatory compliance.

BD is one of the largest global medical technology companies in the world and is advancing the world of health by improving medical discovery, diagnostics and the delivery of care. BD helps customers enhance outcomes, lower costs, increase efficiencies, improve safety and expand access to health care.

(Abhay Kumar Jain)
Head of Plant Operations, BD India Pvt. Ltd. Bawal

## Conclusion

- ✓ **RRCAT has developed 10 MeV E-Beam Linac technology for industrial applications**
- ✓ **10 MeV, 10 kW Linac technology is "Type Approved" by AERB.**
- ✓ **Three Linacs are operational in industry and providing e-beam irradiation service.**
- ✓ **The facility at Indore is operating under the regulatory framework of AERB and FDA and providing sterilization services for medical devices**
- ✓ **Implemented QMS comply the requirements of MDR-2017 and has accreditation for ISO 9001:2015 and ISO 13485:2016**
- ✓ **The facility is being used by medical device manufacturers from across the country for sterilization of their products on regular basis.**

# Thank You

**“Electrons in the Service of Nation”**

# CAPA
CORRECTIVE AND PREVENTIVE ACTION

**Initiation of CAPA**

Non conformance due to-
- Process interruption
- Audits (CDSCO/CE/Vendor/Internal audit)
- Deviation from defined procedures
- Customer complaints related to process

**Assessing potential impact and risk level**

Define the severity & priority based on their effect on impact on safety & sterilization process integrity

**Correction**

"An immediate action"


**Root cause analysis**

"Analyzing the problem and identifying its cause"

**Corrective action**

"Action after root cause analysis to prevent recurrence"

Not effective

**Implementation of control measures & their review & effectiveness evaluation**

Effective

**Preventive action**

"Global action to prevent recurrence"

**Closure of CAPA with the due approval**

Ref: SOP for corrective & preventive action (ARPF/SOP/05, Ver:01, Rev:01, 14-04-2022)