Economical Feasibility of Transitioning from Gamma Sterilization to Accelerator-based Sterilization

REPORT OF A CONSULTANTS MEETING

IAEA Headquarters, Vienna, Austria

19 – 22 August 2019

Working Material Produced by the International Atomic Energy Agency

Vienna, Austria, 2019

1. INTRODUCTION

A group of experts has been tasked to put together criteria to considerer when assessing the economical feasibility of transitioning from gamma to accelerator-based sterilization (both electron beam and X-Ray).

The outline of the discussion is as follows:

- All three modalities used in radiation sterilization processing (Gamma, Electron beam and X-Ray) are discussed.
- Critical aspects of the radiation processing for each modality are presented. These can be compared and assessed for particular scenarios, as applicable. The outcome of such assessment will depend on the country, type of product, Cobalt and electricity availability and many other parameters.
- Costs are not included, as those will be very different per country and are difficult to assess for every condition. Information may be found in some of the documents listed in Section 3 (References 1, 2, 3 and 7).

2. PRESENTATIONS AND DISCUSSIONS

2.1. Sterilization Processing Situation

Over the last 40 years, the sterilization process was mostly based on gamma and Ethylene Oxide technologies.

Electron beam technology was used for several decades for material modification applications. Since the late 90s and availability of more reliable 5-10MeV electron beam irradiators, sterilization processes based on accelerator technology became more common.

The first 7 MeV high power X-Ray irradiator dedicated to sterilization processing started in 2011.

Among other reasons, increasing concerns about Co-60 source availability and Ethylene Oxide emission and residual levels, put pressure on the supply chain of medical device manufacturers.

Due to those concerns and the growing of the sterilization market, electron beam technology developed very fast in last 5 years. As an example, in last 5 years in China many more electron beam irradiators have been established than gamma irradiators.

We believe that in the coming years, electron beam irradiator installations will continue and in addition, several X-Ray irradiators will also be installed.

2.2. Critical aspects to take into account when considering Gamma / Accelerator-based irradiator for sterilization processes

A variety of factors need to be considered when comparing radiation modalities and choosing a sterilization facility. One of the most important and time- and cost-consuming factors is licensing and regulations. All three modes of sterilization require facility licenses; however, gamma requires

additional licensing and costs related to cobalt possession, use, transportation and disposal. Licensing of accelerator facilities is simpler in general, however there are strict energy limits for both electron beam and x-ray. Note that in some countries there are financial incentives to operate accelerator facilities. All three types of facilities must comply with ISO 11137, FDA, and Pharmaceutical standards if applicable.

When considering a facility, one should keep in mind availability and costs of consumables. Uncertainty in cobalt costs and availability is one of the main reasons for increased acceptance of accelerator-based sterilization methods. However, reliability of accelerators still remains an issue. Most of the facilities have more than one accelerator for back up. When choosing a site, the environmental characteristics need to be accessed and potential natural disasters, such as earthquakes, need to be considered. This is especially critical for gamma facilities. Public perception of the radiation technologies is also important, especially in the countries where public approval is required for the facility licensing. In general, public is less concerned about accelerator-based irradiation facilities, and more concerned about facilities containing radioactive material (cobalt).

User acceptance is also critical. As we mentioned earlier, gamma has historically been considered as the main modality of radiation sterilizations. While sterilization processes based on accelerator technology became more common, most of the users still prefer the well-established gamma sterilization process. This is especially true for grandfathered products, which would be too expensive to revalidate. Typically, gamma facilities have good uptime and can be restarted quickly after unplanned maintenance. However, cobalt reload can be time consuming. Accelerator-based facilities have slightly lower uptime and may require longer to restart. Note that electron beam facilities have higher chances of resulting in non-conforming material. While gamma and X-Ray can be used for higher density and bulky products, electron beam is mostly used for low density, thin products. Dose distribution for electron beam is more difficult to predict as it is dependent on product mass and geometry and orientation to the beam in much greater extent than in case of the other two modalities. As a result, process load configuration requires higher control.

Due to their intrinsic “simplicity”, gamma facilities require fewer employees and have overall lower HR requirements compared to accelerator-based facilities. Gamma facility maintenance may be done internally or with local supplier. The spare parts are not expensive and widely available. Maintenance of accelerator-based facilities is more complicated and costly.

As one can see from the table below which summarized the above statements (and more), there is no better or worse facility as it greatly depends on local market and regulations, availability of cobalt, products to be sterilized, and local HR resources. Note that the table has been developed for sterilization processes but also applies to food processes.

ID	Considerations	Gamma	Electron Beam	X-Ray
1	Local Regulation / incentive (See Reference 8)	Facility Licenses Cobalt Licenses Cobalt transportation Source disposal Financial incentive: Not likely Personnel training / certification	Facility Licenses Energy limit <= 10 MeV Financial incentive: More likely Personnel training / certification	Facility Licenses Energy limit <= 5 MeV for food in all country except US (7.5) <= 7.5 MeV for other products Financial incentive: More likely Personnel training / certification
2	Regulation / Norms	ISO 11137 FDA Pharma	ISO 11137 FDA Pharma Product activation assessment required when energy >10MeV	ISO 11137 FDA Pharma Product activation assessment required when energy >5MeV
3	Environment	Natural / environmental disasters (earthquake, tsunami, etc) Ozone emission level	N/A Ozone emission level	N/A Ozone emission level
4	Public acceptance of technology	Low	No concern	No concern
5	User acceptance of technology	Excellent	Good	Low because unknow technology
6	Safety (See Reference 8)	Very high requirements	High requirements	High requirements
7	Consumable	Cobalt 60 Limited suppliers and uncertainty on future availability	Electricity Backup system needed for critical utilities Stable power needed	Electricity Backup system needed for critical utilities Stable power needed
8	Product to be processed	Low to High density Dose distribution easy to predict – OQ data may be used	Low to Middle density Dose distribution: difficult to predict – dependent on product mass and geometry and orientation to the beam	Low to very High density Dose distribution easy to predict - – OQ data may be used

		Process load configuration: Requires lower control	Process load configuration: Requires higher control	Process load configuration: Requires lower control
		Identical Sterilization and maximal acceptable dose qualification method		
9	Human resource (See Reference 10 for example)	Maintenance competence level: Moderate IQ/OQ competence level: Moderate PQ competence level: Moderate QA/QC competence level: High Numbers of employees on site: Low Personnel Training requirements: High	Maintenance competence level: High IQ/OQ competence level: High PQ competence level: High QA/QC competence level: High Numbers of employees on site: Medium Personnel training requirements: High	Maintenance competence level: High IQ/OQ competence level: High PQ competence level: Moderate QA/QC competence level: High Numbers of employees on site: Medium Personnel training requirements: High
10	Commissioning (See Reference 4, 5 and 6)	IQ /OQ: Straight forward May need a lot of dummy material PQ: Straight forward	IQ / OQ: Involved PQ: Involved	IQ / OQ: Involved May need a lot of dummy material PQ: Straight forward
11	Operation (See Reference 4, 5 and 6)	Up Time: Good Time to restart after unplanned maintenance: Good Scheduling: may require attention Throughput: Good Cobalt reload may take significant operation time Risk of non-conforming process: Low	Up Time: Fair Time to restart after unplanned maintenance: Fair Scheduling: very easy Throughput: Good Verification activities can be done during normal operation Risk of non-conforming process: Moderate	Up Time: Fair Time to restart after unplanned maintenance: Fair Scheduling: may require attention Throughput: Good Verification activities can be done during normal operation Risk of non-conforming process: Low
12	Source disposal (See Reference 8)	Cost to be assess, time depends on country	N/A	N/A
13	Maintenance	Spare part:	Spare part:	Spare part:

		Low Cost - High availability Maintenance may be done internally or with local supplier	High Cost - Low availability Maintenance service contract usually required High Qualified personal required Required more personnel	High Cost - Low availability Maintenance service contract usually required High Qualified personal required Required more personnel
14	Dosimetry (See Reference 4, 5 and 6)	One dosimetry system to cover IQ/OQ/PQ. Calibration: easy Routine Monitoring: Moderate because it may be product specific location	Multiple dosimetry system usually required to cover IQ/OQ/PQ Calibration: moderate Routine Monitoring: Easy because it is a fixed location	Multiple dosimetry system usually required to cover IQ/OQ/PQ Calibration: Moderate Routine Monitoring: Moderate because it may be product specific location
15	Effect of processing parameter change on dose delivered	Easy to assess	More difficult to assess (More process parameters may affect the dose distribution)	More difficult to assess (More process parameters may affect the dose distribution)
16	Decommissioning	Process to be defined Cost to be secured	N/A	N/A

3. CONCLUSIONS

- We believe that the transfer from gamma to accelerator-based technology for sterilization is economically viable and should be seriously considered when a new site is selected, or an existing site is updated.

- The final decision on which technology to be selected will depend on the outcome of the assessment made using the table above. This can be Gamma, Electron beam, X-Ray or their combination.

- We believe that some of those technologies (mostly X-Ray) are not well known by the potential users and that effort should be made to educate and inform them about all pros and cons of this radiation modality.

- Economical viability of the X-Ray and electron beam technologies will further improve in the near future when these technologies will be used more.

4. RECOMMENDATIONS

- The IAEA should continue to provide platforms for sharing information and experiences on the use of all radiation modalities that are available for radiation sterilization of healthcare product. This could be done through:
  - Dedicated sessions in the relevant conferences, such as ICARST;
  - Update of the QA/QC guidelines (2013);
  - Development of E-learning modules on technology and processing;
  - Creation of a documented overview of irradiator technologies;
  - Update the database on existing installations in Member States;
  - Share success story from Member states.
- The IAEA should promote versatility in the validation of sterilization processes using ionizing radiation. Medical device manufacturers and the radiation processing industry could benefit from the fact of validating new products for sterilization using all of the existing modalities of ionizing radiation. For example, a public database on existing publication covering those topics, would be very useful.
- The IAEA should support Member States' initiatives to evaluate compatibility of existing products to all three technologies, in order to facilitate the transition from one technology to the other if required.
- The IAEA should support harmonization of existing standards and Member State regulation, for instance the acceptance of radiation processing using X-Ray technology with energy up to 7.5 MeV. This may be done by organizing technical meetings or workshops supporting studies in this area.
- The IAEA should support further development of accelerator technology, in order to improve the operational performance and reduce cost. For example, a dedicated session at AccApp'20 in 2020 could bring together experts in accelerator design and users.

5. REFERENCES

1. White paper: A comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for Sterilization of Medical Devices and Other Products, April 21, 2017, Gamma Industry Processing Alliance (GIPA)
2. A comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for Sterilization of Medical Devices and Healtcare Products, August 31, 2017, Gamma Industry Processing Alliance (GIPA), International Irradiation Association (iia)

3. Thomas K. Kroc, Jayakar C.T., T. Thangaraj, Richard T. Penning, Robert D. Kephart, Accelerator-driven Medical Sterilization to Replace C0-60 Sources, Fermi National Accelerator Laboratory (Fermilab), August 11, 2017
4. ISO 11137-1: 2018: Sterilization of health care products – Radiation- Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
5. ISO 11137-3: 2017 Sterilization of Health Products – Radiation – Part3: Guidance on Dosimetric Aspects of Development Validation, and Routine Control
6. IAEA Radiation Technology Series No.4 - 2013: Guideline for the development, validation and Routine Control of industrial Radiation processes
7. IAEA Report Consultancy Meeting on "Recent Achievements on Irradiation Facilities" 17 to 21 June 2019
8. IAEA Safety Standards Series No. SSG-8: Radiation Safety of Gamma, Electron and X Ray Irradiation Facilities, 2010
9. Gamma irradiators for radiation processing IAEA (2005)
10. Society for Sterility Assurance Professionals – IIA initiative - https://sfsap.org/

Meeting participants on day one of the Consultants Meeting:

From left to right: Zbignew Zimek, Cerina Horak, Herve Michel, Valeriia Starovoitova, Bart Croonenborghs, Dinara Abbasova, Larry Nichols, Peng Wei, Bum Soo Han.

ANNEX I

LIST OF EXPERTS AND IAEA REPRESENTATIVES

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ANNEX II

MEETING AGENDA

Monday, 19 August 2019

9:00 - 9:30	Registration at the Gate 1, IAEA headquarters, VIC
Session I:	**Introductory Session**
9:30 – 10.00	Opening of the meeting by: - Ms Melissa Denecke, Director NAPC (IAEA) - Ms Valeriia Starovoitova, Scientific Secretary, RPRT (IAEA) - Mr Bumsoo Han, RPRT (IAEA) - Ms Celina Horak, RPRT (IAEA) Scope and Objectives of the Meeting, Adoption of the agenda Election of the chairperson of the meeting, introduction of participants
Session II:	**Participants' Presentations**
10:00 – 10:45	Presentation by Mr Bart Croonenborghs **(Sterigenics, Belgium)**
10:45 – 11:15	Coffee Break
11:15 – 12:00	Presentation by Mr Peng Wei **(Vanform Corporation, China)**
12:00 – 12:45	Presentation by Mr Herve Michel **(Steris, France)**
12:45 – 14:00	Lunch break
14:00 – 14:45	Presentation by Mr Zbignew Zimek **(INCT, Poland)**

14:45 – 15:30	Presentation by Mr Larry Nicols **(Steri-Tek, U.S.A.)**
15:30 – 16:00	Coffee Break
16:00 – 17:00	Discussion on Current Status and Recent Issues on Irradiation Facilities
18:00 – 20:00	Welcome Drinks at Melia (sponsored by the IAEA)

Tuesday, 20 August 2019

Session III & IV:	**Recent Achievements on Irradiation Facilities**
09:00 – 10:30	Discussion on Current Status and Recent Issues on Irradiation Facilities
10:30 – 11:00	Coffee Break
11:00 – 12:30	Discussion on Current Status and Recent Issues on Irradiation Facilities
12:40 – 14:00	Lunch Break
14:00 – 15:30	Discussions on How to Move from RI Sources to Machine Sources in Irradiation Facilities (Both for Research and Industries)
15:30 – 16:00	Coffee Break
16:00 – 17:30	Discussions on How to Move from RI Sources to Machine Sources in Irradiation Facilities (Both for Research and Industries)
17:30 – 18:00	*Finalize and document the discussion*

Wednesday, 21 August 2019

Session V & VI:	**The Advanced Approaches in Irradiation Facilities and the Role of the IAEA**
09:00 – 10:30	Discussion on the role of the IAEA on Irradiation Facilities

10:30 – 11:00	Coffee Break
11:00 – 12:30	Discussion on the role of the IAEA on Irradiation Facilities
12:40 – 14:00	Lunch Break
14:00 – 15:30	Recommendations on the Directions and Guidelines for Irradiation Facilities to IAEA Member States
15:30 – 16:00	Coffee Break
16:00 – 17:30	Drafting of the Meeting Report
17:30 – 18:00	*Finalize and document the discussion*

Thursday, 22 August 2019

Session VII:	**Final Review and Acceptance of Meeting Report**
09:00 – 10:30	Finalizing meeting report (scope/contents/structure/conclusions/recommendations)
10:30 – 11:00	Coffee Break
11:00 – 12:30	Review and acceptance of the meeting report
12:40 – 14:00	Lunch Break
14:00 – 16:00	*Closing of the Meeting*