X-Ray Sterilization – Managing Risks

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Agenda

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- Why X-rays?
- Regulatory
- Technology
- Cost and risk management
- Future
    - Medical – Food – Advanced Materials

Why X-rays?

- X-rays compete with gamma
  - Dose uniformity
  - Production capacity
  - Cost
- X-rays can be cheaper than gamma
- Strategy
  - Machine source
  - Electricity vs. cobalt supply

When to consider X-ray?

- Your capacity requirements
  - Pallet Irradiator: > 40.000 m³ p.a.
  - Tote Irradiator: > 60.000 m³ p.a.
- Capacity extensions for gamma-products are needed
- Combining E-beam and X-ray is a possibility, but always a compromise

Evaluation check-list

- Define requirements
  - Regulatory affairs & quality system
  - Type of (accelerator-) source, power
  - Type of material handling
  - Logistic
  - Space and existing facilities
  - Capacity, dose uniformity
  - Automation vs manual
- Define and manage risk
  - Technology
  - Market
- Business plan
  - production capacity
  - investment cost
  - operational cost

Regulatory aspects (EU)

What is needed to sterilize medical devices?

European directive 93/42/CEE gives the answer:

- Implement a quality assurance system
- The CE marking on the device corresponds to all that is obligatory for equipment of class 1
- The Euratom treaty must be obeyed

Regulatory aspects (EU)

- Standard: EN 552 (until ~2005)
- Applies to " […] gamma irradiators using the radio nuclides ^{60}Co and ^{137}Cs and to irradiators using electrons, at or below an energy level of 10 MeV […]"
- EN 552 does not apply to X-rays

Regulatory aspects (ISO)

- ISO 11137:1995(E) – valid today and applies to X-rays
- ISO 11137-1 (2005) – changes for tomorrow
  - these changes are proposed and currently in discussion in the expert committees

ISO 11137

ISO 11137:1995(E)

- No X-ray energy limit
- No requirement for any radiological safety proof
- We can mix E-beam and gamma SOP's and arrive at X-ray SOP's

ISO 11137-1 (2005)

- Below 5 MeV: same as before
- Above 5 MeV:
  - One additional SOP on radiological safety
  - Studies have been published in 2003

ISO 11137

- Sterilization dose setting & maximum dose setting
  - Transfer only between similar equipment
  - No transfer from gamma or e-beam
  - Not enough data yet to prove similarity

➔ dose setting exercise
- Nothing new, normal procedure
- Cost per validation

Technology

- 5 vs 7.5 MeV
- Accelerators
- Material handling systems

5 vs 7.5 MeV

- Production capacity
  - 2x increase at the same beam current
- Dose uniformity
  - Better penetration with higher energy
  - Better dose uniformity with same product
- Directional beam
  - Small treatment zone
  - more flexible material handling solutions
  - Local shielding
- Activation
  - No issues at 5 MeV
  - Paperwork at 7.5 MeV

Accelerators

Today

- 5 MeV
  - Rhodotron (≤ 25mA)
  - Dynamitron (≤ 60mA)
  - Nissin HV (≤ 30mA)
- 7 or 7.5 MeV
  - Rhodotron (≤ 25mA)

New tomorrow

- 5 MeV
  - Rhodotron (≤100 mA)
  - Vivirad (≤ 60mA)
  - …
- 7 or 7.5 MeV
  - TT1000 (≤ 100 mA)

Material handling

Possibilities

- Pallet or tote irradiators
- Continuous, batch, incremental dose
- Flexibility and production capacity

Risks

- Only new designs
- Benchmarking of designs
- Prototype availability

+ Gamma technology

Managing risk

- Ask your supplier to take the risk:
  - You will pay a risk margin. How much?
  - Will he save himself in case of failure, or you?
  - Is the supplier able to take the risk for your complete investment?
  - Will you get what you want? Or what the supplier wants you to have?

➔Manage the risk yourself!

Managing risk

- Use the risk margin, that you don't pay, to outsource or hire competence
- Define your needs and design for it
- Analyze the risk with professional help
  - Technology risks (production capacity, dose uniformity, operation cost, investment)
  - Market risks
- Let the suppliers manage the risks they understand best (standard acceptance tests)

Market risks

- Customer acceptance
  - Your customer's notified body: experience with X-rays
  - Start testing customer products early
  - Reason for change in sterilization method
- Radiation Safety
  - Rules differ. Get an opinion from the regulatory body you deal with
  - Then choose 5 or 7.5 MeV

Technology risks

- Accelerator
  - Guarantee for beam current, scan system, up-time, maintenance and spare part response
  - Make sure it affects your supplier if he can’t deliver the basic parameters.
  - Evaluate maintenance contracts before you invest
  - Evaluate third party spare part supply

Technology risks

- Production capacity & dose uniformity
  - **Do Not** use efficiencies and other vague methods.
  - **Do** simulate the specific material handling solution that you need.
  - **Do** benchmark your simulation in one of the existing facilities.
  - **Do** apply safety margins in your analysis. You also take safety margins when you irradiate, right?

Production capacity

- Example – JMC pallet irradiator
  - 120cm x 100cm x 185cm (2.2m³)
  - Margins taken
  - 25 kGy minimum dose
  - Multi pass, multi layer system

Production capacity

25 kGy				Capacity in m3/h						
	Source	Density g/cm^3	DUR	1 h	2000 h	4000 h	6000 h	8000 h	MCi equiv	Treatment time pallet (min)
Efficient Gamma pallet Irradiator	3.0 MCi	0.25	1.39	5.9	11,800	23,600	35,400	47,200	3.0	22.58
	3.0 MCi	0.10	1.32	7.8	15,600	31,200	46,800	62,400	3.0	17.08
JMC X-ray pallet irradiator 5 MeV	25 mA	0.10	ca 1.5	3.4	6,800	13,600	20,400	27,200	1.3	39.18
	60 mA	0.10	ca 1.5	8.2	16,320	32,640	48,960	65,280	3.1	16.32
	100 mA	0.10	ca 1.5	13.6	27,200	54,400	81,600	108,800	5.2	9.79
	25 mA	0.25	1.5	2.3	4,625	9,250	13,875	18,500	1.2	57.60
	60 mA	**0.25**	**1.5**	**5.6**	**11,100**	**22,200**	**33,300**	**44,400**	**2.8**	**24.00**
	100 mA	0.25	1.5	9.3	18,500	37,000	55,500	74,000	4.7	14.40
JMC X-ray pallet irradiator 7 MeV	**25 mA**	**0.10**	**1.4**	**6.8**	**13,600**	**27,200**	**40,800**	**54,400**	**2.6**	19.59
	60 mA	0.10	1.4	16.3	32,640	65,280	97,920	130,560	6.3	8.16
	25 mA	0.25	1.46	5.1	10,240	20,480	30,720	40,960	2.6	26.02
	60 mA	0.25	1.46	12.3	24,576	49,152	73,728	98,304	6.2	10.84

V1

Technology risks

- Material handling
  - Use standard technology. Help the supplier with radiation resistant materials and components.
  - Do Not over-automate
  - Make sure it affects your supplier if he can’t deliver the basic parameters.
  - Evaluate maintenance contracts before you invest
  - Evaluate spare parts supply

Technology risks

- Space requirements
  - Get a safe shield design and price it
  - Determine your warehouse floor space and product flow.
  - Ensure adequate loading and unloading area
  - Today's economy allows significant reduction in negotiated prices compared to A&E estimates

Cost overrun risks

- Take your time before you invest
  - Lock the production capacity down before too long
  - RFQ based on specifications. Write specifications. Look at civil works and equipment.
  - Estimate personnel cost.
  - Understand your utility requirements and get offers based on forecast consumption

The quality of your evaluation is the key to your risk reduction.

Investment
X-ray vs cobalt

- + Bunker for accelerator
- + Accelerator
- + Material handling
- - Material handling cobalt
- - cobalt load
- Net: +/- 0

- Accelerator OEMs seem ready to price accelerator competitive with cobalt load (>2 MCi)
- Production capacity & DUR comparable

Operation cost ranking

- X-ray
  1. Depreciation
  2. Personnel
  3. Utilities
  4. Maintenance
- Gamma
  1. Co decay 12% pa
  2. Depreciation
  3. Personnel
  4. Utilities & maintenance

Operation & strategy

Operation Cost

- + Electricity
- + Maintenance
- - Cobalt decay
- Estimated net: pro X-ray (if initial load > 2 MCi)

Strategy & Risks

- Cobalt or electricity availability
- Government restrictions on cobalt
- Machine source: on/off
- Future price of electricity & cobalt
- EtO residuals in product

Risk summary

You will find:

- The risk is manageable and can be reduced
- You will be able to make sound decisions
- You save money

Future of X-rays in sterilization

All systems are GO:

- X-ray is well understood – medical device manufacturers are well aware of the potential
- ISO standards are known for decades. They apply.
- Material qualifications are similar to gamma
- Customers want to have a reason to change
  - Reducing cost per unit
  - Improving dose uniformity
  - Full pallet integrity

Future in other markets

The same approach is valid also for other applications

- Food pasteurization
  - E-beam can be cheaper, but packaging is an issue
  - Gamma and X-ray can treat food in boxes
  - X-ray can treat full pallets – that will be the winner for production centers
- Advanced Materials
  - Some Bulk polymers require better dose uniformity than electron beam – market is shared with gamma
  - Composite materials, especially when very thick may need X-rays instead of electron beam

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