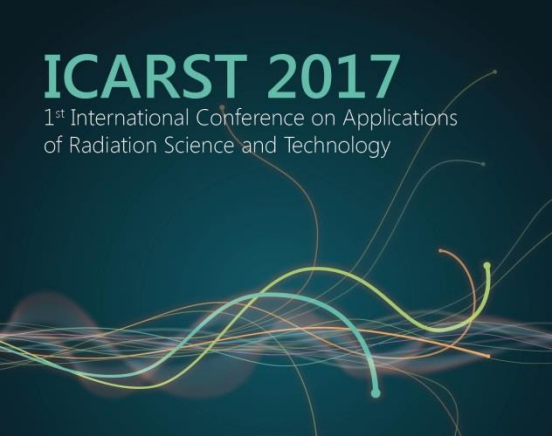


Emerging Areas of Radiation Sterilisation

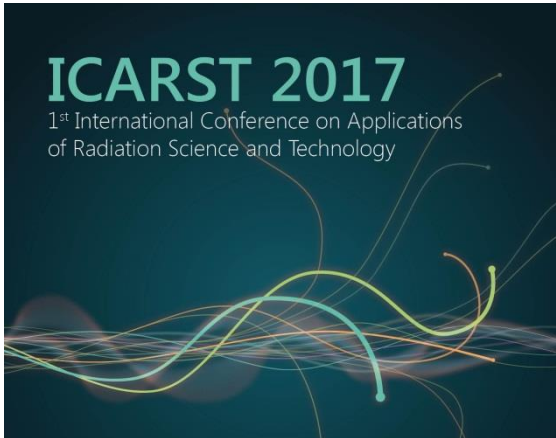
Dr. BART CROONENBORGHS

Sterigenics International

Outline

- “Traditional” vs “non-traditional” processes

- 3 examples of “non-traditional” irradiation processes qualified at Sterigenics



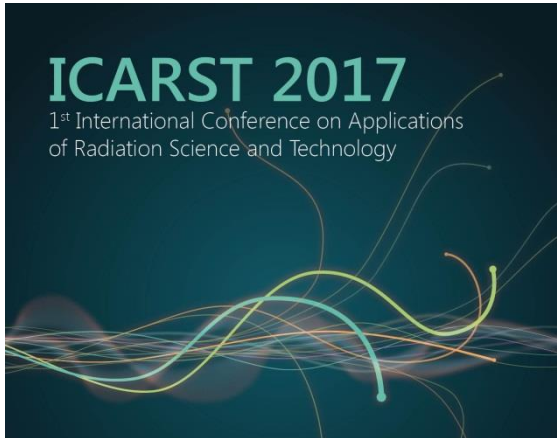
Non-traditional Radiation Sterilisation

Traditional Approach

- High sterilisation doses and wide specs (e.g. 25 kGy – 50 kGy)
- Ambient conditions during storage and irradiation
- Large batch volumes, "simple" products

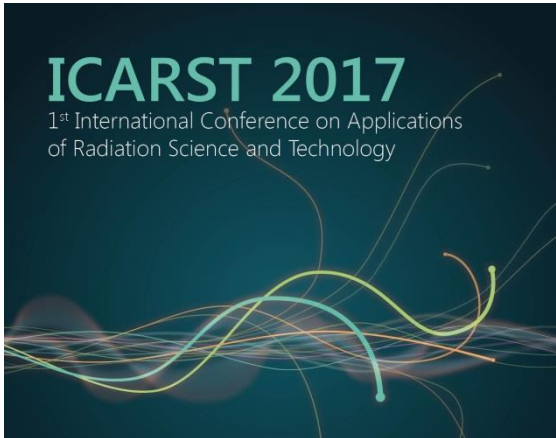
New Challenges

- Lower (customised) sterilisation doses and narrow dose specifications
- Low (controlled) temperature may be necessary during storage and irradiation
- Dose rate restrictions may apply
- Inert atmosphere or other means of product protection
- (Very) low batch volumes, expensive product
- Just In Time manufacturing
- Safety aspects e.g. cytotoxicity, cephalosporine



“Either you decide to stay in the shallow end of the pool or you go out into the ocean”

Christopher Reeve



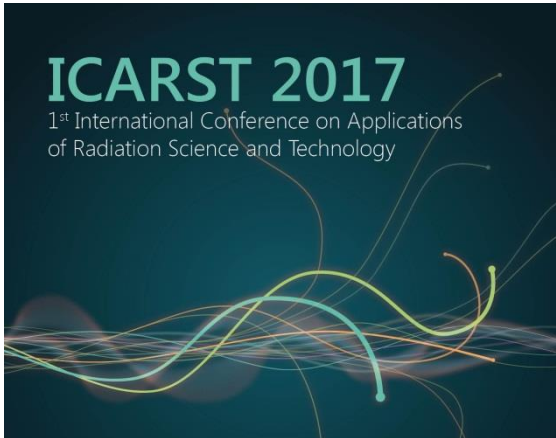
Dosimetry at Low Temperature

- Apply temperature correction factor
- Calibrate dosimeter at refrigerated / frozen temperature as encountered during product irradiation

Or

- Use simulated refrigerant & PQ at ambient temperature
- Reference location at ambient temperature for routine process monitoring

↳ Done at Sterigenics



Complex dosimeter response, alanine example

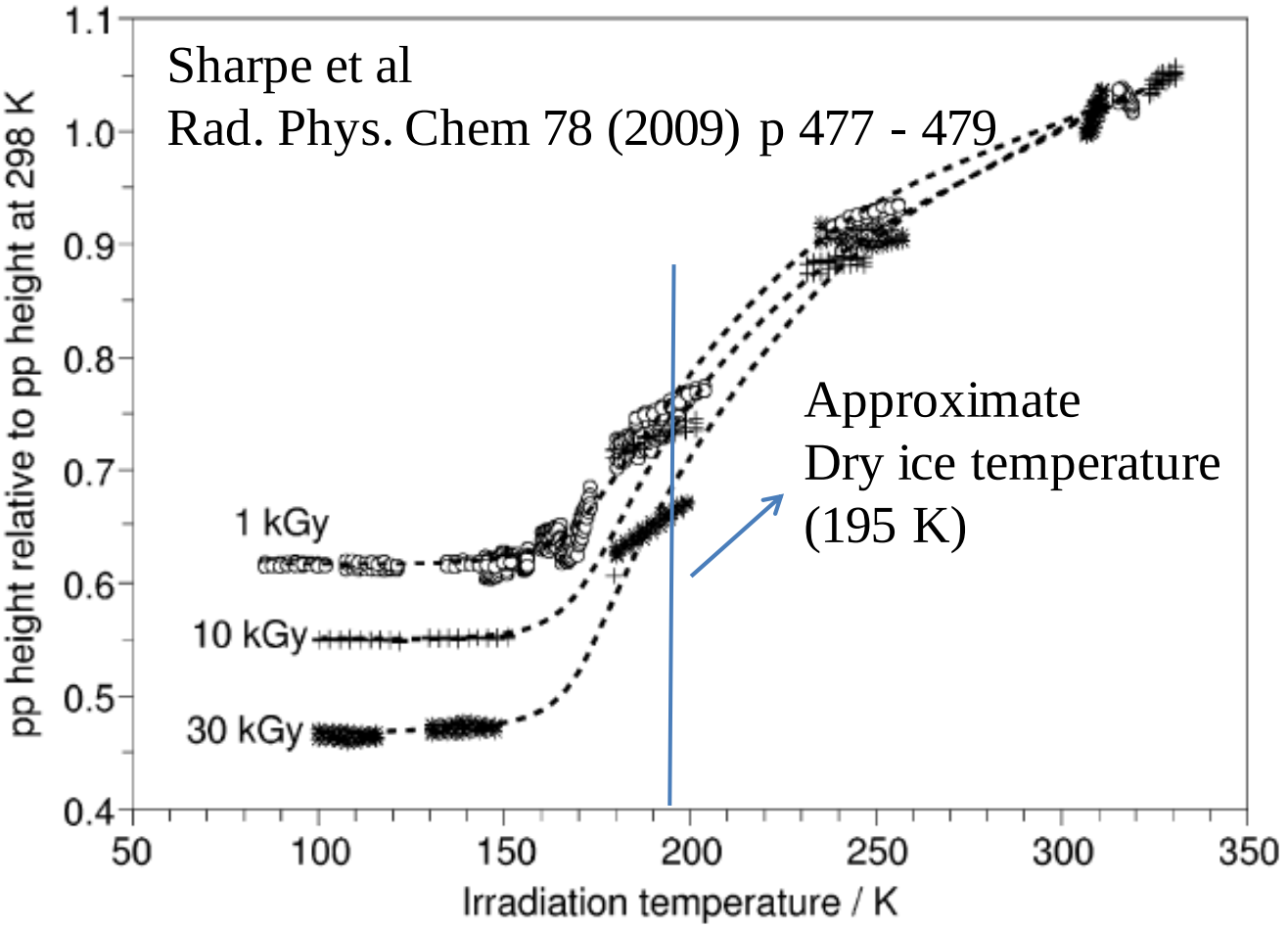
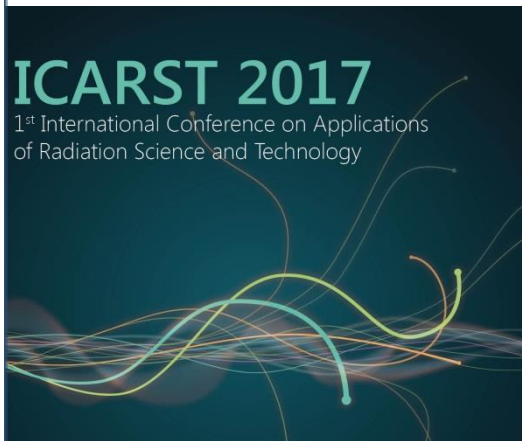


Fig. 3. Relative response of alanine dosimeters irradiated to 1, 10 and 30 kGy at temperatures between 80 and 310 K.



Example 1: High energy electron beam

Dangerous goods packaging

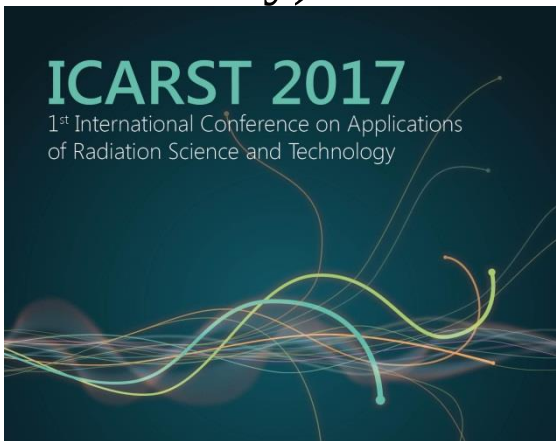
20 ml glass vial with approx. 50 mg product

"Dangerous goods"

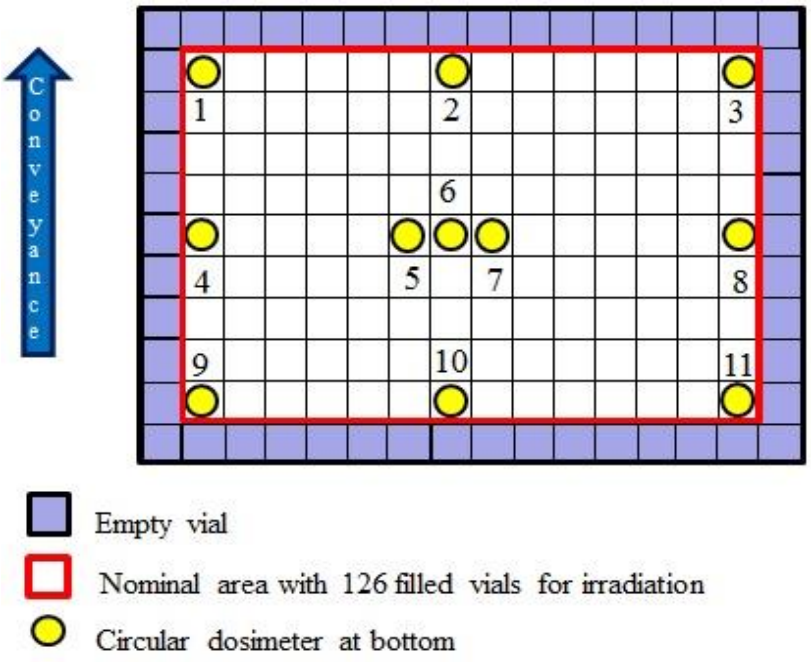
Storage at irradiation site 2 °C – 8 °C

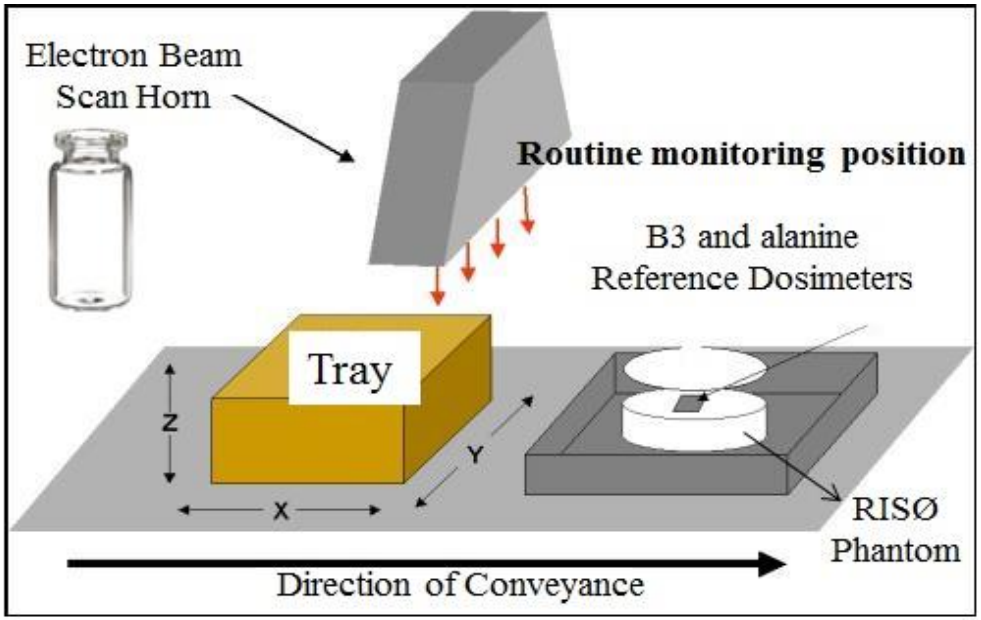
11 kGy – xx kGy

(Average bioburden ≤ 0.1 CFU
Method 1 dose setting ISO 11137-2
Verification dose 1.3 kGy)



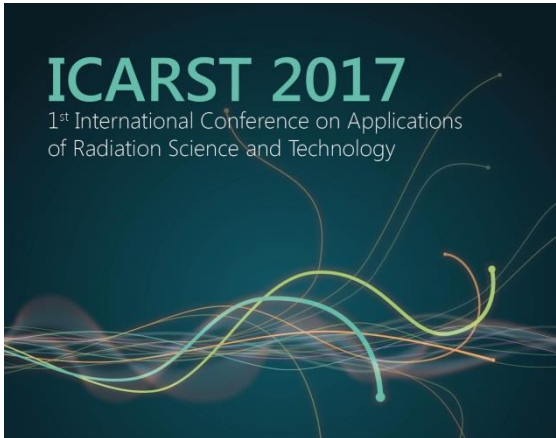
Example 1: High energy electron beam



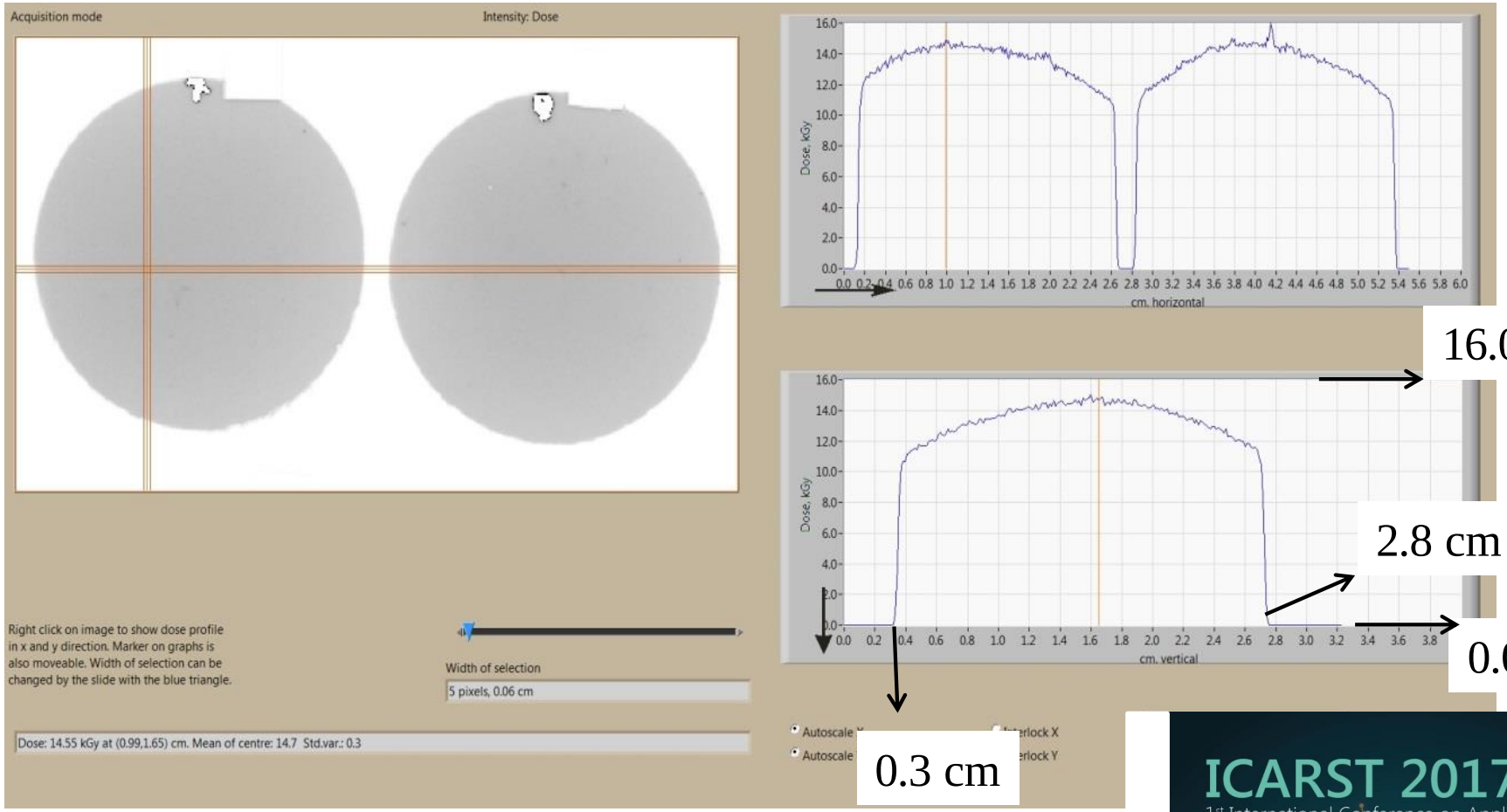


Single sided irradiation, 10 MeV electrons
Outer ring of empty vials

PQ dose mapping at ambient temperature:
Circular dosimeter at bottom of selected empty vials



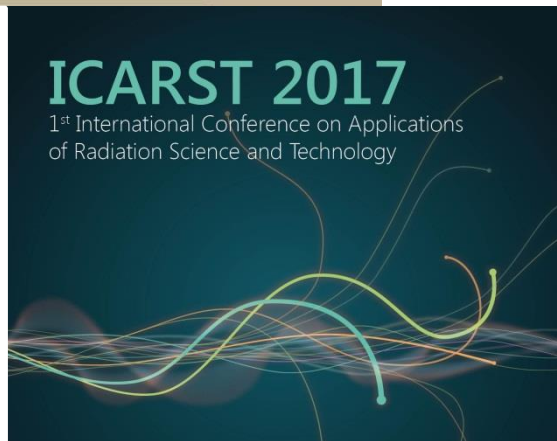
Example 1: High energy electron beam



Dose distribution:

Circular dosimeter at bottom of selected vials

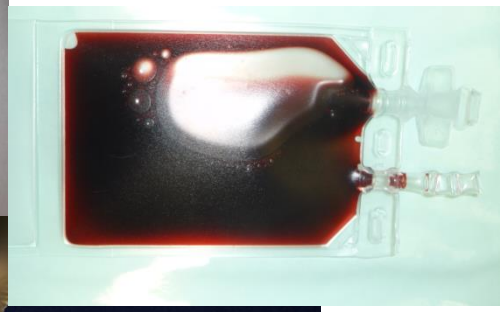
Avg. DUR at bottom of vial is 1.40 (CV 3.1%)



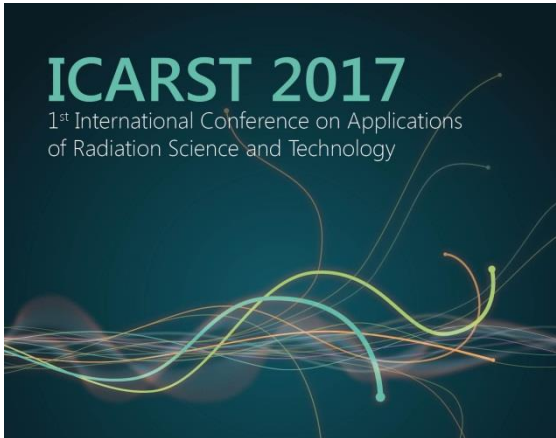
Example 2: Gamma

xx kGy – yy kGy

Generally below -20 °C during storage
and irradiation



Biological products



Example 2: Cold chain management

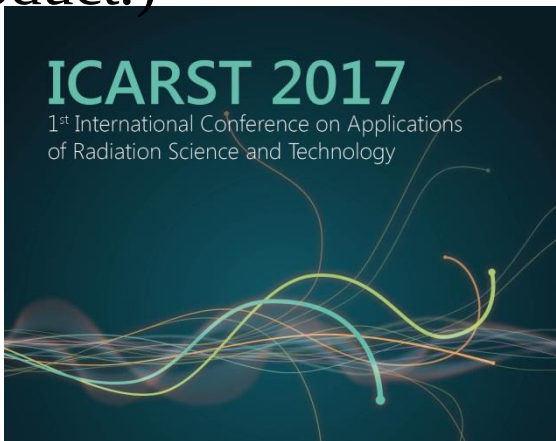

Product under dry ice sent to the irradiation site


Product removed from transport container and stored on-site in -80 ° C freezers


Loading Sterigenics cryotainers: At controlled T
Coolant during irradiation: Dry ice
(validated positions where it is demonstrated there is no effect on dose delivery to product.)

After irradiation:
transferred at controlled T to -80 ° C freezer.


Product shipped under dry ice



Example 2: Cold chain management

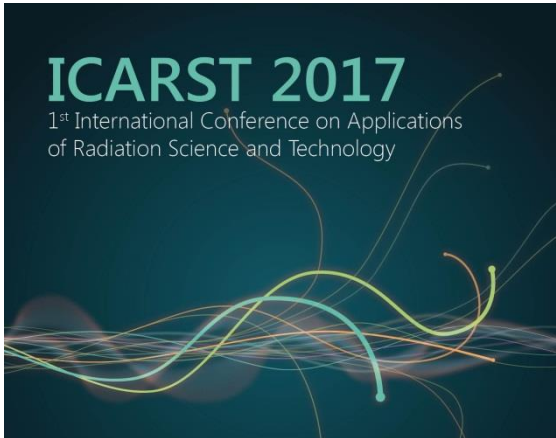
Irradiator:

Batch irradiator; because of customised and tight dose ranges, Small volumes and short turn-around times.

Performance Qualification dose mapping:

Ambient temperature using simulated product (and coolant)

Building in operational flexibility to accomodate different volumes in shipment



Example 3: Gamma

20 ml glass vial with approx. 500 mg product

“Dangerous goods”

Storage at irradiation site below -20 °C

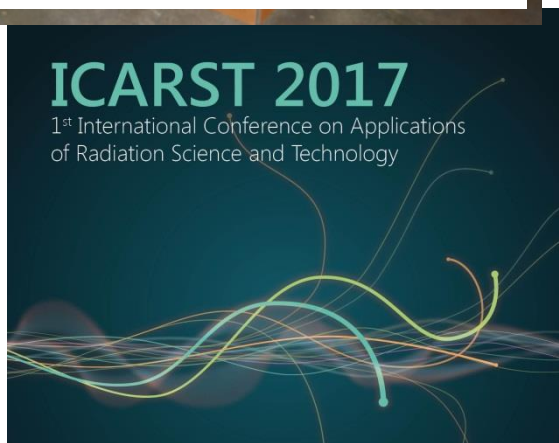
Irradiation under cold chain management

xx kGy – yy kGy

Method VD_{max}^{SD} (ISO TS 13004)

Batch irradiator (full manufacturing batch = 1 run)

Dangerous goods packaging



Conclusions

In order to succeed in the environment of ever-more complex sterile health care products one needs to think outside of the box and provide a customised solution:

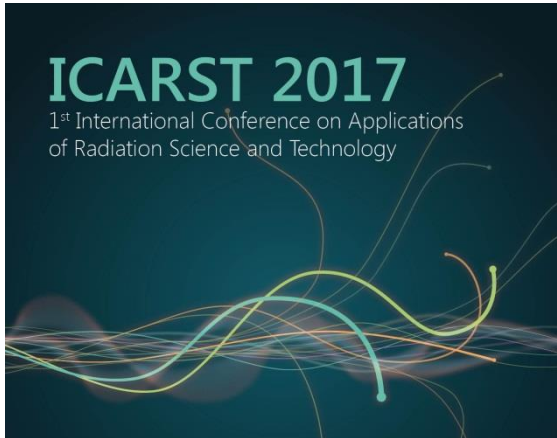
- Techniques to minimise radiation damage
(e.g. Low temperature, inert atomosphere, radioprotectants)

- New methods for establishing a sterilisation dose, performed under the same conditions as the ones that are found to minimise radiation damage of the product

- Mathematical modelling, specialised irradiators and dosimetry

- EHS procedures (and possibly licenses)

→ Partner with a diverse group of people and already early on in development



… It’s in our hands

Thank You!!

Questions?

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