

**TC PROJECT RER/8/010**

**“Regional Workshop on Harmonization, Implementation, and use of  
Quality Assurance & Quality Control Methods”**

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# **Gamma – Dose mapping in IQ/OQ and PQ**

**Rodica Georgescu**

**IRASM Radiation Processing Center**

**Horia Hulubei National Institute of Physics and Nuclear  
Engineering, Bucharest, Romania**

# Absorbed - dose mapping

- **Measurement of absorbed dose within a process load using dosimeters placed at specified locations to produce a one, two or three-dimensional distribution of absorbed dose, thus rendering a map of absorbed - dose values**

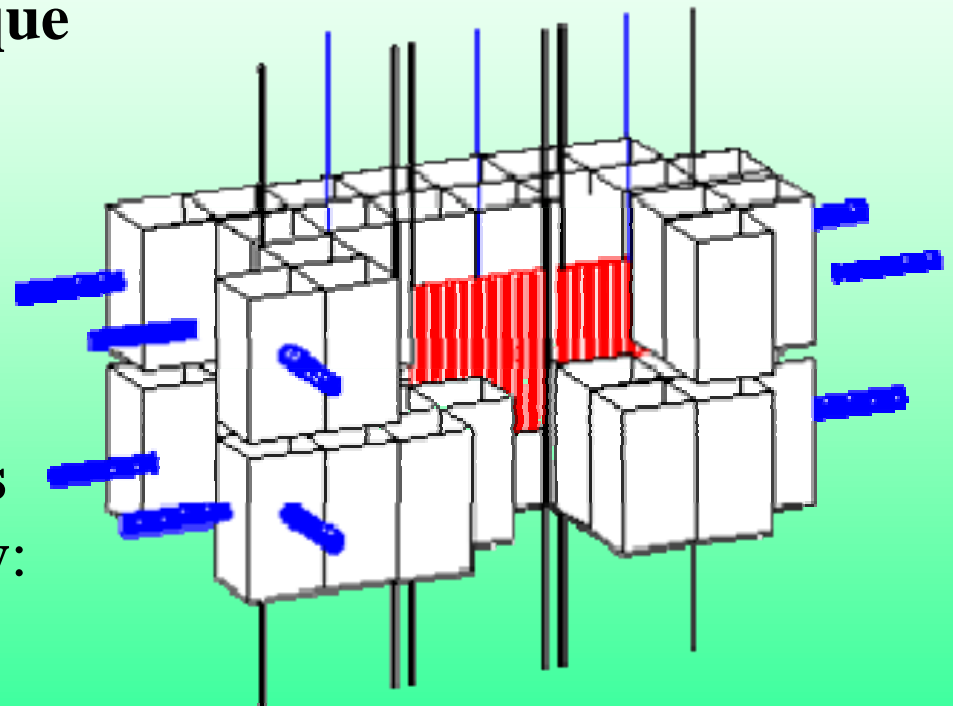
The SVST Co-60/B type irradiator of IRASM is a wet storage, tote-box irradiator produced by the Institute of Isotopes Ltd. Co. from Budapest - Hungary

- commissioned in year 2000;
- was loaded with 100 kCi of Co - 60; replenishment - 2004

- **product overlap irradiation technique**
- **3 source racks, with a split source hoist system;**
- **shuffle-dwell conveyor system**
- **52 irradiation position**

- **Radiation technological parameters for  $0.2 \text{ g/cm}^3$  average product density:**

- **efficiency - min. 27 %**
- **$D_{\text{max}}/D_{\text{min}} = 1.30 \pm 0.13$**



## **Guiding Standards :**

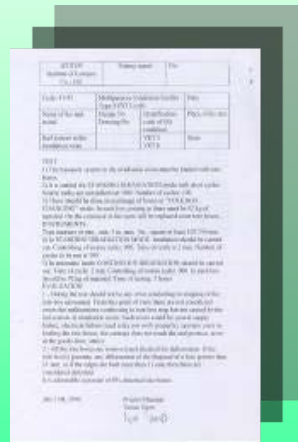
- **ISO/ASTM 51702 : 2004 - Standard Practice for Dosimetry in Gamma Irradiation Facilities for Radiation Processing**
- **EN ISO 11137 : 2006 - Sterilization of health care products - Radiation**
  - Part 1 - Requirements for development, validation and routine control of a sterilization process for medical devices;
  - Part 2 - Establishing the sterilization dose;
  - Part 3 - **Guidance on dosimetric aspects.**
- **ASTM E 2303 - 03 - Guide for Absorbed-Dose Mapping in radiation Processing Facilities**

# Installation qualification (IQ)

Process of obtaining and documenting evidence that the irradiator, with all its associated equipment and instrumentation, has been provided and installed in accordance with specifications



Quality Plan



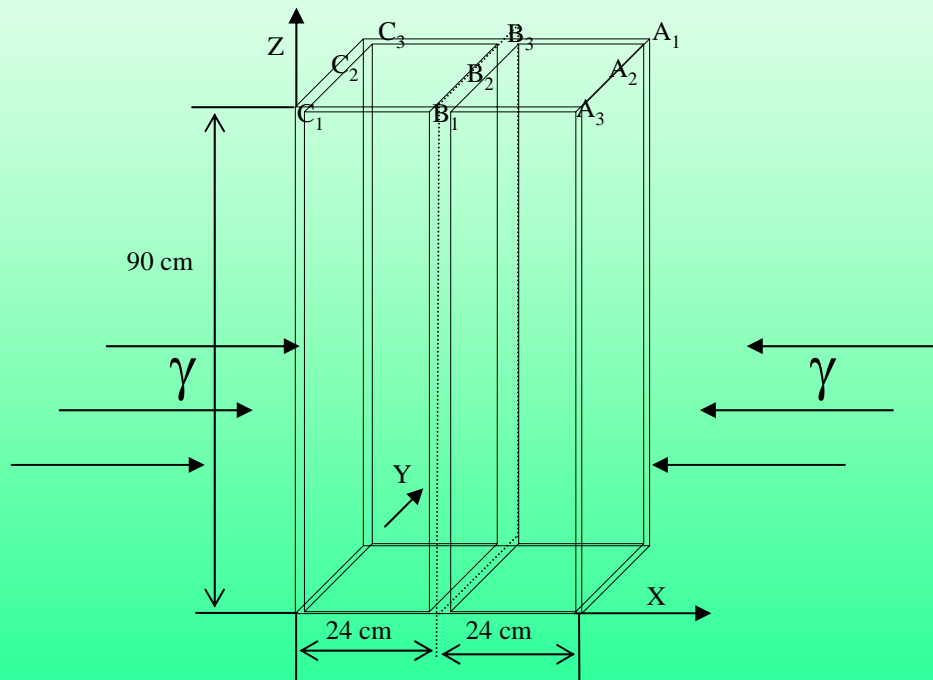
Test reports



**IQ: OK!**

# Dose-mapping for IQ

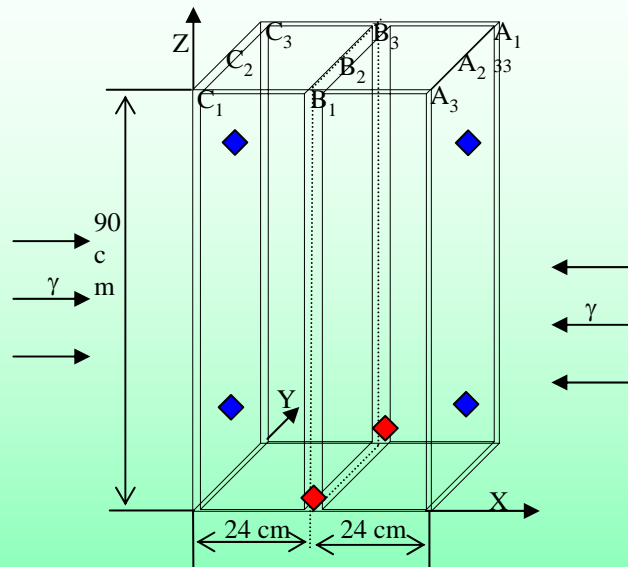
- was carried out by supplier of the plant - September 2000;
- tote boxes were loaded with dummy material of nominal density  $0.2 \text{ g/cm}^3$ ;
- ECB dosimeters were placed in 3 tote boxes, in 45 positions;
- in each position 2 parallel ampoules were placed.



1	2	3
4	5	6
7	8	9
10	11	12
13	14	15

To demonstrate the correct installation of gamma sources and positioning system

# Dose-mapping for IQ - results:



◆  $D_{\min}$

◆  $D_{\max}$

The minimum and maximum dose positions were found in accordance with the theory and other international experiences

→ the gamma sources were installed in correct positions

-other information → OQ

# Operational qualification (OQ)

**Process of obtaining and documenting evidence that the installed equipment and instrumentation operate within predetermined limits when used in accordance with operational procedures.**

- The purpose of OQ is to demonstrate that the irradiator as installed is capable of operating and delivering appropriate doses within defined acceptance criteria. This is achieved by determining dose distributions through dose mapping exercises and relating these distributions to irradiator and process parameters.

# Operational qualification (OQ)

- **The absorbed dose received by any portion of product in a process load depends on both irradiator parameters and process parameters.**
- **Irradiator parameters :**
  - source activity**
  - source geometry**
  - irradiation geometry**
  - the process paths**
- **Process parameters :**
  - irradiation time**
  - product composition and density**
  - product loading configuration**

# Dose mapping for OQ

- Is carried out for evaluating facility effectiveness and to characterize the irradiator with respect to the distribution and reproducibility of absorbed dose in product for each set of irradiator parameters and process parameters used for irradiating product.
- Should be performed placing dosimeters in irradiation containers filled with materials of homogeneous density to its designed limits, or with the amount expected during typical production runs → **locations of Dmin and Dmax zones, the magnitudes of Dmin and Dmax for the chosen density.**
- At least three irradiation containers should be dose mapped at each chosen density → **determine the variability of absorbed dose when process parameters fluctuate statistically during normal operations.**

# Dose mapping for OQ

- At least two dose mapping should be carried out, with materials close to the lower and upper limits of the density range for which the irradiator is intended to be used → the relationships between the magnitude of dose at defined locations within the irradiation container and the product density.
- A separate dose mapping exercise should be carried out or a calculation of transit dose should be performed in order to assess the effect of process interruption.
- Dose mapping should be carried out to determine the effects on dose and dose distribution that may occur in irradiation containers as a result of changing to product of different density - by sequentially processing two products with different densities and dose-mapping the last container of the first product and the first container of the second one → the acceptable range of densities that can be processed together .

# Dose mapping for OQ

- If there is more than one conveyor path, dose mapping shall be carried out for each path to be used for processing product.
- Separate dose mapping exercise should be performed for fixed locations in the irradiation chamber designated for manual placement of products (e. g. - for sample irradiation for dose setting)

# Dose mapping for OQ at IRASM (I)

- batch mode - 52 irradiation positions - all Co-60 sources (1 1 1) -
  - 2 - sided irradiation, 52 passes - conveyor
- Absorbed-dose mapping in 2 homogeneous dummy materials of nominal densities **0.084 and 0.197 g/cm<sup>3</sup>** were made at installation commissioning and after replenishment of sources.
  - containers filled to their design limits;
  - ECB dosimeters in 3 containers (49-53 dosimeters /container);
  - three-dimensional placement of dosimeters;
  - evaluation of the effects of process interruption;
  - sequentially processing of dummy with the two densities;

# Results for dose mapping for OQ at IRASM (I)

• From absorbed-dose mapping in dummy material of nominal density **0.2 g/cm<sup>3</sup>** made at irradiator commissioning

→ The efficiency of Gamma Irradiator: **27.7 %**;  
(specification : min 27 %)

$$D_{\max}/D_{\min} = 1.29 \text{ (specification : } 1.30 \pm 0.13\text{)}$$

# Results for dose mapping for OQ at IRASM (I)

- Locations of Dmin and Dmax zones - in accordance with the expectations and unchanged after the replenishment, especially for Dmin;

- Dose-mappings after replenishment :

- 197 kg / m<sup>3</sup> (20. 11. 2004)

$$\dot{\bar{D}}_{\min} = \frac{\bar{D}_{\min}}{T_i} = 899 \text{ Gy} / h$$

$$\dot{\bar{D}}_{\max} = \frac{\bar{D}_{\max}}{T_i} = 1263 \text{ Gy} / h$$

- 84 kg / m<sup>3</sup> (26. 01. 2005)

$$\dot{\bar{D}}_{\min} = \frac{\bar{D}_{\min}}{T_i} = 1013.5 \text{ Gy} / h$$

$$\dot{\bar{D}}_{\max} = \frac{\bar{D}_{\max}}{T_i} = 1333.5 \text{ Gy} / h$$

# Results for dose mapping for OQ at IRASM (I)

- Evaluation for 01. 02. 2005

$$\dot{D}_{\min} \text{ (Gy / h)} = 1111,35 - 1,19469 * \text{Dens. (kg/m}^3\text{)} \quad u = 2.1 \%$$

$$\dot{D}_{\max} \text{ (Gy / h)} = 1406,08 - 0,89381 * \text{Dens. (kg/m}^3\text{)} \quad u = 1.5 \%$$

$$DUR = \frac{D_{\max}}{D_{\min}} = 1,24984 + 0.00079 * \text{Dens. (kg/m}^3\text{)} \quad u = 2.5 \%$$

- The **effects of process interruption** are negligible - the transit time ~ 7 s and the maximum dose rate < 20 kGy/h (**< 40 Gy**).

# Results of dose mapping for OQ at IRASM (I)

- The effects of presence of products with different densities:
  - **46 tote-boxes** (1 ... 10 and 17 ...52) loaded with dummy - **84 kg / m<sup>3</sup>**
  - **6 tote-boxes** (11 ... 16) loaded with dummy - **197 kg / m<sup>3</sup>**
  - ECB dosimeters – in minimum and maximum absorbed dose positions in **(1 ... 26)** and **(37 ... 39) tote-boxes**

$$\bar{D}_{\min} (84 \text{ kg} / \text{m}^3) = 1.16 * \bar{D}_{\min} (197 \text{ kg} / \text{m}^3)$$

**at interfaces**

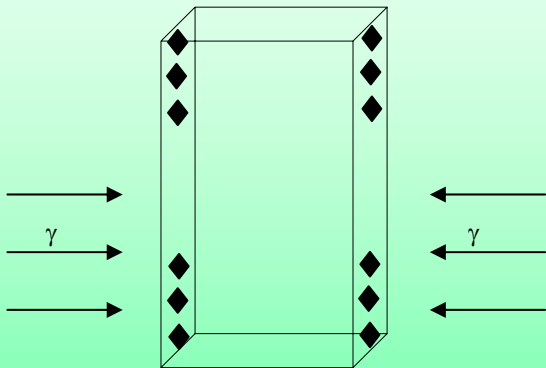
**1.04**

$$\bar{D}_{\max} (84 \text{ kg} / \text{m}^3) = 1.04 * \bar{D}_{\max} (197 \text{ kg} / \text{m}^3)$$

**1.01**

# Results of dose mapping for OQ at IRASM (I)

- The effects of presence of unloaded tote-boxes:
  - **46 tote-boxes** (1 ... 10 and 17 ...52) loaded with dummy - **84 kg / m<sup>3</sup>**
  - **6 tote-boxes** (11 ... 16) unloaded

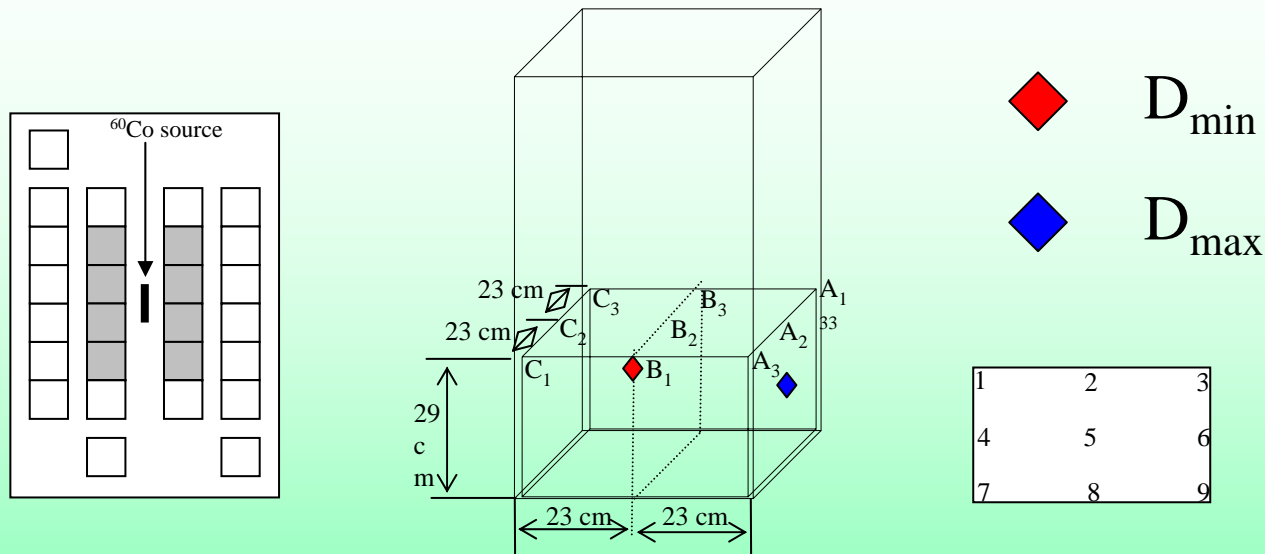


ECB dosimeters were placed in the maximum dose zones at interfaces (tote-boxes 10 and 17) and in two reference totes (38 and 39).

The effects were not statistical significant.

# Dose mapping for OQ at IRASM (II)

- batch mode - 8 irradiation positions - central Co-60 sources (0 1 0) -
- 2 - sided irradiation - conveyor

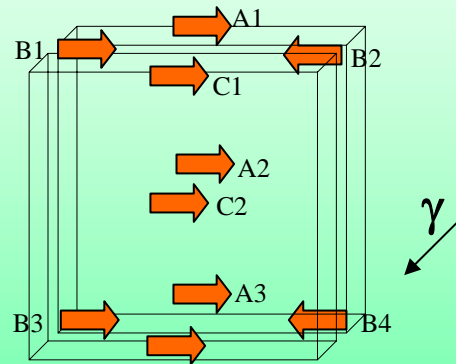
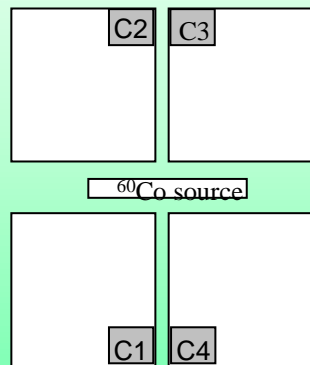


- Dose mappings with and 0.2 and 0.02 g/cm<sup>3</sup>  
→ cycle times for different product densities

# Dose mapping for OQ at IRASM (III)-samples

- stationary - 1 irradiation position - central Co-60 sources (0 1 0) -
- 2 - sided irradiation - manual

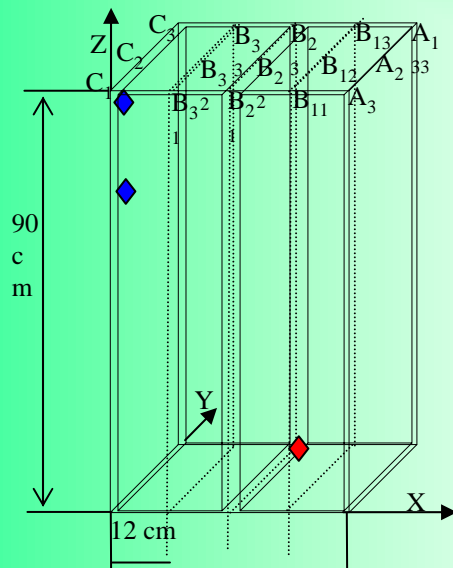
- Cardboard boxes 15 cm x 15 cm x 10 cm - dummy - 0.1 g/cm<sup>3</sup>



-asymmetry  
DUR  $\leq$  1.1

# Dose mapping for OQ at IRASM (IV) – (SIT)

- batch mode - 52 irradiation positions - the small Co-60 source (0 0 1) -
- 2 - sided irradiation, 52 passes - conveyor

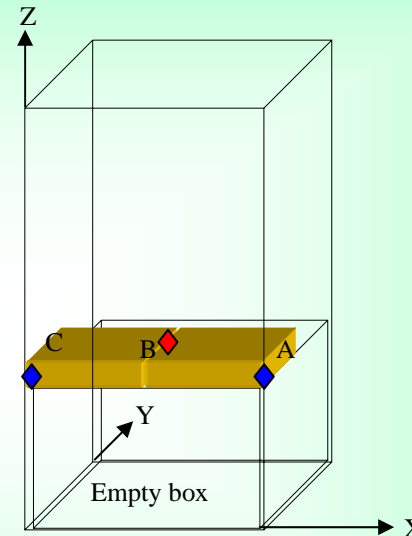


0,2 g/cm<sup>3</sup>

1 dosimetric tote

5x15 alanine

DUR = 1.67



0,4 g/cm<sup>3</sup>

3 dosimetric totes

4x4 alanine

DUR = 1.18 (u = 1.7 %)

# Performance qualification (PQ)

- **Process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification.**
- **PQ Is carried out to determine the appropriate process parameters (timer setting, product loading configuration) for ensuring that the absorbed dose requirements for a particular product can be satisfied.**

# Dose mapping for PQ

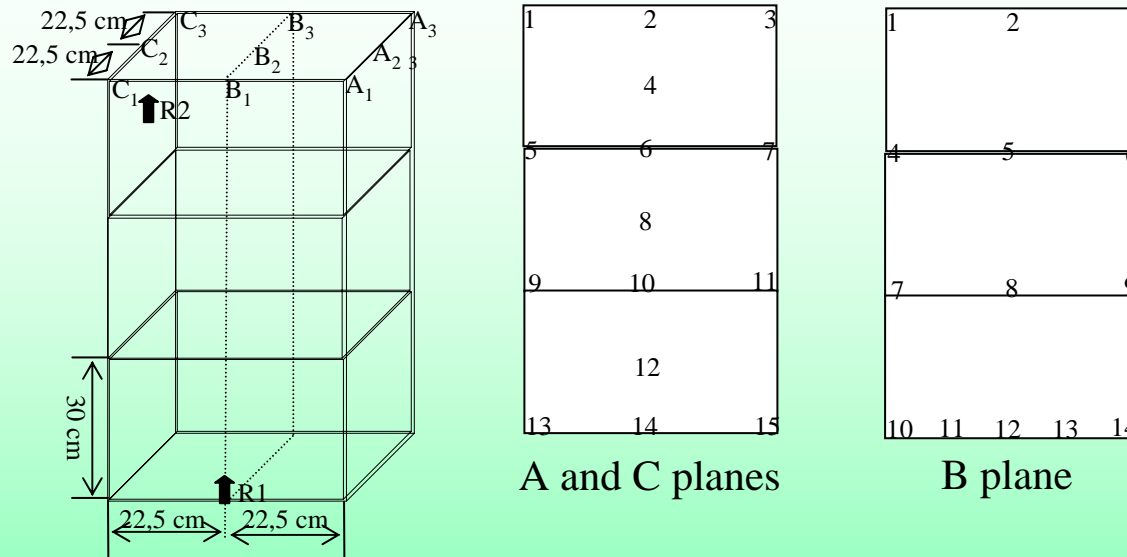
- Dose mappings should be performed for specific products and loading configurations to identify locations and magnitudes of minimum and maximum doses within product and the relationship between these doses and the dose(s) at the routine monitoring position(s).
- Dose mapping may be performed in actual product or in simulated product materials with similar densities and distributions as the actual products.
- Different products with similar densities and distribution may be considered as a single processing category and the dose map data can be applied to all products in this group.
- Process load exhibiting the same dose distribution characteristics as those used in the operational qualification dose map can be considered to have met the product dose mapping requirements for PQ.
- The location of the dosimeters used in dose map is established taking into consideration voids, density variations or any material interfaces that may cause significant localized dose gradients that could affect the location of minimum and/or maximum dose within the process load.

# Dose mapping for PQ

- At least three irradiation containers should be dose mapped, especially in areas of dose extremes, in order to obtain statistically valid data.
- Information from doses measured during dose mapping is used to determine the values for process parameters, such as timer setting or conveyor speed, which are set to obtain the specified absorbed dose without exceeding the maximum acceptable dose and to establish the process specification.
- The effect on dose to product of different densities present in the irradiator shall be determined to define product that can be processed together.
- Dose distribution and the effect of partially filled containers shall be determined.

# Dose mapping for PQ at IRASM (example)

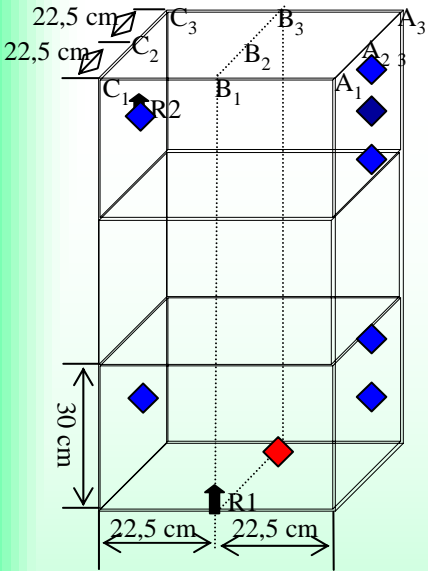
**cotton compresses – cardboard boxes 45 x 45 x 29 cm<sup>3</sup>, 9 kg, ( 0,15 g/cm<sup>3</sup>)**  
**batch mode - 52 irradiation positions - all Co-60 sources (1 1 1)**



**R1 and R2 – routine monitoring positions**

- ECB dosimeters
- 3 mapped containers

# Results -dose mapping for PQ at IRASM (ex.)



Container	Dmin/ D <sub>R1</sub>	Dmax/ D <sub>R2</sub>	Dmax/ D <sub>R1</sub>	Dmin/ D <sub>R2</sub>	Dmax/Dmin
1	0,975	1.026	1.270	0,788	1,302
2	0,958	1,017	1,247	0,781	1,303
3	0,979	1,014	1,278	0,777	1,305
Mean	0,971	1,019	1,265	0,782	1,303
SD	0.011	0,006	0,016	0,006	0,002
Int. 95 %	0,971± 0,027	1,019 ± 0,015	1,265 ± 0,040	0,782 ± 0,015	1,303± 0,005

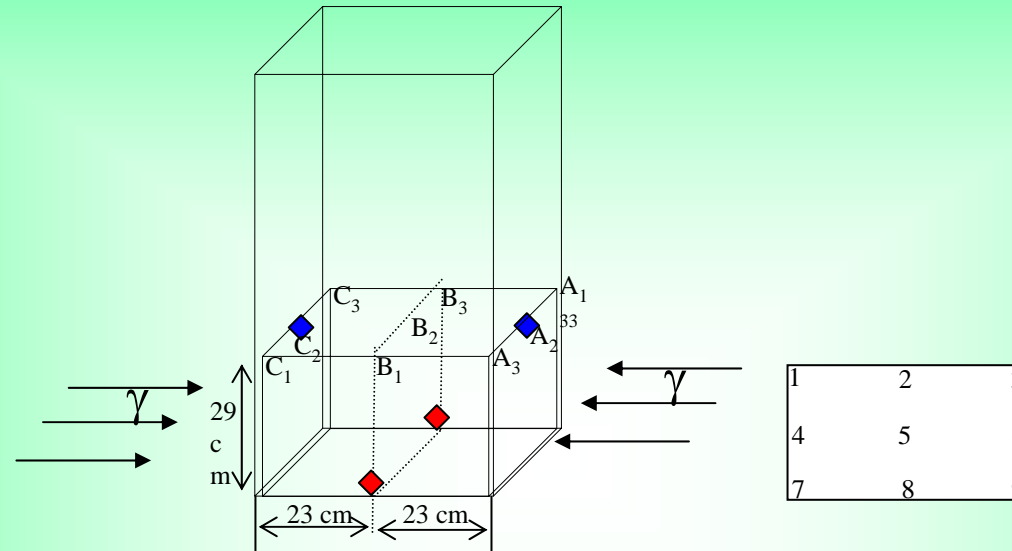
## The timer setting for the production runs

$$T_{i, \min} = \frac{D_{\min}^{req} T_{i, dm}}{D_{\min}^{calc}} \quad D_{\min}^{calc} = [D_{Ri} - U(D_{Ri})] * \left[ \frac{D_{\min}^{dm}}{D_{Ri}} - U\left(\frac{D_{\min}^{dm}}{D_{Ri}}\right) \right]$$

$$T_{i, \max} = \frac{D_{\max}^{acc} T_{i, dm}}{D_{\max}^{calc}} \quad D_{\max}^{calc} = [D_{Ri} + U(D_{Ri})] * \left[ \frac{D_{\max}^{dm}}{D_{Ri}} + U\left(\frac{D_{\max}^{dm}}{D_{Ri}}\right) \right]$$

# Dose mapping for PQ at IRASM

- partially filled containers -



- The effects of presence of partially filled or unloaded tote-boxes were non important for the processing of our products (the maximum acceptable absorbed doses are quite high)

# THE PROCESS SPECIFICATION

- The description of the packaged product with the acceptable variations;
- the loading pattern of product within the irradiation container;
- the dose requirements;
- the routine dosimeter monitoring position(s);
- the relationships between the routine dosimeter measurement(s); and the minimum and maximum doses;
- the timer setting;

Products (over 20) → **product categories** → **processing categories**  
**6 process specifications**, each of them with multiple processing categories and, some of them, with multiple doses (ex. pharmaceuticals)

**THANK YOU FOR YOUR ATTENTION**