Validation and routine control for low energy electron accelerators in medical and pharmaceutical applications

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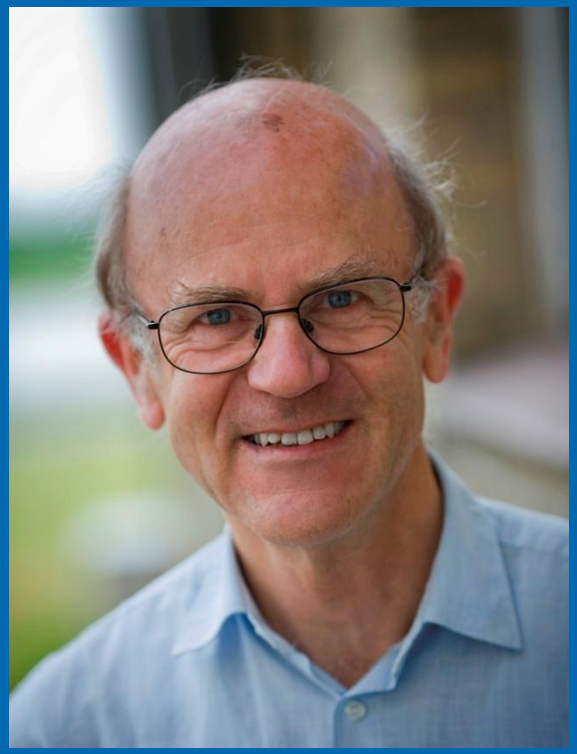


Low Energy Validation

- Content of presentation:

  Requirements for using radiation in medical device sterilization and in pharmaceutical industry:

  - 1. Dose (absorbed dose) must be traceable to national standards.
  - 2. Measurement uncertainty must be known.
  - 3. The irradiation process must be validated.

Low Energy Validation

- 1. Dose (absorbed dose) must be traceable to national standards.

- Two methods are recommended for calibration required for traceability (ISO/ASTM 51261 (new), NPL CIRM 29):

- 1. Irradiation of dosimeters in-plant (in-situ).
  - - requires irradiation of routine dosimeters together with reference dosimeters

- 2. Irradiation of dosimeters at calibration laboratory.
  - - must be followed by in-plant verification

Low Energy Validation

Irradiation in-plant.

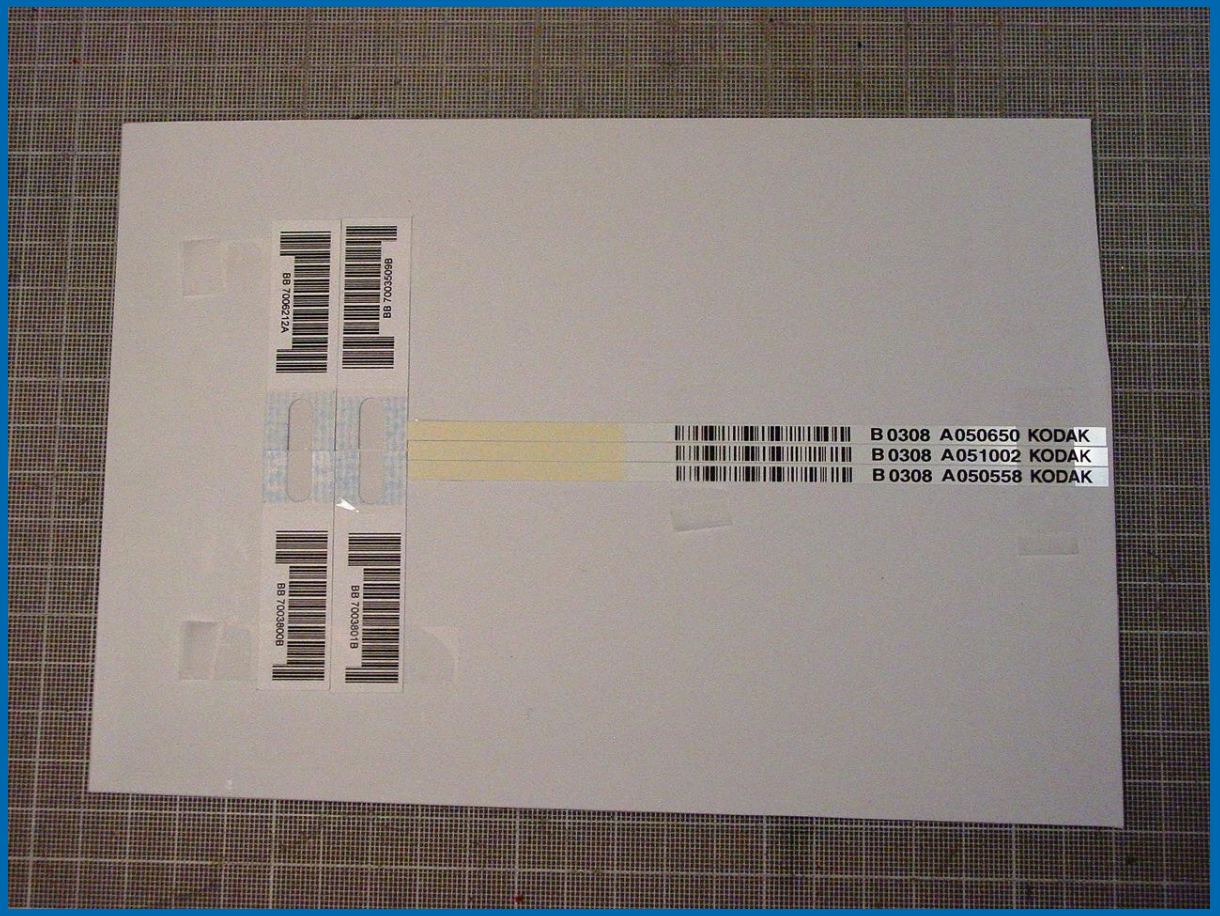
Reference geometry for low energy e-

Reference dosimeters:

Alanine film

Routine dosimeters:

GEX DoseStix

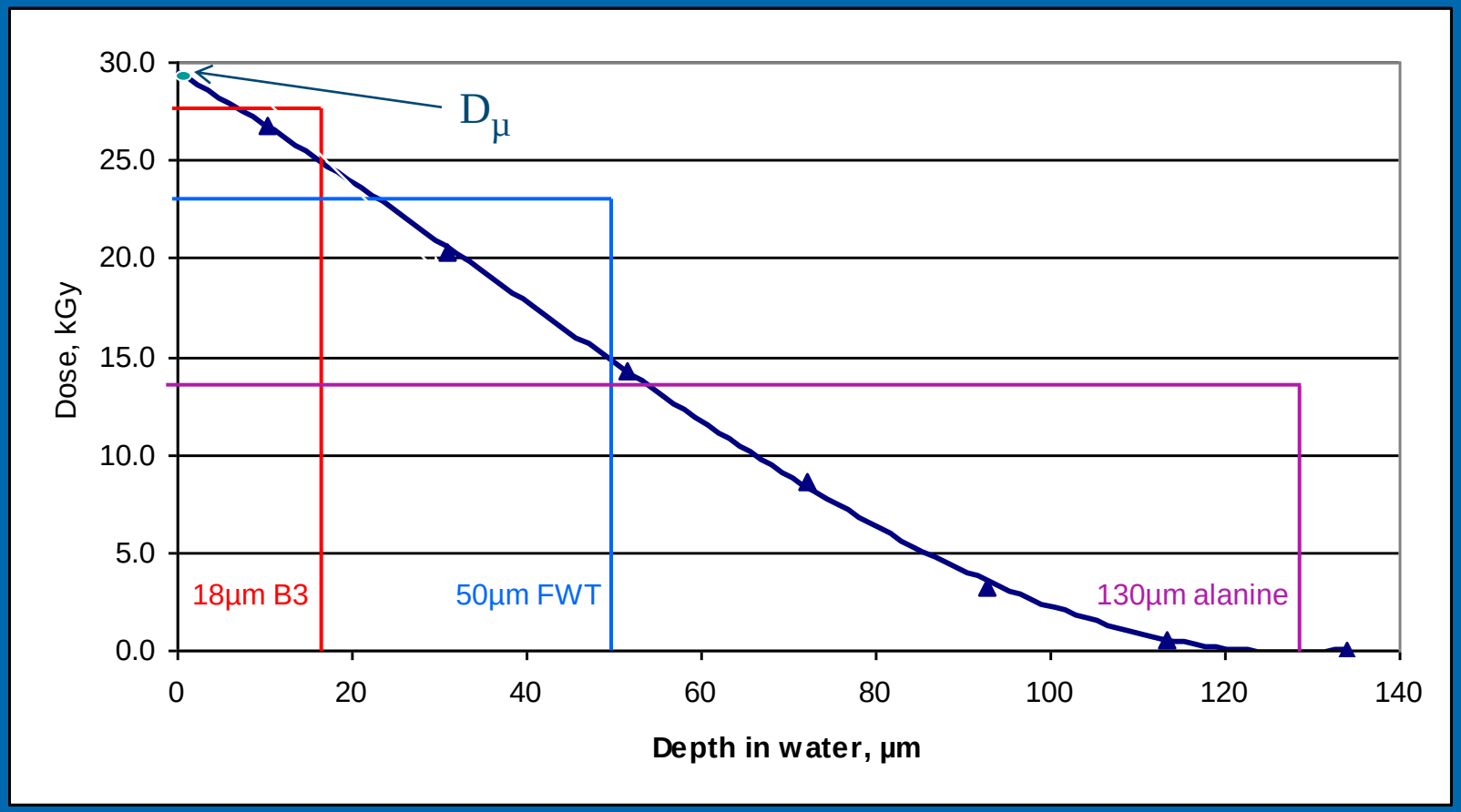


Low Energy Validation

- Concept of D_{μ}

Different thickness dosimeters calibrated at
high energy e-beam or gamma
will measure different doses
when irradiated at low energy e-beam

Concept of D_μ



Low Energy Validation

- Concept of D_μ

D_μ is the dose in the first micron of the absorbing material.

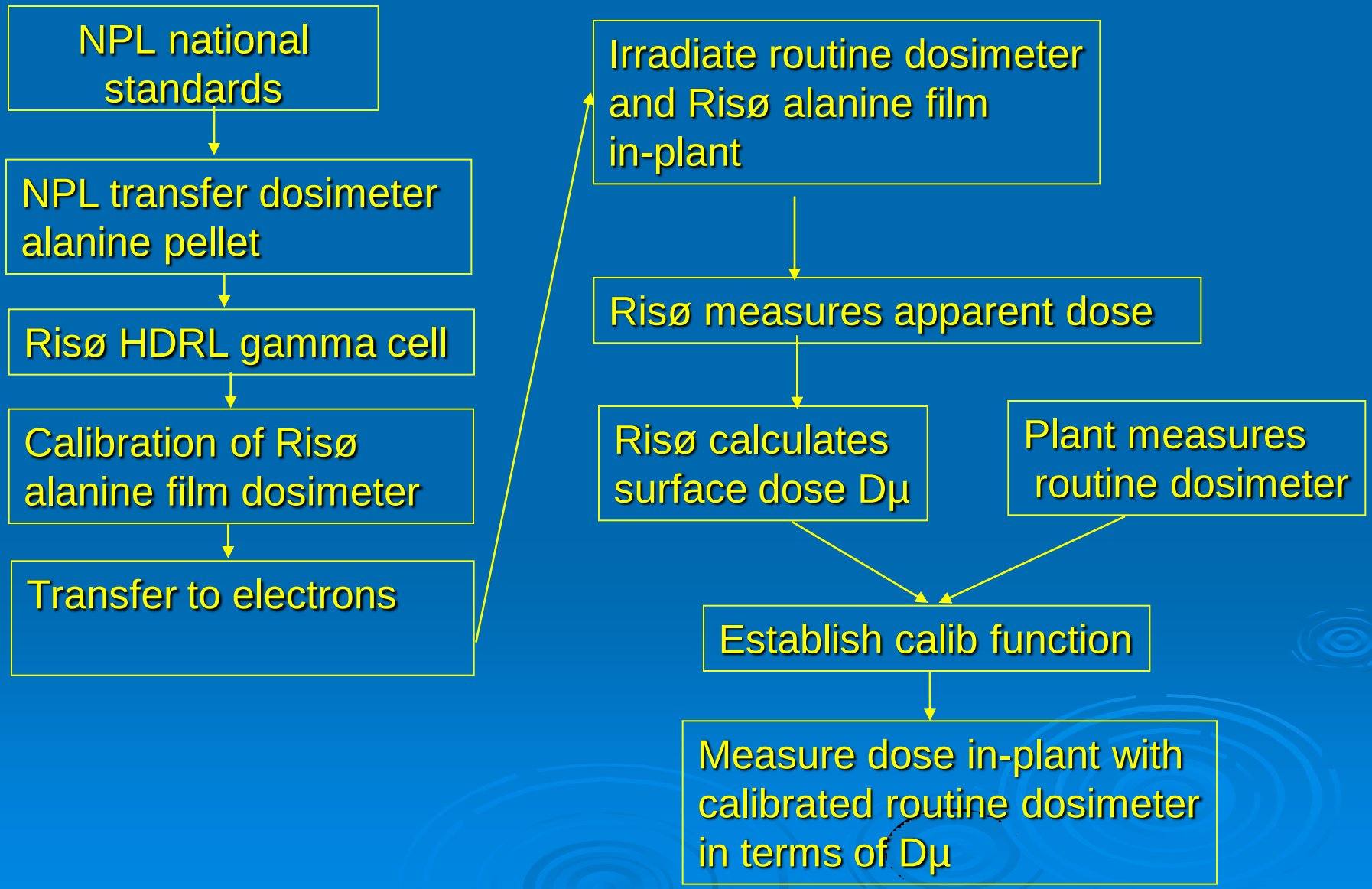
Different thickness dosimeters measure the same D_μ value.

Routine dosimeters are calibrated in terms of response as a function of D_μ

D_μ is evaluated by the calibration laboratory.

The user of the routine dosimeter does not need to evaluate D_μ

Traceability of Low-Energy Electron Dose Measurement using D_μ concept



Low Energy Validation

2. Measurement uncertainty must be known.

An uncertainty budget must be established.

This is an evaluation of all uncertainty components related to the measurement of dose at the plant.

- starting with the uncertainty of the national standard and moving through each step of the traceability chain.

The uncertainty components are summed in quadrature.

Low energy Validation

3. The irradiation process must be validated.

Validation principles are described in

ISO 11137, part 1 – Sterilization of Health Care Products – Radiation – Requirements for the Development, Validation and Routine Control of a Sterilization Process for Medical Devices

(1. Scope)

Note: Although the scope of this part of ISO 11137 is limited to medical devices, it specifies requirements and provides guidance that may be applicable to other products and equipment.

Major content of ISO 11137-1:

- Equipment characterization (6)
- Product definition (7)
- Process definition (8)
- **Validation (9)**
  - **Installation Qualification (9.1)**
  - **Operational Qualification (9.2)**
  - **Performance Qualification (9.3)**
- Routine monitoring and control (10)

EN ISO 11137-1

9.1 Installation Qualification - IQ

- Agreement supplier – customer

A.9.1 IQ is carried out to demonstrate that the sterilization equipment and any ancillary items have been supplied and installed in accordance with their specification.

Whether or not data are “in accordance with their specification” depends on agreement between supplier and user.

Measurements are often the same as for Operational Qualification.

Low Energy Validation

- 9.2 Operational Qualification - OQ
  - "OQ shall demonstrate that the irradiator, as installed, is capable of operating and delivering appropriate doses within defined acceptance criteria."
  - - provides baseline data to show consistent operation of the facility.

OQ Electron beam

- Characteristic parameters to be measured

  - dose distribution reference product
  - beam width
  - energy
  - dose as function of speed, current, scan width
  - beam spot
  - process interruption

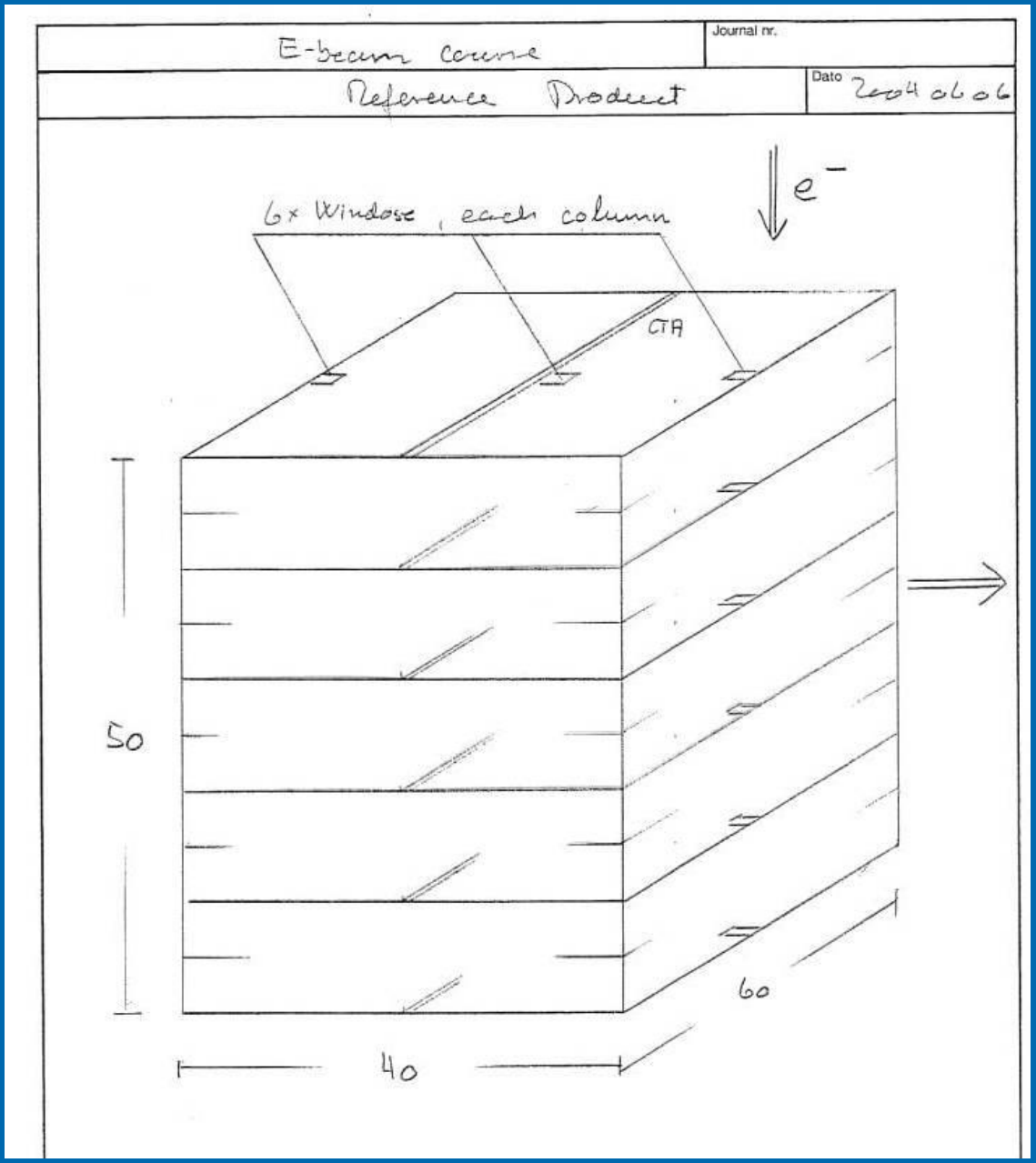
- Ref: ISO / ASTM 51649
  ISO / ASTM 51818

OQ E-beam cont..

Reference product for high energy E-beam

Placement of dosimeters in reference product

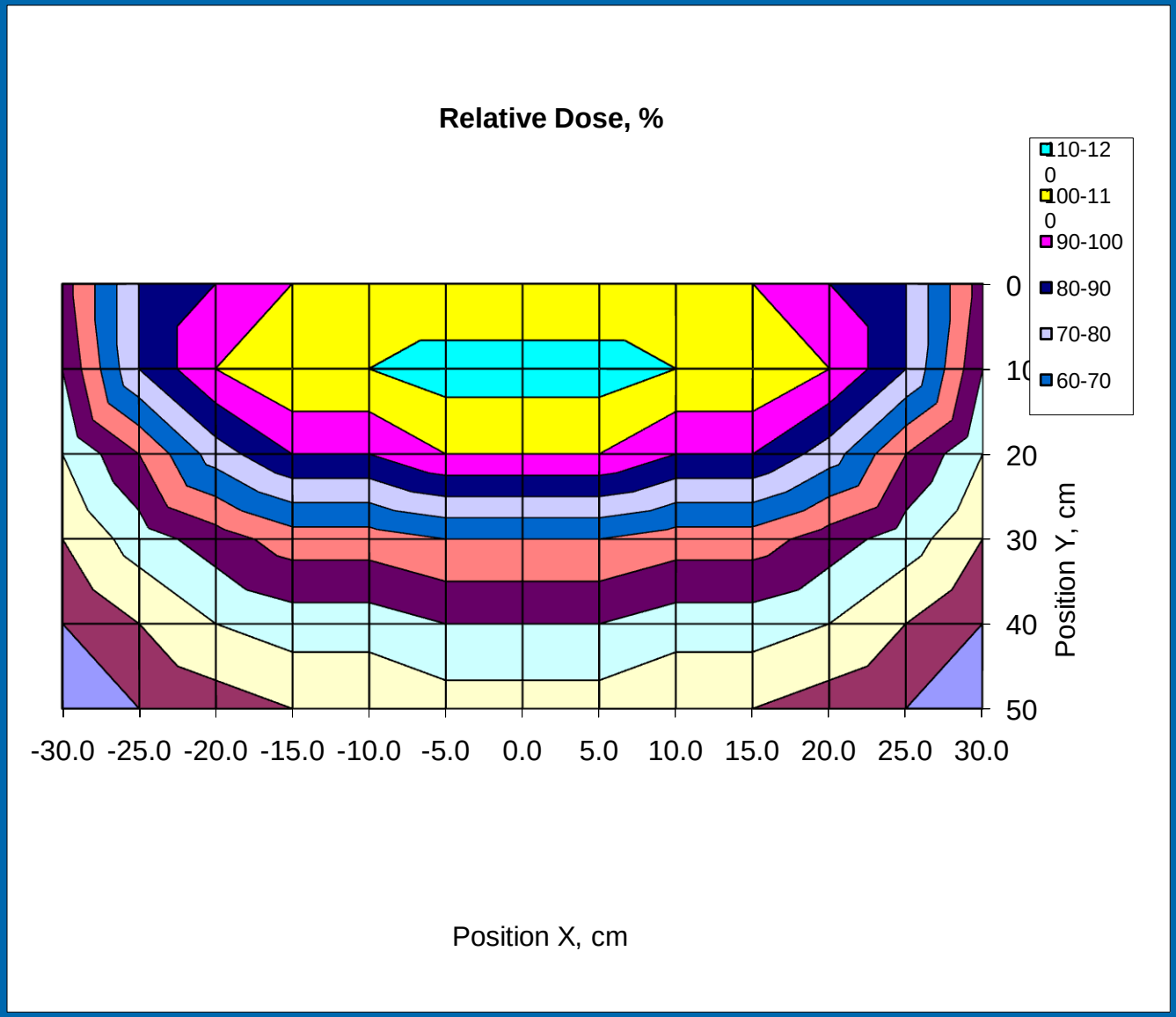
Ref product:
Polystyrene
$\rho = 0.1\ g/cm^3$



OQ E-beam cont..

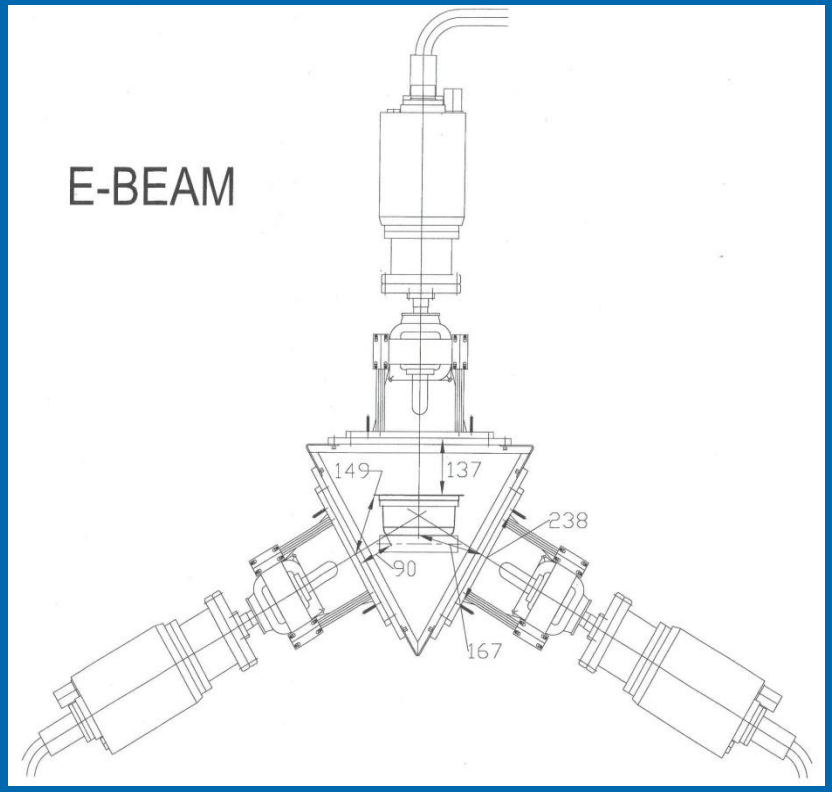
Dose Distribution in high energy e-beam reference product

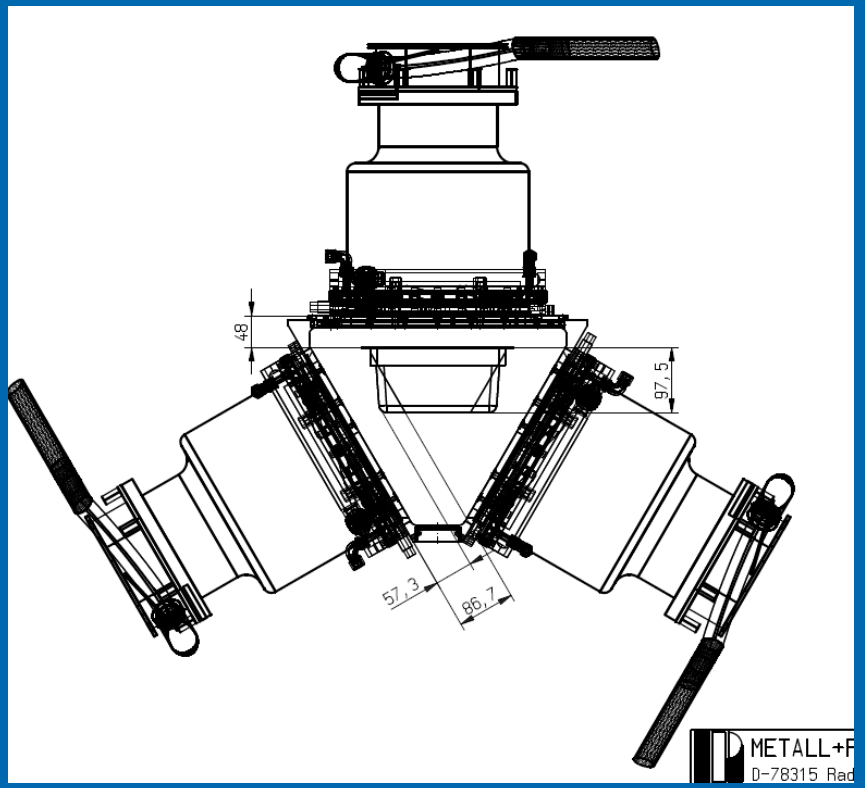
Limits for acceptable variations can be defined.



OQ E-beam cont..

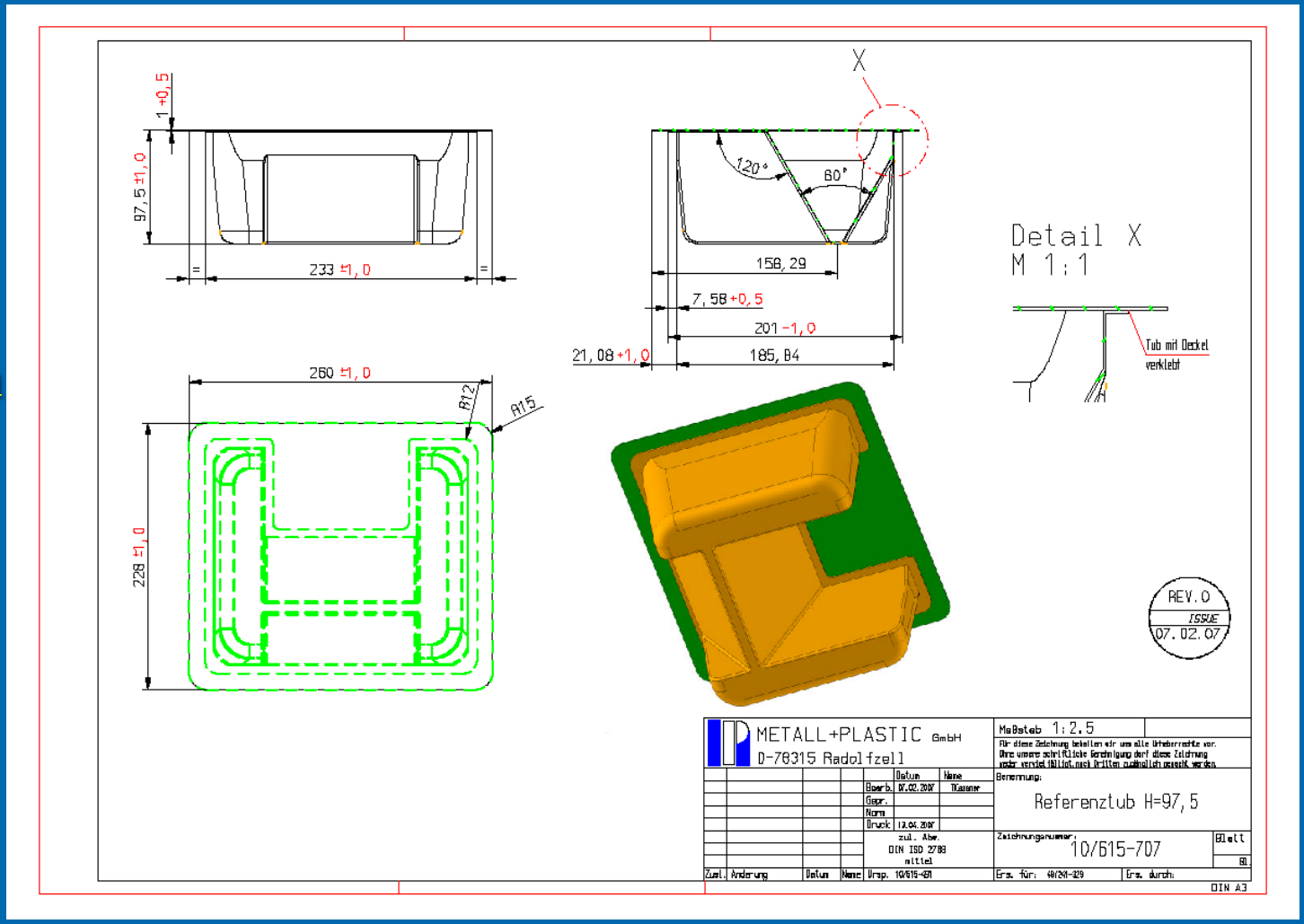
Low energy e-beam installations for sterilization





OQ E-beam cont..

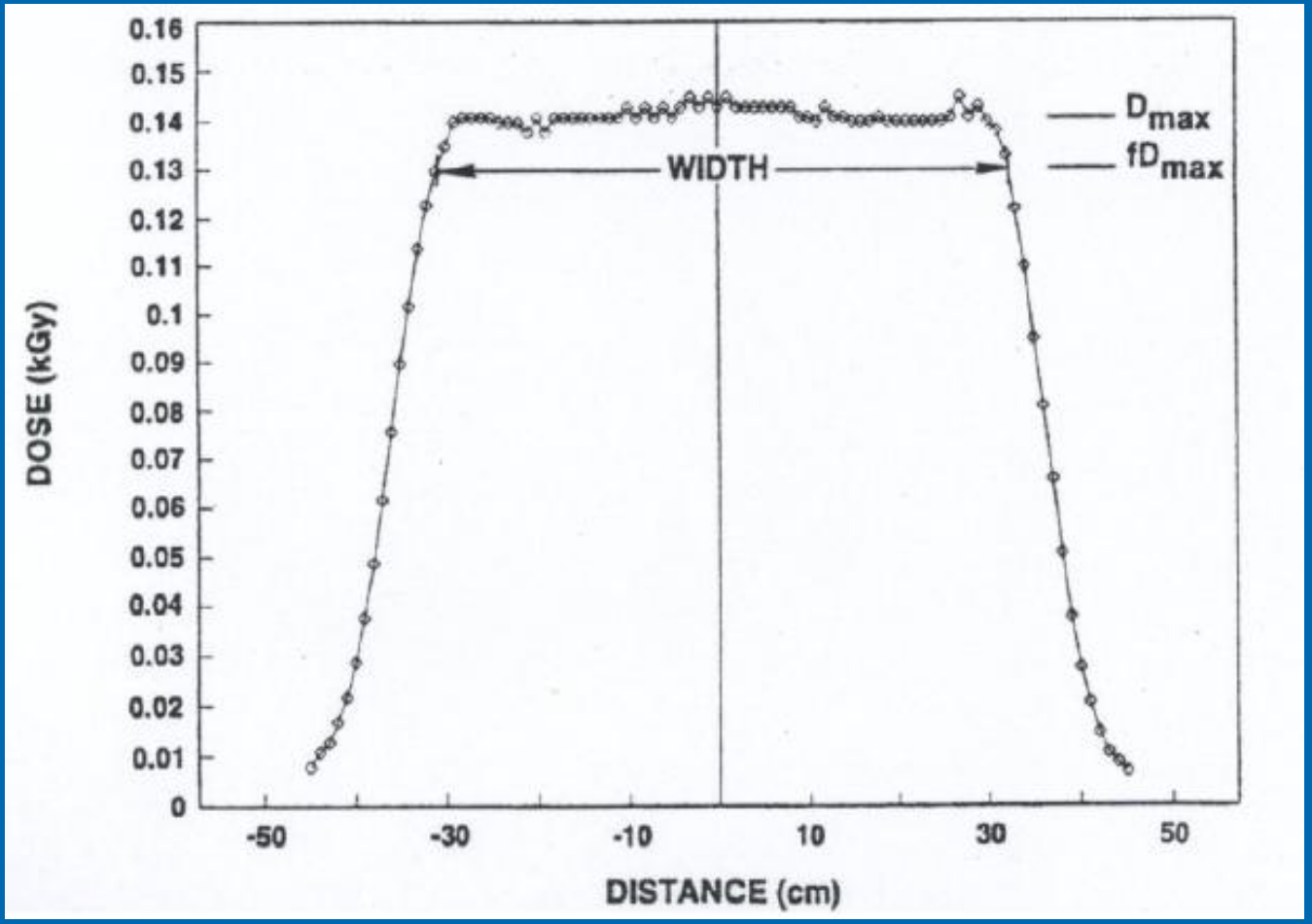
Reference product for low energy electron beam tunnels



OQ E-beam cont..

Beam width measurement

Limits for acceptable variations can be defined.



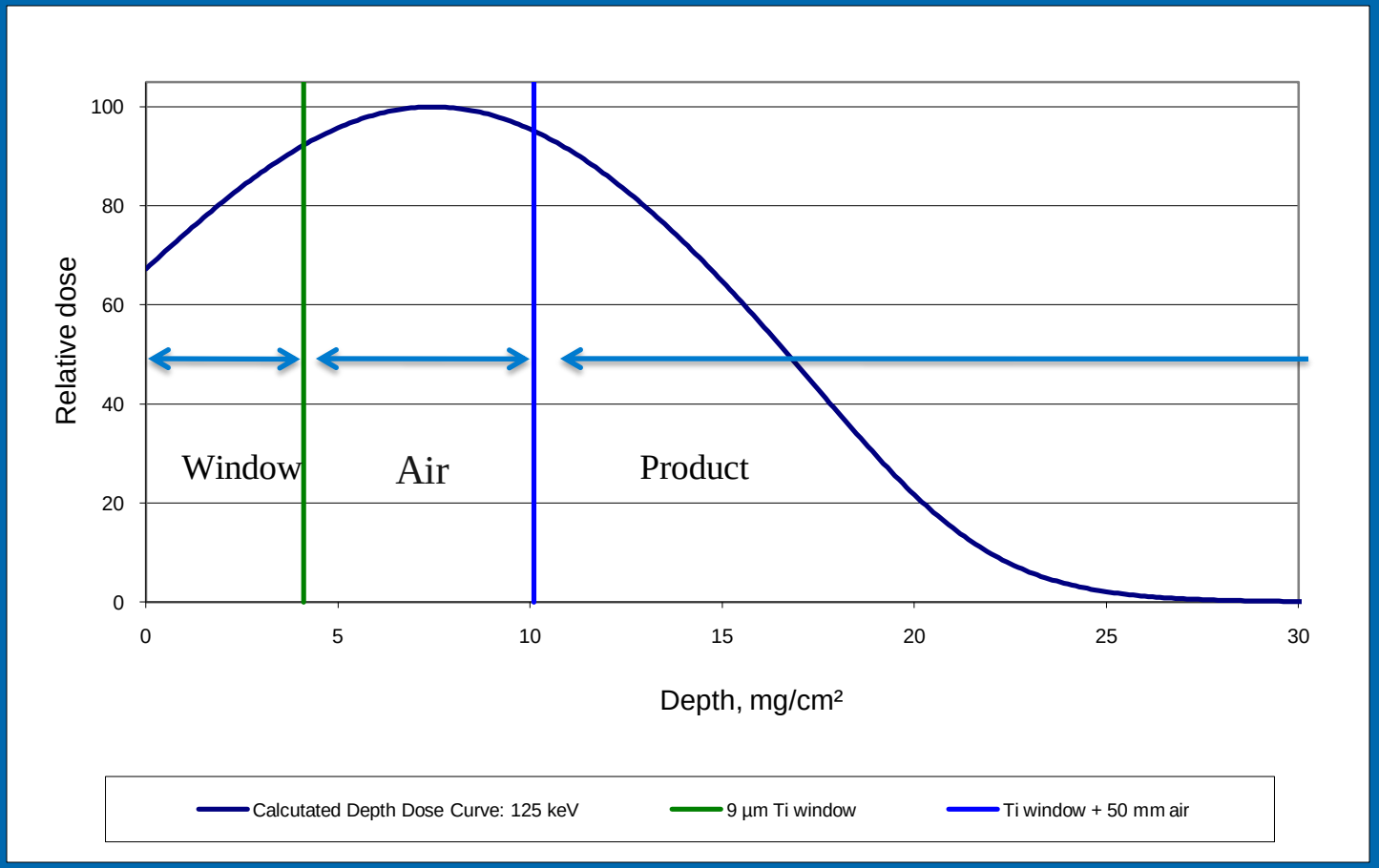
OQ E-beam cont..

Depth dose measurement

125 keV

Window:
9 µm Ti

Air:
50 mm



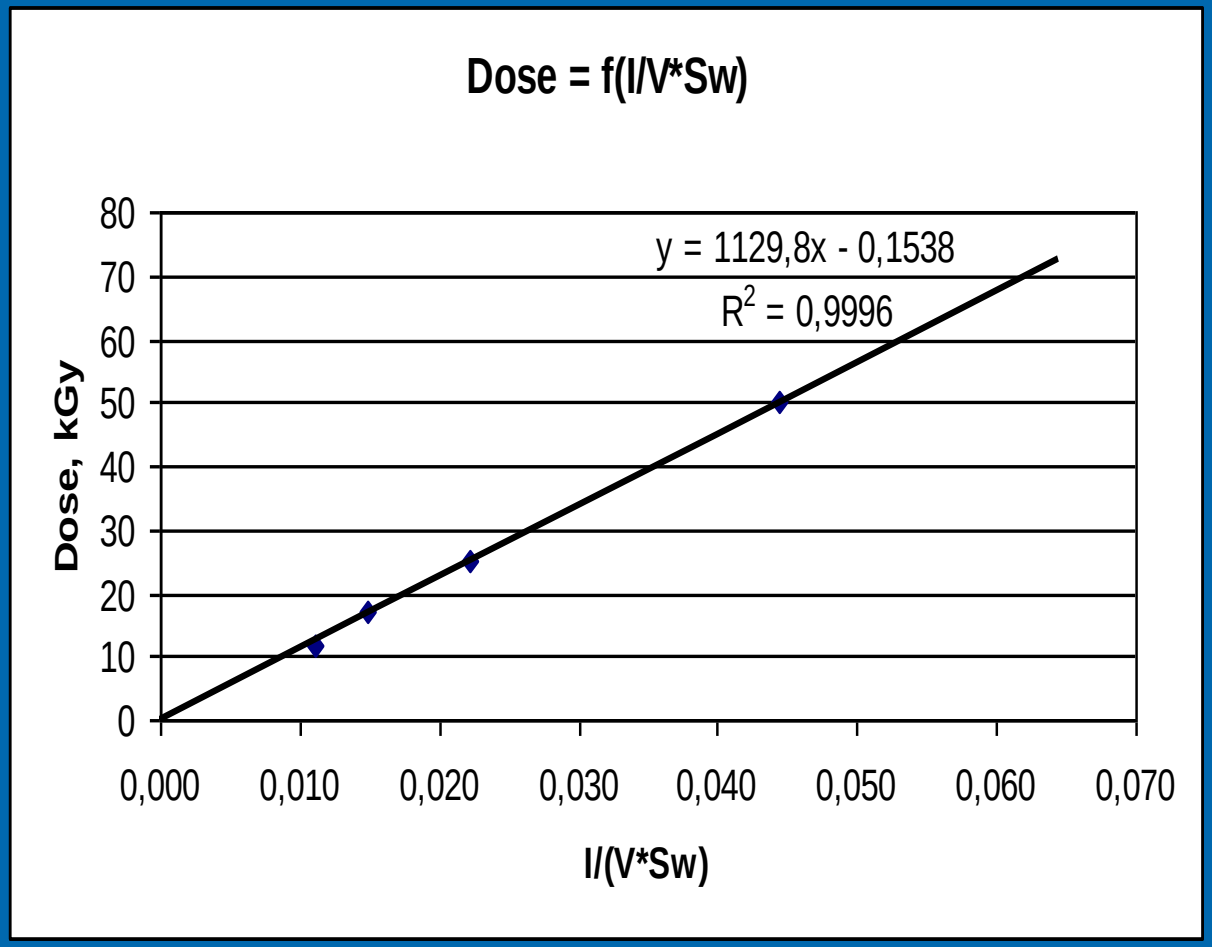
OQ E-beam cont..

Dose as a function of

- beam current
- conveyor speed
- scan width

Straight line through (0,0)

Slope of line = k



Low Energy validation

9.3 Performance Qualification – PQ

Dose mapping of real product in order to

- identify the location and magnitude of the minimum and maximum dose and
- determine the relationships between the minimum and maximum dose and the dose(s) at the routine monitoring position(s).

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Dose map example

Risø B3 dosimeters placed on tub for an isolator in a filling line.

Low energy Validation

Sect 10: Routine Process Control

- show that the process runs within specifications

"Dosimeters shall be placed at the predetermined routine monitoring position(s).

Following irradiation, the dosimeters shall be measured and the results recorded and analysed"

Low Energy validation

GEX DoseStix dosimeters placed on reference tub for routine dose measurement

Low Energy Validation

Concluding remarks

The principles of validation for high energy (1 - 10 MeV) irradiation can be applied in low energy (100 – 300 keV) irradiation.

The Dμ concept must be used to obtain measurement traceability.