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Risø HDRL Technical note E3

Evaluation of dose map for irradiation at verification dose D_{ver}.

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The standard for radiation sterilization of medical devices EN / ISO 11137, part 2 specifies how product samples shall be irradiated at verification dose, D_{ver}, in connection with establishing, substantiating or auditing a dose for sterilization, D_{ste}. The procedure used for sterilization dose establishment for Method 1 as described in the standard is used as an example in this note. The same principles can be applied for Method 2, and Method VD_{max}.

EN / ISO 11137, part 2:
7.2.5.2
Irradiate the product items at the verification dose. Determine the dose. If the highest dose to the product items exceeds the verification dose by more than 10 %, and the sterilization dose is to be established using Method 1, the verification dose experiment shall be repeated. If the arithmetic mean of the highest and lowest doses delivered to product items is less than 90 % of the verification dose, the verification dose experiment may be repeated. If this mean dose is less than 90 % of the verification dose and, on performance of the tests of sterility, acceptable results are observed (see 7.2.6.1), the verification experiment need not be repeated.

In case of gamma irradiation it is normal to measure the delivered doses during irradiation of product samples, and obtain maximum and minimum doses to product samples. In case of e-beam irradiation dose mapping can be carried out in order to determine a monitoring dose D_{mon} that shall be used for irradiation of product samples in order irradiate these at D_{ver}. Measurement uncertainties must be taken into account in order to determine the required D_{mon} and to fulfill the requirement above.

Electron accelerator irradiation of product samples is usually carried out in a geometry that is designed to minimize the difference between maximum and minimum dose to product. The geometry is often selected to be single layer of product samples placed between two 3-mm polystyrene plates. This package is irradiated from two sides. The polystyrene plates serve to scatter the e-beam leading to a more uniform dose distribution and also to limit backscatter from metal components of conveyor or carrier.

Dose mapping is usually carried out by irradiating with doses that are conveniently measured, and based on the results a required monitoring dose D_{mon} for irradiation of product samples at D_{ver} can be calculated.

For e-beam irradiation it can be expected that there is significant difference between maximum and minimum doses, even within a single product sample. It might therefore be needed to place several dosimeters at the product samples in order to obtain valid dose map results. The results of the dose map can be expressed in terms of average minimum dose D_{min} and average maximum dose D_{max} at each of the individual dosimeter positions accompanied by their respective uncertainties. The minimum dose D_{min} and the maximum dose D_{max}, which shall be considered with respect to the requirements of the standard, are the lowest and the highest of the individual average minimum and maximum doses, respectively.

The mean dose is calculated as $D_{mean} = (D_{max} + D_{min}) / 2$.

The required D_{mon} should be determined to be in a range that will allow D_{mean} to be more than 90% of D_{ver}, while D_{max} does not exceed D_{ver} by more than 10%.

In order not to overdose product samples, the upper 95% confidence limit of D_{max} (DU) is used to calculate the maximum limit of D_{mon}.

The maximum limit of D_{mon} is calculated as

$$D(_{mon,max}) = D(_{mon,\ meas})*D_{ver}*1.1 / DU$$

The minimum limit of D_{mon} is calculated as

$$D(_{mon,min}) = D(_{mon,\ meas})*D_{ver}*0.9 / D_{mean}$$

An Excel file is attached that shows an example for calculations of the required range of monitor dose D_{mon}.

RISØ HIGH DOSE REFERENCE LABORATORY

Template 05 (1) Risø B3 / RisøScan

Date: 2013.10.17

Operator: tk

Report number: 13R-xx
Customer: I.D.
Product: product i.d.
Facility E-beam, 2-sided
Irradiation for Dver
Irradiated between PS plates

Env. Temp: 22
Env. R.H.: 37%

RisøScan Data

Alan. Ref.AR602/1140		14.84	0.993 Correction factor
	B3 ref	14.95	

BOX 1

	D(min)		D(max)	
	Uncorrected	Corrected	Uncorrected	Corrected
1.1	25.5	25.3	28.2	28.0
1.2	27.4	27.2	29.8	29.6
1.3	26.8	26.6	29.5	29.3
1.4	26.1	25.9	30.0	29.8
2.1	25.3	25.1	28.1	27.9
2.2	26.2	26.0	29.2	29.0
2.3	25.8	25.6	29.5	29.3
2.4	25.4	25.2	29.9	29.7
3.1	24.5	24.3	28.1	27.9
3.2	25.8	25.6	29.4	29.2
3.3	26.3	26.1	30.2	30.0
3.4	25.8	25.6	30.4	30.2
4.1	25.7	25.5	27.7	27.5
4.2	25.6	25.4	29.3	29.1
4.3	26.7	26.5	29.9	29.7
4.4	26.0	25.8	30.9	30.7
5.1	25.7	25.5	28.6	28.4
5.2	26.6	26.4	29.0	28.8
5.3	26.4	26.2	29.8	29.6
5.4	26.6	26.4	29.6	29.4

B3 ref measurement	
1	15
2	14.9
Average	14.95

Dmon, requested 2 x	15	kGy
Dmon, measured 2x	14.8	kGy

Average	**D(min)**			**D(max)**		
position #	Average kGy	s.d. kGy	%	Average kGy	s.d. kGy	%
1	25.2	0.5	2.0	27.9	0.3	1.1
2	26.1	0.7	2.7	29.1	0.3	1.0
3	26.2	0.4	1.5	29.6	0.3	1.0
4	25.8	0.4	1.7	29.9	0.5	1.7

Dmin	25.2	0.5	2.0			
			Dmax	29.9	0.5	1.7
D(mean)	27.5			D(max)/Dmin		1.19

	Uncertainties (k=1), %			
	D(min)	D(max)	Dmon	Estimated from
Dose map	2.0	1.7		this dose map
Calibration	2.1	2.1		calibration
			2.3	facility info
Facility var.	1	1		facility variation with Dmon measured
at k = 1, %	3.8	3.7		
at k = 1, kGy	0.96	1.10		

Upper 95% conf. Limit of D(max), DU	32.1	kGy
Dver, kGy	7.0	Insert value based on bioburden data

Dmon(max), 2x	**3.55**	**kGy**	Dmon(max) = D(mon, meas)*Dver*1.1/DU
Dmon(min) 2x	**3.38**	**kGy**	Dmon(min) = D(mon, meas)*Dver*0.9/Dmean
Required Dmon = (Dmon(max)+Dmon(min)) / 2 =	**3.47**	**kGy**	

The maximum dose to product may be 10% greater than the verification dose
The mean dose to product may be 90% of the verification dose