Validation of the Gamma Irradiation of Margron femoral implants – Dosimetry validation

Prepared by:	**Date:** 18/2/04	**Position:** Manufacturing Engineer Vimek P/L
Checked by:	**Date:** 18/2/04	**Position:** Production Manager Vimek P/L
Approved by:	**Date:** 18/2/04	**Position:** Chief Technology Officer Portland

1 Purpose

This document is intended to define the requirements for dosimetry validation of the gamma irradiation of the Margron femoral implant range.

2 Scope

This document covers the requirements of ISO 11137:1995 paragraph 6.4 – process qualification.

Implants covered by this validation process include all Stems, Modular Extension Components and Necks in the Margron THR range as contained in drawings SGHP-001, SGHP-002, SGHP-003 and SGHP-004.

3 References

- ISO 11137:1995 – Sterilization of health care products – Requirements for validation and routine control – Radiation sterilization
- SPEC-002 – Manufacture – Implants
- SGHP-001 – Femoral Stem Component Set and Details
- SGHP-002 – Femoral Neck Component Set and Details
- SGHP-003 – Modular Extension Component Set and Details
- SGHP-004 – Femoral Neck Component XYZ Set and Details

4 Description of product.

There are 3 broad ranges of device covered in this document.

4.1 Necks

Neck implants range from size X as the smallest up to size C+6 as the largest. These devices are manufactured from Cobalt Chrome alloy to either ASTM-F-1537 or ASTM-F-799. The masses vary from 74 grams up to 210 grams. See appendix A for the entire range.

All necks are packaged in the same package – a peelable pouch nested in foam, contained in two Tyvek lidded PETG trays with a cardboard outer box. The dimensions of the outer box are 145mm x 145mm x 48mm.

This gives an overall range of individual package densities from 0.073 to 0.208.

4.2 Stems

Stem implants range from size X+0 as the smallest size increasing in diameter in increments of 2mm up to size 7+0. Each size also has a range of lengths from +0cm up to +6cm. The masses vary from 43 grams up to 706 grams (This assumes that the range does not include implants above 7+2). See appendix A for the entire range.

Stems are packaged in two different sized trays, dependant on length and diameter (see Vimek work instruction 6470094).

The packaging system is similar for each tray size, comprising a peelable pouch nested in foam, contained in two Tyvek lidded PETG trays with a cardboard outer box. The dimensions of the short outer box are 225mm x 103mm x 47mm. The dimensions of the long outer box are 307mm x 108mm x 55mm.

This gives an overall range of individual package densities from 0.039 to 0.393.

4.3 Modular Extension Components (MECs)

MEC implants range from size XX6 as the smallest size increasing in diameter CC7. The masses vary from 79 grams up to 339 grams. See appendix A for the entire range.

MECs are packaged in the short tray used for the short stems. The packaging system is the same, comprising a peelable pouch nested in foam, contained in two Tyvek lidded PETG trays with a cardboard outer box. The dimensions of the short outer box are 225mm x 103mm x 47mm.

This gives an overall range of individual package relative densities from 0.073 to 0.311.

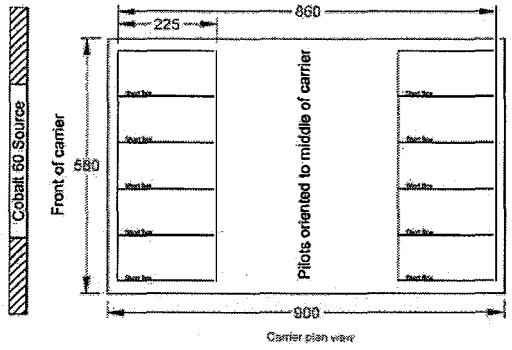
5 Loading Pattern

Steritech, Wetherill Park, is the contract steriliser used in Sydney. They have carriers with plan form dimensions of 580mm wide by 900mm deep and a height of 2330mm (see Appendix B).

The loading patterns are as follows:

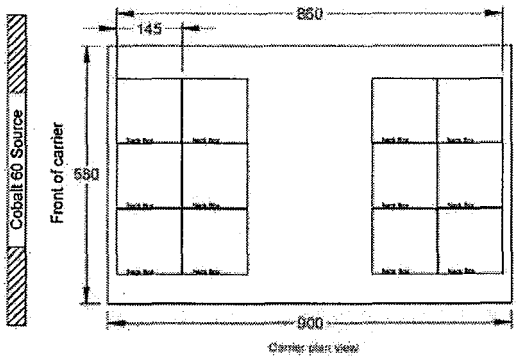
5.1 Stems and MECs (long and short trays)

Stems and MECs will be oriented as shown below, with the axis perpendicular to the source and the proximal ends facing the outside of the carrier.



5.2 Necks

The neck implants should not be affected by orientation like the stem and module implants, given that they do not have any cavities. Therefore, the implants may have random orientation in their trays and can be distributed over the area of the carrier as shown below:



6 Loading Containers

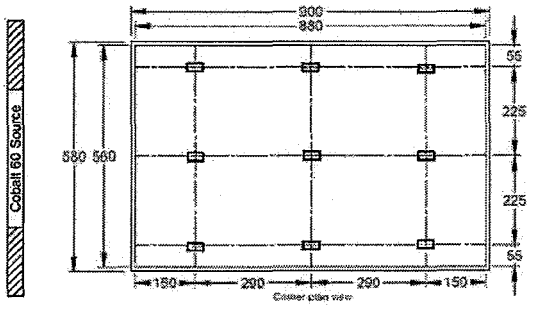
Cardboard boxes 543mm x 430mm x 275mm (internal dimensions) will be used to package the devices for sterilisation. These are designed to stack 2 per level on the carriers and maintain orientation. Each box will allow stacking of implants to a level of 5 high.

Boxes will be stacked only 2 high in each carrier.

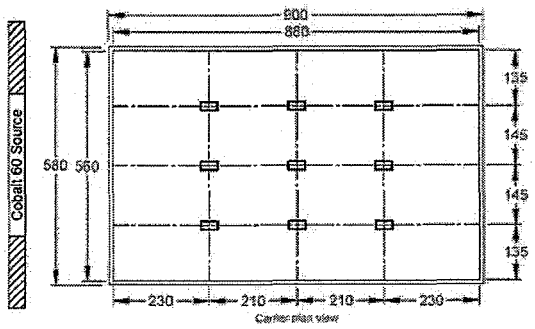
7 Dosimetry Mapping

Each arrangement of implants must be validated for adequate exposure and uniformity of dose at the beginning of processing in that arrangement and every time that the source is changed.

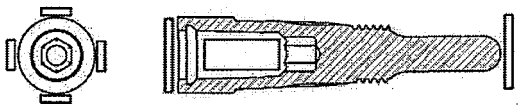
Dosimetry will, as a minimum, require a layer of cardboard to be laid between the boxes. This cardboard layer will have 9 dosimeters distributed for stems as shown below:



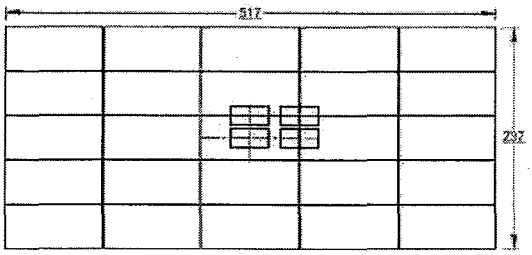
and for necks as shown below:



In addition, for the stem, a number of dosimeters may be placed around and inside the bore of a CoCr sample as shown below.



On the front face of the most dense box, a dosimeter pattern will be laid out as follows



Elevation view of front of carrier

8 Dose

From preliminary investigations, the probable dose uniformity ratio (DUR) is 1.18. Given

$$DUR = Dose_{max} / Dose_{min}$$

then to guarantee a minimum dose of 25kGy, the minimum dose must be calculated

$$\begin{aligned} Dose_{max} &= Dose_{min} \times DUR \\ &= 25 \times 1.18 \\ &= \underline{29.5kGy} \end{aligned}$$

The contract steriliser will guarantee a dose between 100% and 200% of the required minimum dose.

9 Interpretation of Results

The results will be reviewed on return from the contract steriliser.

The doses on the front face of the carrier will be reviewed to see if there are any areas on the face that may be affected by attenuation. Using this data, a range of locations for routine dosimeters will be defined.

The doses around and inside the implants will be reviewed for the worst case attenuation for the implant. Minimum dose requirements for future batches will be based upon this figure.

10 Results, December 2003

10.1 Stems and MECs

On 16 December, 2003 eight boxes of implants were irradiated at Steritech to a minimum dose of 30kGy.

The implants were placed into boxes in descending order of density. That is, box 1 contained the most dense implant packages and box 7 and box 8 contained the least dense implant packages. Box 8 only contained 7 implants and one sample, the rest of the 25 positions being taken up using a cardboard filler.

The boxes were placed in two carriers. Carrier one contained Box 1 and Box 2 on the bottom and Box 3 and Box 4 on top. Carrier two contained Box 5 and Box 6 on the bottom and Box 7 and Box 8 on top.

A routine dosimeter, placed at the front and lowest point of the load in the carriers, registered 30.3 kGy.

10.1.1 Stem Sample Dosimetry

The following table gives the dose registered by the dosimeters placed on samples as shown in paragraph 7.

Sample 1 - Box 1 – Size 6+6

Position	Dose
Inside bore	24.1
On top of implant	27.2
Right side of implant	25.6
Bottom of implant	26.8
Left side of implant	26
Proximal end	28
Distal end	30.4

Max	30.40
Min	24.10
DUR	1.26
$DUR_{\text{Routine dosimeter reference}}$	1.25

Sample 2 – Box 3 – Size 5+0

Position	Dose
Inside bore	27.1
On top of implant	28.3
Right side of implant	26.8
Bottom of implant	28
Left side of implant	27.7

Max	28.30
Min	26.80
DUR	1.06
$DUR_{\text{Routine dosimeter reference}}$	1.13

Sample 3 – Box 5 – Size 4+0

Position	Dose
Inside bore	27
On top of implant	29
Right side of implant	27.1
Bottom of implant	29
Left side of implant	27.7

Max	29.00
Min	27.00
DUR	1.07
DUR $_{\text{Routine dosimeter reference}}$	1.12

Sample 4 – Box 7 – Size 1+5

Position	Dose
Inside bore	27.5
On top of implant	28.4
Right side of implant	28.8
Bottom of implant	29.2
Left side of implant	27.8

Max	29.20
Min	27.50
DUR	1.06
DUR $_{\text{Routine dosimeter reference}}$	1.10

Sample 5 – Box 4 – Size 3+2

Position	Dose
Inside bore	28
On top of implant	28.7
Right side of implant	28.1
Bottom of implant	29.3
Left side of implant	28.8

Max	29.30
Min	28.00
DUR	1.05
DUR $_{\text{Routine dosimeter reference}}$	1.08

Sample 6 – Box 8 – Size 3+0

Position	Dose
Inside bore	30.4
On top of implant	30.2
Right side of implant	32.1
Bottom of implant	30.6
Left side of implant	31.8

Max	32.10
Min	30.20
DUR	1.06
DUR $_{\text{Routine dosimeter reference}}$	1.00

Note that box 8 only had seven out of 25 spaces occupied by implants.

10.1.2 Inter-Box Dosimetry

A layer of cardboard with dosimeters attached was laid on top of each pair of boxes. The doses registered by these dosimeters was as follows:

Carrier 1

On top of box 1/2		
Back of carrier		
36.6	30.4	35.9
28	37.7	36.7
34.7	35	29.3
Front of carrier		

DUR box 1/2	1.35
Max	37.7
Min	28.0
Average	33.81

On top of box 3/4		
Back of carrier		
32.5	34.5	29.4
32.6	35.1	37.1
31.1	33.4	37
Front of carrier		

DUR box 3/4	1.26
Max	37.1
Min	29.4
Average	33.63

Carrier 2

On top of boxes 5/6		
Back of carrier		
37.8	36	34.6
31.9	29.9	37.2
35.7	29.5	28.5
Front of carrier		

DUR box 5/6	1.33
Max	37.8
Min	28.5
Average	33.46

On top of boxes 7/8		
Back of carrier		
35.4	37.4	37.8
35.4	36.7	35.8
32.8	35.8	30.5
Front of carrier		

DUR box 7/8	1.24
Max	37.8
Min	30.5
Average	35.29

The doses from carrier 1 range from 28 kGy up to 37.7 kGy. The doses from carrier 2 range from 28.5 kGy up to 37.8 kGy.

10.1.3 Box 1 Face dosimeters

A cluster of 4 dosimeters was placed on the front of box 1 in the pattern shown paragraph 7. These registered between 30.5 and 31.1. Comparing these results

with the routine dosimeter result of 30.3, there is only a small rise in dose up the face of the box.

10.1.4 Comments

As can be seen from all the above results, the critical area for attenuation of the gamma rays is in the bore of the large implants (Size 6+6 stem was the largest tested).

The doses received by the inter-box dosimeters are higher than the routine dosimeter reading. There was no recognisable pattern to the variations, except that the layer above boxes 7/8 had a higher average dose, probably due to the space in the box above the implants.

The dosimeters on the face of Box 1 were very consistent and correlated well with the routine dosimeter.

Comparing the dose on the routine dosimeter to the dose registered in the bore of the size 6+6 stem, the Dose Uniformity Ratio (compared with the routine dosimeter) was 1.25. Therefore the minimum dose required as measured by the routine dosimeter is 1.25 x 25kGy, or 31.3kGy.

11 Results, January 2004

11.1 Necks

On 28th of January, 2004 two and a half boxes of neck implants were irradiated at Steritech to a minimum dose of 32kGy.

The implants were placed into boxes in no particular order. There were 55 size B, B+4 or BA necks, 14 AZ necks and 7 Y necks.. There were 29 implants and 1 dosimetry sample each in boxes 1 and 2. Box 3 contained the remaining 18 implants and 1 dosimetry sample – the rest of the box being filled with empty trays.

The boxes were placed in one carrier with Box 1 and Box 2 on the bottom and Box 3 on top. A box of short tray stems was included as part of the load on top of Box 2.

5 boxes of short stems were sterilised in the same batch.

A routine dosimeter, placed at the front and lowest point of the load in the carriers, registered 31.4 kGy.

11.1.1 Neck Sample Dosimetry

Dosimeters were placed around three samples in similar style to the illustration in paragraph 7. They were placed around the distal taper. The following tables give the doses registered by these dosimeters.

The Routine Dosimeter registered 31.4kGy.

Sample 1 - Box 1 – Size C sample

Position	Dose
On top of implant	33.2
Right side of implant	33.5
Bottom of implant	33.2
Left side of implant	32.6

Max	33.50
Min	32.60
DUR	1.03
DUR Routine dosimeter reference	0.96

Sample 2 – Box 2 – Size B sample

Position	Dose
On top of implant	31.9
Right side of implant	31.3
Bottom of implant	32.9
Left side of implant	32

Max	32.90
Min	31.30
DUR	1.05
DUR Routine dosimeter reference	1.00

Sample 3 – Box 3 – Size BA sample

Position	Dose
On top of implant	32.5
Right side of implant	31.4
Bottom of implant	31.6
Left side of implant	29.7

Max	32.50
Min	29.70
DUR	1.09
DUR Routine dosimeter reference	1.06

11.1.2 Inter-Box Dosimetry

A layer of cardboard with dosimeters attached was laid underneath each pair of boxes. The doses registered by these dosimeters was as follows:

Carrier 1

Underneath box 1/2		
Back of carrier		
32.8	31.2	32
34.2	33.2	33.7
32.6	31	34.2
Front of carrier		

Underneath box 3/4		
Back of carrier		
35.4	34.3	35
36.9	35.9	37.4
36	34.5	35.2
Front of carrier		

DUR box 1/2	1.10	DUR box 3/4	1.09
Max	34.2	Max	37.4
Min	31.0	Min	34.3
Average	32.8	Average	35.6

The doses from carrier 1 range from 31 kGy up to 37.4 kGy.

11.1.3 Box Face dosimeters

A cluster of 4 dosimeters was placed on the front of box 1 in the pattern shown paragraph 7. These registered between 32.2 kGy and 32.8 kGy. Comparing these results with the routine dosimeter result of 31.4, there is a small rise in dose up the face of the box.

Box 2 and Box 3 also had dosimeters placed on the face in the centre. These dosimeters registered 32.6 and 33.7 kGy respectively. The dosimeter on box 2 was at the same height as the dosimeters on box 1 and records a similar dose. The dose increased slightly to the dosimeter on box 3.

11.1.4 Comments

The dosimeters on the face of Box 1 were very consistent and correlated well with the routine dosimeter. There was a rise of approximately 1kGy between the routine dosimeter and the dosimeters on box 1 and box 2, and then an additional 1kGy rise to the dosimeter on box 3.

The doses received by the inter-box dosimeters are higher than the routine dosimeter reading. There was no recognisable pattern to the variations, except that the layer below boxes 3/4 had a higher average dose, probably due box 3 only being half full and box 4 containing low density short stems.

The doses measured around the distal tapers of the neck implants were reasonably consistent, with the worst DUR being 1.09 with reference to the implant dosimeters and 1.06 with reference to the routine dosimeter. Therefore the minimum dose required as measured by the routine dosimeter is 1.06 x 25kGy, or 26.5kGy.

11.2 Stems

A set of 6 Size 6 stems was also sent through with the neck batch to determine the effect of processing the stems parallel to the plane of the source. The six stems were arranged in the following configuration (looking at the ends of the boxes):

Sample 6 - 6+2	Sample 2 - 6+5	Sample 5 - 6+4
Sample 3 - 6+6	Sample 4 - 6+5	Sample 1 - 6+6

Samples 1, 2 and 3 had one dosimeter placed up the bore and four dosimeters placed around the outside on the top and bottom and the left and right sides. The following tables give the doses registered by these dosimeters.

The routine dosimeter reading of 31.4kGy was used.

Sample 1 – Size 6+6

Position	**Dose**
Inside bore	29.6
On top of implant	28.7
Right side of implant	30.9
Bottom of implant	30.5
Left side of implant	30.3

Max	30.90
Min	28.70
DUR	1.08
DUR Routine dosimeter reference	1.09

Sample 2 – Size 6+5

Position	**Dose**
Inside bore	28.4
On top of implant	30.2
Right side of implant	30.2
Bottom of implant	29
Left side of implant	29.4

Max	30.20
Min	28.40
DUR	1.06
DUR Routine dosimeter reference	1.11

Sample 3 – Size 6+6

Position	Dose
Inside bore	29.3
On top of implant	29.8
Right side of implant	31.7
Bottom of implant	30.4
Left side of implant	30.9

Max	31.70
Min	29.30
DUR	1.08
DUR Routine dosimeter reference	1.07

11.2.1 Comments

The doses registered by the dosimeters in the bores of the size 6 implants are much closer to the outside doses when the implants were processed parallel to the source. The largest DUR comparing the stem dosimeters was 1.08 and the largest DUR compared against the Routine Dosimeter was 1.11. This compares favourably against processing the stem implants perpendicular to the source. The minimum dose required as measured by the routine dosimeter would be 1.11 x 25kGy, or 27.8kGy.

12 Conclusion

In this study, we have demonstrated that the minimum dose required for sterilising large stems when processed perpendicular to the source is 31.3kGy (measured on the routine dosimeter).

We have also demonstrated that the minimum dose required for sterilising necks is 26.5kGy (measured on the routine dosimeter).

The routine dosimeter location should remain where Steritech are already putting it, i.e., on the front side of the load at the bottom centre.

An additional investigation during a production run with significant quantities of the high density stems should be conducted to validate the use of 27.8kGy (measured on the routine dosimeter) as the minimum dose for stems processed parallel to the source. This investigation is currently being carried out under Portland Project PRPR012, but will be reported separately by mid March, 2004.

The following documents need to be reviewed in light of the above findings:

- SPEC-002 Specification – Manufacture Implants
- Vimek Work Instruction 64700095 – Sterilisation of MARGRON Implants
- GMP Agreement with Steritech

The dosage during production shall be controlled until the additional investigation is completed and these documents are updated.