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FIRST METHOD OF ISO STANDARD 11137 FOR TROFIN CAP BOTTLE STERILIZATION

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ABSTRACT

Trofin is a natural nutritional supply principally used for children and old people. The sterilization dose for gamma radiation of Trofin bottle cap was calculated according to the method I of ISO standard 11137. The dose setting validated method to reduce the sterilization dose is described. It was used an sterility assurance level (SAL) of 10^{-3} enough for this kind of product. The sterilization dose was reduced from 25 kGy to 15 kGy and as a result it is possible to increase product quantity irradiated.

INTRODUCTION

Ionizing radiation is an acceptable and reliable method of sterilizing disposable medical devices which has been available for 30 years. Microbial life is susceptible to the lethal effects of radiation but there is a substantial degree of variability in the susceptibility of microbial species to radiation [5].
Sterility is classically as an absolute condition, the complete destruction or removal of all forms of life. It is my view that the sterility of medical devices be assured to the extent that the probability of microbial contamination or survival is one in a thousand(10^{-3}) or less for each topical medical device an one in a million (10^{-6})or less for each implantable device[1].
The use of gammaradiation for radiosterilization of disposal medical devices takes,in the world,the biggest percentage in reference that work over the tecnology of radiation.This procedure applies to products.that because characteristic of ist components do not suffer any change under the action of radiations.Keeping Characteristics Which permit overcome the funtion they were designed for.
The ionizing radiations are widely used sterilize devices and disposal medical products, also exist one good experience for the treatment for radiation of medication,mostly in useless conventional sterilized process(heat ,filtration....).One of the most important point is the radiation dose,because certain unwished phisical and chemical changes which come along with the treatment,specially the 25kGy dose tradicionally used(Schuttler,et al,1978)[7].
Sterilization is an example of a process for which efficacy cannot be verified by retrospective inspection and testing of the product. It is important to be aware that exposure to a validated and accurately controlled sterilization process is not the only factorassociated with ensuring that the product is sterile and suitable for its intended use. Attention has to be given to the microbiological status of raw materials and/or components, the microbiological barrier properties of the packaging, and to the control of the environment in which the product is manufactured, assembled, packaged and stored[4].
According to Whitby y Gelda[1] figures had been made showing the dependence of the Bioburden and the sterility assurance level obtained, Is shown the dose required to get the sterility of those. Several Pharmacopoeia and EUCOMED[1] recommend 25 kGy as sterilization dose for medical products[3].
The subject of this work was according to METHOD 1 of ISO 11137 standard, determine the sterilized dose for Trofin cap.

MATERIALS AND METHODS

The acurracy in the stage of sterilization depends in the absortion dose.This is evaluated on relation with the time of exposition,the distance of the object in relation with the source, the distribution of doses in the radiation field with close relation to the minimun doses in the field and finally the determination of the probability that no survivor will exit ,This depend on the microorganisms initially in the product and this must be calculated with exact methods[2].

Validation of the methods of desadsortion of cell:

1.a-Desadsortion of cell by wash and filtration of the samples:

This experiment was developed using two different diluters :peptone water with tween 80 at 1 % and phosphate buffer (pH=7) with tween 80 at 2% .Done following this procedure:

- 5 caps were taken and sunk separately in 100ml erlenmeyers with diluters and shaken for 45 min at 75 rpm .
- Later the content of each erlenmeyer were filtered through Milipore (HA,0.45µm type).
- Membranes were put on plates with Agar Tryptone Soya at 32°C for 48 h. Later counting the colonies to determine the Bioburden.

1.b-Determine wash accuracy.

The following formula $\varepsilon=(X+Y+Z)/X \times 100$, **Where** X, Y, Z are the percentage of bioburden values obtained in each diluters ,after the first ,second and third wash of the caps.

2-Determination of the minimum sterilization doses according to method 1 ISO 11137 standard(doses stabilized using information of Bioburden):

2.a-Determination of Bioburden

- We took 30 caps selected from different batch ,which were separately sunk into 100 ml diluter selected as optimum(phosphate(pH-7) buffer)reinforced with tween 80 at 2 % and shaken 45 min at 75 rpm.
- Later the content of each erlenmeyer were filtered through Milipore (HA,0.45µm type).
- Membranes were put on plates with Agar Tryptone Soya at 32°C for 48 h. Later counting the colonies to determine the bioburden.

2.b- experiment checking sublethal doses

-taking the average values of bioburden per caps(average of bioburden of samples (ABS))the bioburden values was determined for each sample item portion(caps)(SIP)The following expression was used:

SIP = ABS x number of caps per lots

- Using the correspondent figures of standard ,Was selected the doses values of verification according to SIP values obtained.
- 100 samples were taken from the same lot and were irradiated with doses values of verification
- The sterilization test was done to the samples for 7 days at 32°C and 7 days ambient temperature from which we made the lecture
- The value of sterilization doses were selected from the previous figures for sterility assurance level 10^{-3} enough for this product .

3- Irradiation:

It was used a Co^{60} installation model PX-γ-30, located in Radiobiology and Irradiation Techniques Department belonging to Center of Applied Studies to Nuclear Development (CEADEN). The dose mapping of both installation and irradiation was made trough Fricke dosimetric system [6]. Batches were irradiated in the end baggage.

RESULT AND DISCUSSION

To validate the desabsortion methods two different diluters were used,reinforced with Tween 80.Taking in acount hidrofobic characters of the material in the caps.

The results obtained are shown in figure 1,2 and 3

Table 1. Validation of the method of desadsortion using peptone water which Tween 80 at 1%.

Erlenmeyer	Wash 1	Wash 2	Wash 3
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1	1
5	3	1	1

Efficiency of the wash: 42.86%

Table 2. Validation of the method of desadsortion using buffer phosphate (pH-7) which Tween 80 at 2%.

Erlenmeyer	Wash 1	Wash 2	Wash 3
1	4	1	0
2	1	0	0
3	0	0	0
4	0	0	0
5	0	0	0

Efficiency of the wash: 83. 33%

According to the data in figure 1 and 2 came to the conclusion that the best deluter was the phosphat(PH-7)with tween80 at 2% because tzhe efficency obtained was up to the recommended(80.0%).selecting this procedure as valid.Using this selected deluter,the bioburden was determine by filtration to 30 caps selected from defferent lots.The result are shown in figure 3

Table 3. Values of the bioburden for caps.

Cap No.	Ufc/ Cap	Cap No.	Ufc/ Cap	Cap No.	Ufc/ Cap
1	3	11	-	21	1
2	2	12	1	22	2
3	4	13	-	23	2
4	2	14	2	24	1
5	2	15	4	25	2
6	-	16	3	26	1
7	-	17	5	27	1
8	5	18	7	28	2
9	1	19	7	29	3
10	1	20	2	30	2

percentage of bioburden of the samples : 2.27 ufc/cap

For this bioburden value ,according to the figure of all standard of verification dose that correspond to 8.4kGy to which 100 lots were irradiated.The reason for this uniformity of doses obtained for the radiation dose s was 1.09 while the average absorbed dose was $15,130^{+}$-0,076kGy.

To reach this objective we made the sterility test where no positive sample were detected.This shows the values of this procedure used and permited to find the right sterilization dose for the SAL(10^{-3}). The dose was 14.8 kGy, in practice 15 kGy for the process.
Applying the method 1 the reguired dose for radiosterilization for caps was 15 kGy.Increasing the cuality of product for timme unit .Decreasing the time of exposure to radiation.
We got to the conclution that with 15kGy dose the results are the same as when we used 25kGy.

CONCLUSIONS:

Applying the Method 1, of the ISO 11137 Standard, the required dose for radiosterilization for cap was 15 kGy. Increasing this the quantity of product for time unit decreasing the time of exposure to radiation .
We got to the conclusion that with 15 kGy dose the results are the same as we 25 kGy.

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