Bioreactor Design and Analysis
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Lecture - 32
Heat Transfer Operations in Bioreactors – Practice Problems

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Welcome back students. So, now, today we are going to take some practice problems on sterilisation and heat transfer operations in reactors.

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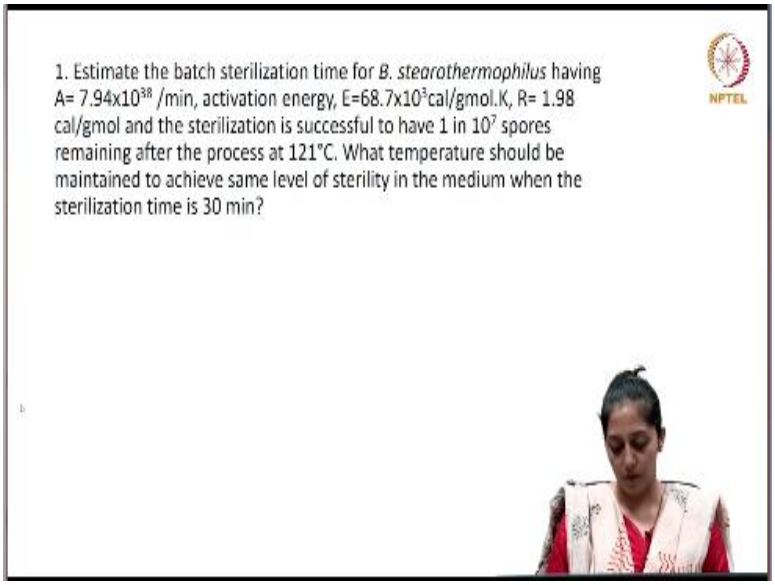

let us see the problem given on the slide where we need to estimate the batch sterilisation time for beta stearothermophilus organism and the Arrhenius constant is given. The activation energy is also given and the universal gas constant value is also known. The

sterilisation is set to be successful if we can have one only remaining in 10 to the power of 7 spores after the process of sterilisation done at 121 degrees centigrade.

They have also asked us to calculate what temperature should be maintained to achieve the same level of sterility when the sterilisation time is given as 30 minutes. So, let us first solve the first part of the problem, which was to estimate the batch sterilisation time. Now, first, we will consolidate all the information which is given to us about the process.

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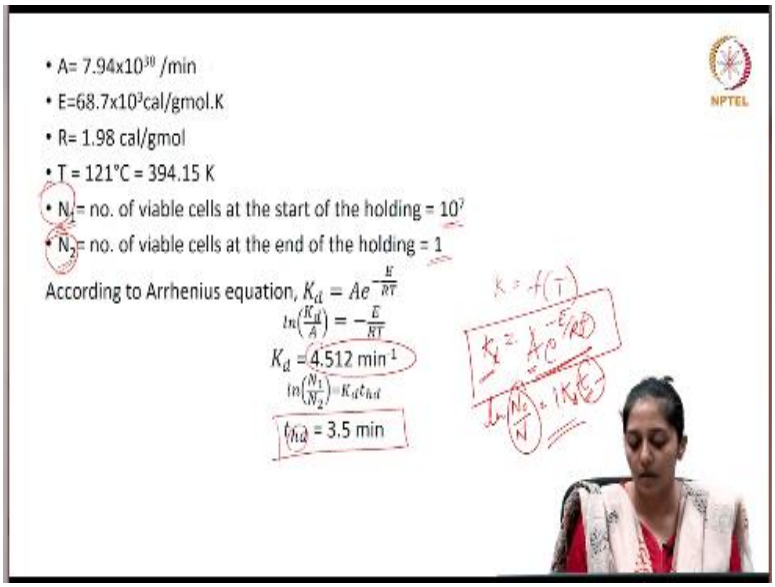

So, here is the list of information which is given to us. So, Arrhenius constant is given; activation energy is known,; R is also given and temperature for sterilisation is also given which is 121 degrees centigrade. So, to keep the consistency of units, we will convert it into Kelvin. Now, what else is given? The number of viable cells, we can assume to be 10 to the power of 7 spores in the beginning.

So, for successful sterilisation to happen, only one should be remaining. So, we can assume the N 0 value which is given here as N 1 is 10 to the power of 7, while the final number of organisms after sterilisation cycle is 1. So, this is N value. Now, we know that as per Arrhenius equation here, thermal death rate constant is a function of temperature given as the Arrhenius model or equation. And we know, this is what is Arrhenius equation.

Now, here K d which is thermal death rate constant, A is Arrhenius constant, E is the activation energy and T is the temperature for sterilisation. Now, we also know assuming that the thermal death kinetics follows a first order kinetics. Then, ln N 0 by N will be equal to K

d t, where t is your sterilisation time. So, minus sign has gone therefore, the N 0 came up. So, now, we have to find the batch sterilisation time.

For that, we must calculate the value of K d first, because we need K d here. So, K d can be calculated using our Arrhenius equation, where t is known; the constant values are given. So, then if you substitute all the values, you can find the value of k d which is given here as 4.5 minute inverse, because rest of the values are given to us in the Arrhenius equation.

And using that, value of K d in the first order degradation kinetics, we can find the value of time required to reach the desired sterility where N 0 is your N 1 as shown here. And N is your N 2 which is shown here. So, if you substitute all the values here to the rearrangement to get the value of t, then t is being represented as t hd which is holding time for batch sterilisation and you get the time for sterilisation.

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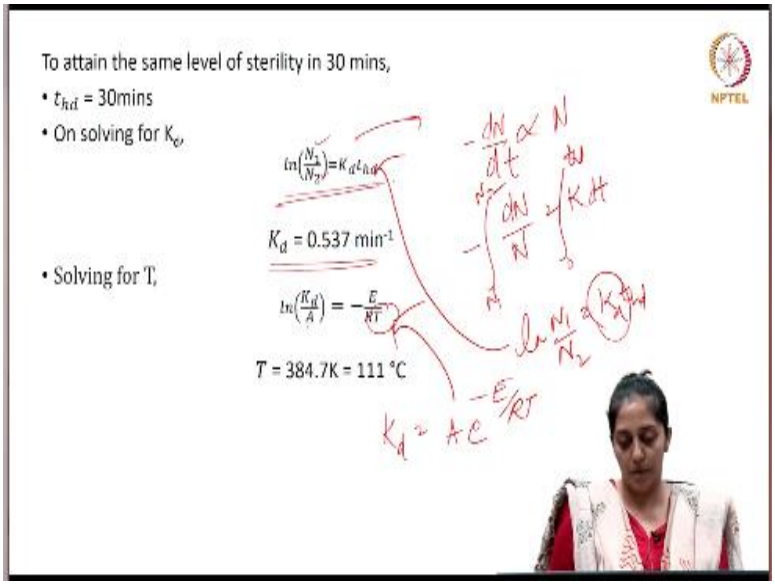

We are assuming if it is holding time, we assume no killing during heating and cooling, it is being sterilised at 121. Now, in the second part of the problem, if the same level of sterility is to be achieved in 30 minutes. Then, what should be the temperature at which the sterilisation can be done? So, if this time for sterilisation can be changed to here in this equation, if this can be changed to from 3.5 to 30 minutes.

So, now, using the first order degradation kinetics, the value of the thermal death rate constant will be calculated giving the same sterility to be maintained. So, N 1 and N 2 remains the same and N 1 is the initial number and N 2 is your final number. So, here ln N 1

by N 2 is equals to k d t, this has come from dN by dt being a first order kinetic equation is proportional to N. So, your dN by N was K dt.

So, this was for the batch sterilisation time and this is from some N 1 to N 2. This is first order degradation kinetics minus. So, this becomes ln N 1 by N 2 which is equal to K t hd. This is what is given here. So, then N 1 and N 2, the sterility level is the same. So, this becomes you can obtain in the N 1, N 2 values from the problem given here and you can substitute in this equation to get the value of K d.

Now, once we have got the value of K d by the Arrhenius equation, we can obtain the temperature because ENR will remain the same. K is given. So, we can find the using Arrhenius equation, what was Arrhenius equation? K d is equals to A e to the power of minus E by RT. So, this is how we can calculate the temperature.

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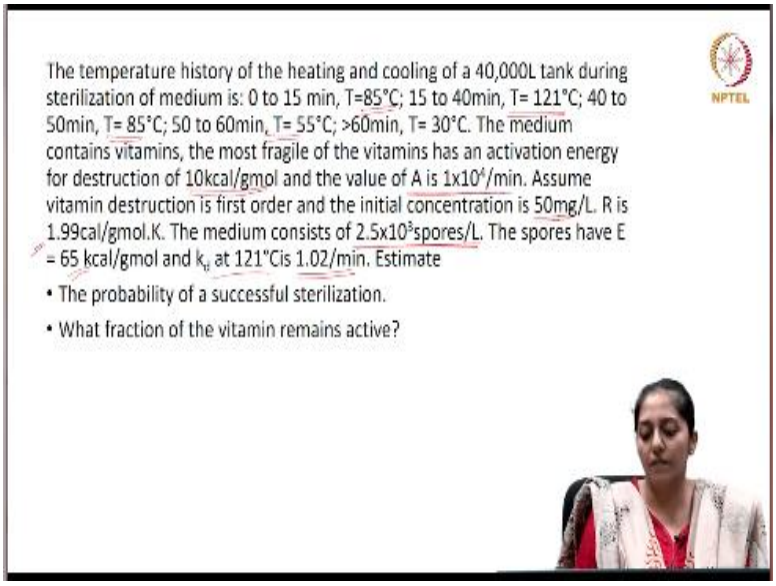

Let us, see the second problem. The temperature history of heating and cooling of a 40,000 litre tank during sterilisation of the medium is. So, we have given a profile of how the temperature is changing. So, from 0 to 15 minutes, the temperature is at 85; from 15 to 40 minutes the temperature is at 121; from 40 to 50 minutes, again it drops to 85 and from 50 to 60 minutes, it is at 55. And this is how it cools down, greater than 60 minutes, the temperature then is 30.

This medium contains vitamins which are heat level by, they have an activation energy of 10 kilo calorie per gram mole. The Arrhenius equation constant is given. Assume the destruction

by heat is following the first order and the initial concentration of vitamins in the medium is 50 mg per litre. The R universal gas constant value is given and the initial number of spores present in the medium. For sterilisation is also given per litre.

Now, spores have the E value of 65 kilo calorie per gram mole and the thermal death rate constant at 121 is 1.02 per minute. We need to first find the probability of successful sterilisation.

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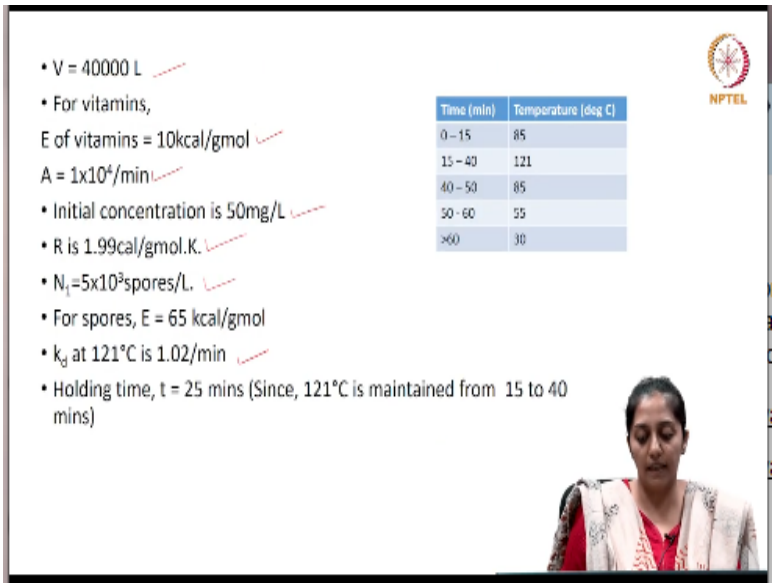

First, let us, list down what is given in the problem. So, here is the list of information which is given in the problem. The volume is given as 40,000 litres. For vitamins, the E value is given and the A value is given for the Arrhenius equation. The initial concentration is known; R value is given; the initial number of spores per litre, the concentration of spores in the medium is given. And for the spores, the E and the K d value is also given.

Now, if you see the profile of temperature at 121 which is the holding temperature generally for sterilisations. The time is between 15 to 40 minutes, so, which is 25 minutes. So, for 25 minutes, the temperature is being maintained at 121 degrees C, which is generally the sterilisation temperature. So, we will take that the holding time.

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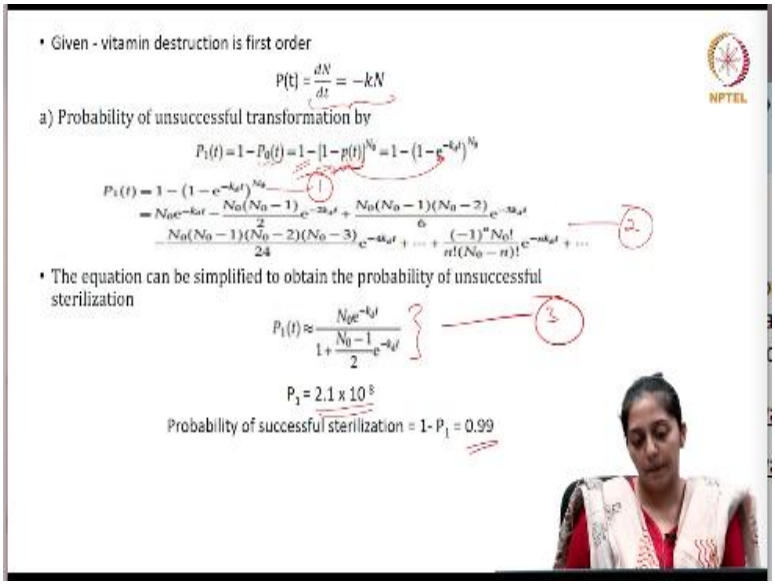

Now, vitamin destruction is the first order. So, dN by dt is equals to minus kN. So, the probability of unsuccessful sterilisation would be 1 – P 0 t, where P 0 t is the probability of successful sterilisation. And what is probability of successful sterilisation? That none of the organisms remain. So, if p t is the probability of survival for each of the organisms, then for them not to survive, the probability will be 1 minus small p t and none of these organisms should not survive.

So, their probability would be 1– p t to the power of N 0. So, the probability of successful sterilisation would be 1 – p t to the power of N 0. And the probability of unsuccessful sterilisation therefore, will be 1 minus the probability of successful sterilisation. So, the probability of survival is e to the power of minus k d t. So, this has been substituted here and this is obtained from the first order degradation kinetics, the death rate kinetics of the organism.

So, if we substitute here, we will get this equation for probability of unsuccessful sterilisation. Now, this can be expanded using Taylor series expansion. So, when you expand equation 1, you get equation 2 and then taking the first term constant out common. It can then be an infinite exponential series, where the sum can be given us for this infinite series, can be given as shown here in equation 3.

So, you can check back on the Taylor series for expansion as shown in equation 2. So, then if you substitute now, k d value, the time for sterilisation, the initial number of spores present all that is known in the problem. So, if we substitute that, we will see that probability of

unsuccessful sterilisation comes out to be, the probability unsuccessful sterilisation is this. Then, the probability of successful sterilisation would be 1 minus this value, which will be 0.99.

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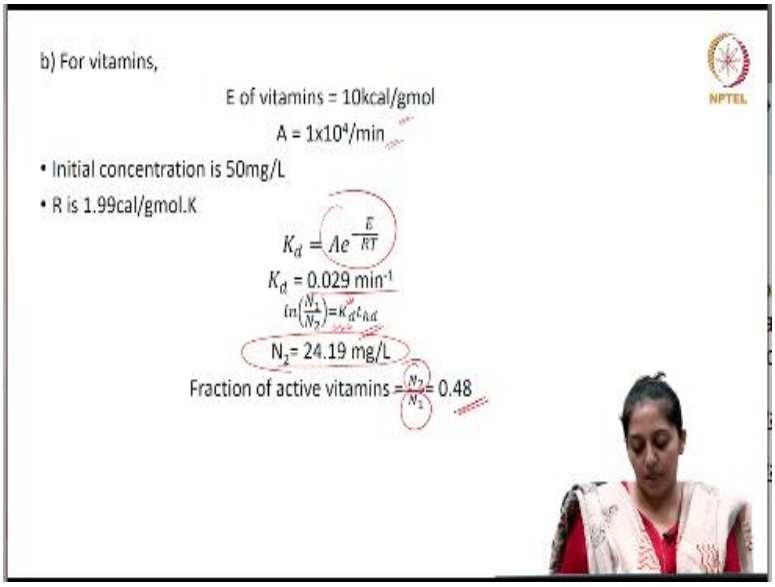

So, let us see the second part. The second part is what fraction of vitamins which are heat level components during this process of sterilisation will remain active. So, how do we find that? The initial concentration is given; the final concentration is to be obtained; the time for which they are exposed to sterilisation temperature is given. So, we can determine the value of the degradation constant.

To obtain the value of degradation constant, we will use Arrhenius equation, where the activation, deactivation energy and the Arrhenius constant value is given. And it was calculated as 0.029 minute inverse. Then the same K d value has been substituted in the first order degradation kinetics. And we get the final concentration of the vitamins during the sterilisation operation after degradation. So, the fraction of active vitamins would be the final concentration to the initial concentration which comes out to be 0.48.

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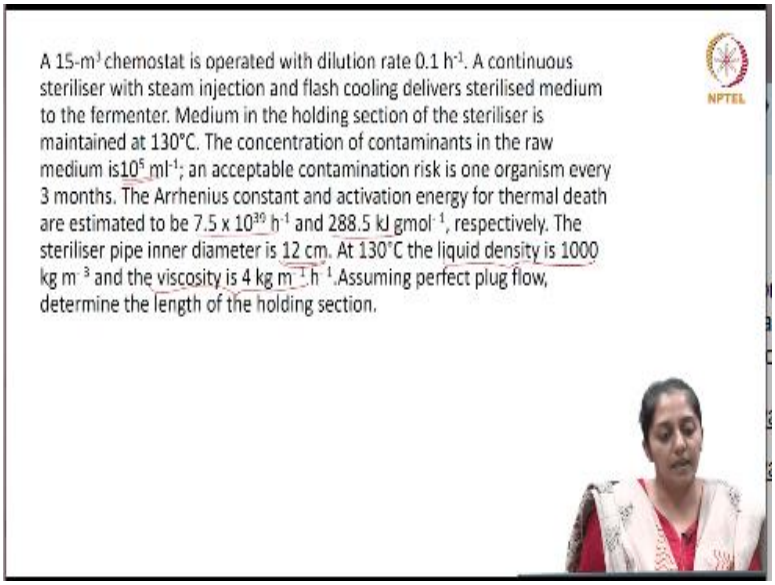

Let us, see another problem. A 15 metre cube chemostat is operated with dilution rate of 0.1 hour inverse. A continuous steriliser with steam injection and flash cooling delivers sterilised medium to the fermenter. So, this is a continuous heat sterilisation process. Medium in the holding section of the steriliser is maintained at 130 degrees C. So, the holding temperature, we know is 130 degrees C.

The concentration of the contaminants in the raw medium is known which is 10 to the power of 5 organisms per ml. This is the load. An acceptable contamination risk is one organism every 3 months, we cannot go beyond that. So, after every 3 months, there is only one organism. The Arrhenius constant and the activation energy for thermal death is given. A value is given and the activation energy is given. The inner diameter of the steriliser, the pipe diameter is given as 12 centimetres.

Now, at the sterilisation temperature, which is 130 degrees C here, the fluid properties including the density and the viscosity is known. Now, it is said to assume that the fluid is under perfect plug flow conditions and we need to determine the length of the holding section.

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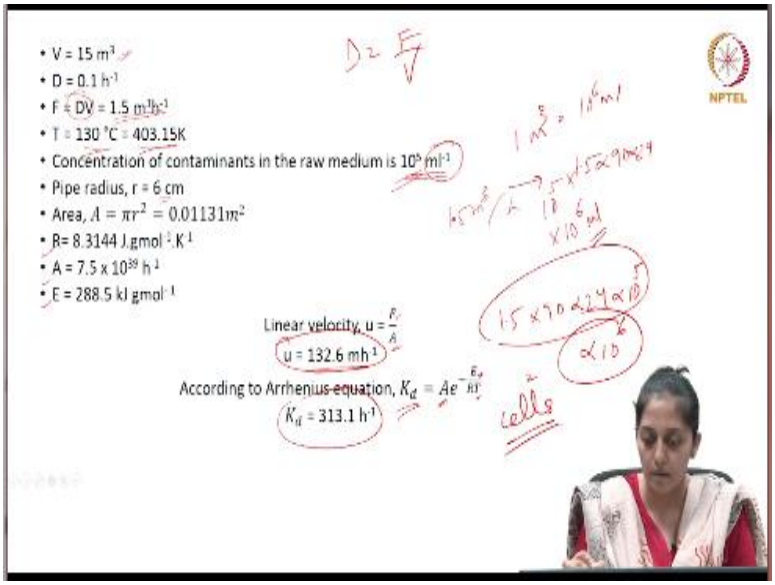

Now, again listing down the information which is given in the problem. So, the volume given to us is 15 metre cube of the raw medium in this chemostat continuous steriliser. The dilution rate is 0.1 hour inverse. So, the volumetric flow rate can be calculated using the dilution rate and the volume. We know how they are related which comes out to be 1.5 metre cube hour inverse.

So, dilution rate is nothing but F by V, where F is the volumetric flow rate and V is the volume. Then the temperature is given as 130 degrees C. So, we convert it into Kelvin. The initial load is 10 to the power of 5 number per ml. So, we must find out how much will be the total number as per the volume. The pipe radius is 6 centimetre. the area would then be, it is a pipe, so, the cross sectional area is phi r square and the R, A and E value are given.

Now, from the information which is listed, we can calculate the linear velocity, the fluid velocity in the pipe which can be given us the volumetric flow rate divided by the area of cross section. So, it comes out to be 132 metre per hours. Now, the Arrhenius constant is given; the activation energy at temperature 130 degrees C is also given. So, we can find out the thermal death rate constant. So, 2 things can be obtained. One is the linear velocity. The other is the thermal death rate constant.

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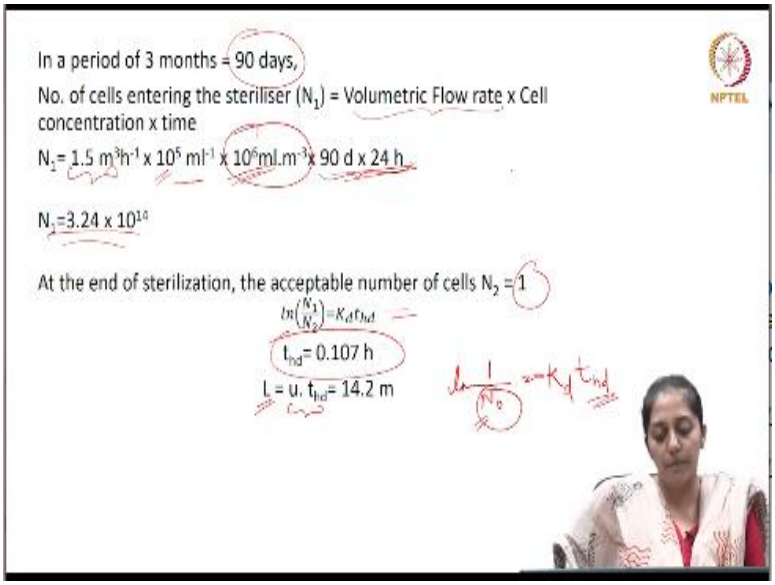

Now, because 1 in 3 months is acceptable once organisms surviving. So, in 3 months, which means, what would be the total amount of organisms? So, we need to calculate the number of cells entering the steriliser. So, per ml of the raw medium is 10 to the power of 5 ml. So, we need to see, how much medium would have been processed in 3 months, 1.5 metre cube per hour.

So, this will be 1.5 into 90 into 24, this much metre cube processed into 10 to the power of 5, 6 ml. So, this will be the total amount of cell. So, if we know that the acceptable limit. Let us assume, only one organism remains and N 0 is not known. We need to calculate, it is equals to the thermal death rate constant into the holding time. Now, K d value, we have obtained from here. Time for holding needs to be calculated. If we know the other, unknown is the initial number of cells.

So, the initial number of cells can be calculated by finding the total amount of raw material, the volume of raw material which will be processed in 90 days, because 1 in 3 months is acceptable. So, we will find. If the final is one organism, the initial would be whatever number of organisms have entered in these 90 days. So, we can calculate the volumetric flow rate is given; total time is given and 10 to the power of 5 per ml.

So, therefore, we will multiply it to get the total number of initial amount of cells in the medium. So, at the end of the sterilisation, we can find what will be the time of sterilisation required by the first order degradation kinetics. Now, if the time of sterilisation is known, we

know in the holding section of the continuous steriliser, this time is related to the length of the holding section by the linear velocity.

So, linear velocity we calculated previously, which if multiplied by the time it spends in the holding section, we will get the total length of the holding section. So, this will be 14.2 metres.