NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

Technical Report 32-1191

Determination of Terminal Sterilization Process Parameters

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Abstract

The time/temperature effects on the reliability of spacecraft components and assemblies require that the terminal heat sterilizing process for spacecraft be adequate, but minimal. Accordingly, an analytical model was developed to study the effects of various facets of the terminal sterilization process and to establish the relationship which exists between the thermal characteristics of the spacecraft and microbial contamination.

For the purposes of this study, a simple geometrical configuration of the spacecraft was assumed. The effects upon the process parameters of times and temperatures of various heating and cooling rates were studied. In addition, various distributions of microbial load were postulated and the processes necessary to achieve sterility of the model spacecraft were determined. These variables, as well as the microbial heat-resistance parameters, are shown to affect significantly the derived process time at any temperature.

Determination of Terminal Sterilization Process Parameters

I. Introduction

The time/temperature effects on the reliability of spacecraft components and assemblies require that the terminal dry-heat sterilizing process for spacecraft be adequate, but minimal. To ensure that this objective is met, consideration must be given to all facets of the sterilization process, and a complete understanding of their effects is necessary to determine the actual process times and temperatures. The factors which must be considered include the heat-transfer coefficients for various levels of assemblies, the temperature driving force of the heating medium, the species and numbers of the microorganisms present, their distribution on the hardware, and their thermal resistance parameters, D and Z, (see Ref. 1).* The latter are affected by the water activity of the microorganisms, which is in turn influenced by the conditioning of the organisms prior to the heat exposure and the relative humidity associated with the heating environment. Because of the magnitude of the problem, a conceptual analytical model was developed to study the effects of various facets of the terminal sterilization process and to establish the relationships which exist between the thermal characteristics of the spacecraft and the characteristics of the microbial contamination which is present.

For the purposes of this study, a simple geometric configuration of the spacecraft was assumed. The configuration is illustrated in Fig. 1. The spacecraft model is a cylinder, 8 ft in radius and 16 ft high, of homogeneous material and, for ease in performing the thermal analysis, assumed to be insulated at the ends. It was also assumed that the model could be divided into zones or shells (as shown in Fig. 1) of constant altitude. The criterion for establishment of the zones of the model is the thermal behavior of the zone. For the real case, other factors such as the functional attributes of subsystems and geometry of the configuration, in addition to the thermal properties, will undoubtedly influence the selection of the zones for the calculation of process parameters.

*The term D is defined as the decimal reduction time or the time at temperature required to destroy 90% of the cells. It represents the slope of the survivor curve. The term Z is numerically equal to the number of degrees F (or C) required for a thermal destruction curve to traverse one log cycle. It is the negative reciprocal of the slope of the TD curve.

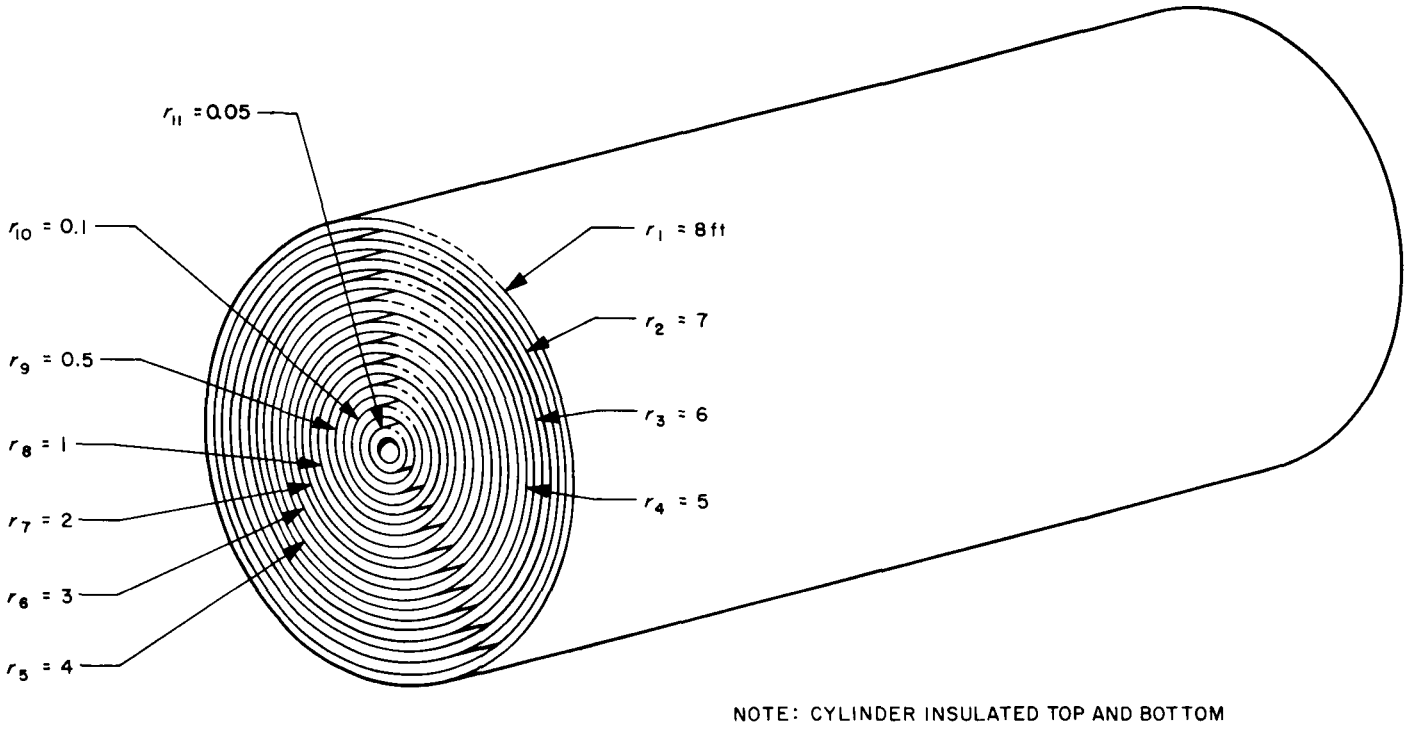

Fig. 1. Analytical sterilization model

II. Analysis and Discussion

A thermal analysis of the model was performed. For this purpose, it was assumed that the heating and cooling rates of the heating medium were constant at 11° C/h, and the initial temperature of the medium and the model was 22° C, as shown in Fig. 2. The rate of heating (or cooling) was chosen to be consistent with information from previous programs that indicated a change of 10 to 15° C/h could be tolerated without degrading effects upon spacecraft performance. The temperature profile of the surface of the spacecraft model (i.e., the profile of the 8-ft shell) was assumed to be equal to the profile of the heating medium. The temperature profile for the most heat-resistant zone of the spacecraft, i.e., the innermost shell of the model, was extrapolated from a published report of a study of the heat transfer for a titanium aeroshell (see Ref. 2). The profile for the model differs from the published profile because of the difference in heating and cooling rates of the heating medium.

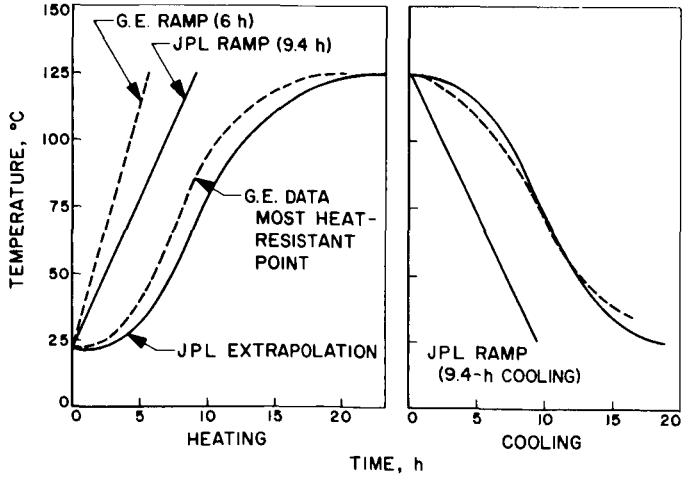

Fig. 2. Heating and cooling a titanium aeroshell (extrapolation of G.E. aeroshell analysis)

The temperature profiles shown in Fig. 3 for the intermediary shells were calculated using the equation for heat flow in an infinite cylinder

$$\frac{q_i}{\ell} = \frac{2\pi k(T_i - T_{i+1})}{\ln (r_{i+1})/r_i}\ ;\ i = 1 \cdots 10 \qquad (1)$$

where

q = heat-flow rate
k = thermal conductivity
T_i = temperature at r_i shell
ℓ = length of cylinder

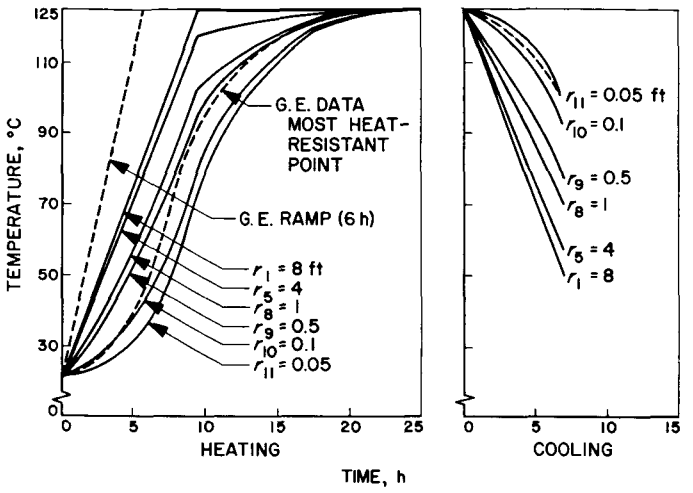

Fig. 3. Temperature profiles of cylinder shells during heating and cooling (extrapolation of G.E. aeroshell analysis)

Since the cylinder is homogeneous, the heat flow is constant throughout the cylinder at any given instant.

For an actual spacecraft, the transient thermal behavior will have to be determined by combining the results of temperature control model tests and a transient analysis. However, for the scope of this study, the simple thermal model, described above, appeared to be adequate.

The lethal effects of the transient temperatures during the heating and cooling phases of the sterilizing cycle can be readily determined with the model, and the sterilizing process parameters for the model can be calculated. This approach has been suggested previously by both Schalkowsky (Ref. 3), Lorsch (Ref. 4), and one which has been used in the food industries for many years (Ref. 5).

The details of the approach are included in a paper by A. R. Hoffman and J. A. Stern (Ref. 6) and therefore will not be presented here. However, for ease of understanding, definitions of the basic factors in the calculations are presented, as follows, in this report.

To determine the process parameters of time and temperature for the heating medium, it is necessary to account for the reduction in microbial population which occurs during the transient phases of heating and cooling of the model as well as at steady state.

To accomplish this, factors called "Lethality" (L) and called the "equivalent sterilizing time or process" (F_T) are introduced.

"Lethality" is defined as a measure of the sterilizing process that, when equal to unity, is indicative that sterility has been achieved.

The "equivalent sterilizing time or process" is that time sufficient to achieve sterility, i.e., unit lethality, at a steady-state temperature assuming instantaneous cooling and heating. Since a logarithmic microbial survival model was assumed for the study, and sterility was assumed to be obtained when the microbial population has been reduced to a level where the probability of survival is P_s, the "equivalent sterilizing time" (F_T) may be obtained by use of the equation

$$F_T = D_T \log N_o/P_s \quad ** \tag{2}$$

where

N_o = initial number of microorganisms
D_T = time to reduce the specific microbial population at temperature T by 90%

The "equivalent sterilizing time" at any given temperature and for any ratio of N_o/P_s may be calculated by use of a thermal death-time curve as shown in Fig. 4.

If a population of microorganisms (N_o) with given D_T characteristics is subjected to a process of F_T minutes at temperature T, sterility will be achieved and the lethality of the process will be equal to 1. If the population had been exposed to only one minute at temperature T, the resultant lethality would be equal to $1/F_T$. The term $1/F_T$ will be referred to as the lethal rate.

Lethality, therefore, is the product of the lethal rate and time, or

$$L = 1/F_T \times t_T \tag{3}$$

The total lethality of a sterilizing process for a particular point in the configuration may be obtained by calculating the lethality for each temperature during the cycle and summing all of the lethalities. Thus,

$$L_{TOT} = \sum_{i=1}^{m} 1/F_{Ti} \times t_{Ti} = 1 \tag{4}$$

**The equation is sometimes expressed as $F_T = D_T$ [log (N_o) — 1 — log P_s] to account for the initial reduction which is often encountered in the first few minutes of heating a microbial population. This form of the equation is used in calculating all results presented in this report (except for those in Fig. 6).

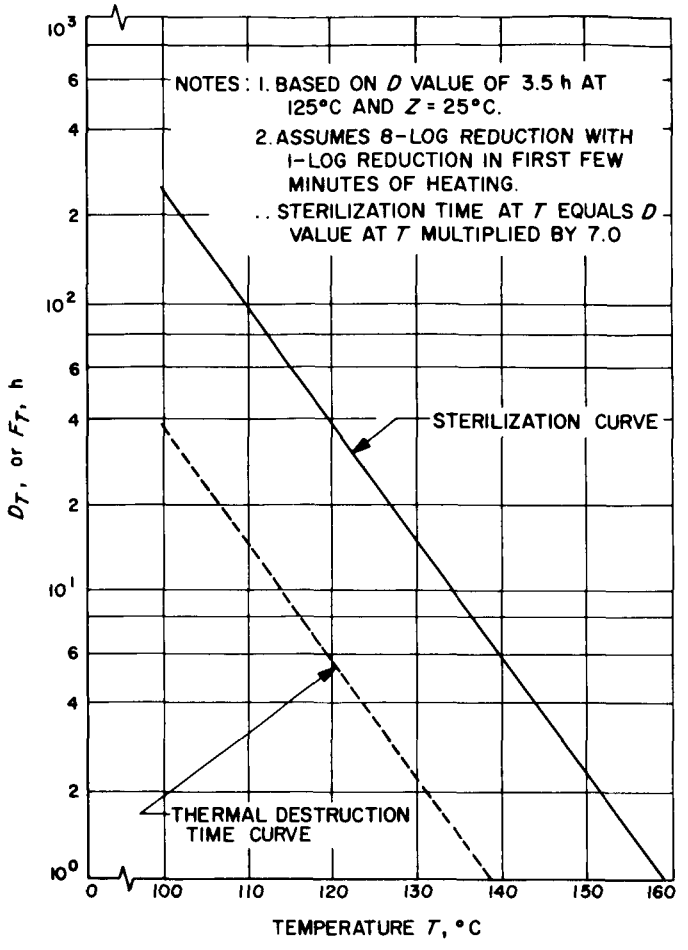

Fig. 4. Thermal destruction and equivalent sterilization time curves

The total lethality of the process is also equal to the sum of the lethalities occurring during the heating and cooling phases of the cycle and the lethality occurring at the steady-state temperature, or

$$L_{TOT} = L_H + L_S + L_C \tag{5}$$

where

L_H = lethality during heating
L_S = lethality during steady state
L_C = lethality during cooling

The lethality occurring during heating (L_H) can be calculated by integrating all of the instantaneous lethalities occurring during the heating phase. This may be simply accomplished by graphical integration of a plot of lethal rate against time. In a similar manner, the lethality occurring during the cooling phase can be determined.

Then, since by definition the total lethality of the process must equal 1,

$$L_S = 1 - L_H - L_C \tag{6}$$

The process parameter of time at steady-state temperature can then be calculated by solving the equation

$$L_S = 1/F_{T_s} \times t_s \tag{7}$$

where the subscript s is indicative of the steady state condition.

The total process time can then be determined by the addition of the times of the transient phases (for the particular point in the model under study) to the time calculated at steady state temperature.

All of the studies which have been performed to date with the model have assumed a steady-state temperature of 125°C, lethality occurring at all temperatures above 100°C, a homogeneous microbial population of 10^5 organisms (N_0) with a D_{125} of 3.5 h and a Z of 25°C, and P_s, for sterilizing the population of microorganisms on the model, equal to 10^{-3}.

Using the model and the concept of integration of lethalities, it was possible to demonstrate a reduction of 23% in time of application of heat to achieve sterility, assuming that all of the organisms are at the most heat-resistant point (see Ref. 6).

Therefore, establishment of sterilizing-process parameters without considering the lethal effects of the transient phases of the process would appear to be an overly conservative approach. The effects of transient phase lethality integration upon total process time are seen in the data presented in Table 1.

If the distribution of microorganisms upon the zones of the model is considered, rather than assuming that all of the organisms are present at the most heat-resistant point, the process parameters may be affected.

The results of some studies of different microbial distributions upon the model zones are also shown in Table 1.

Table 1. Effects of model microbial distribution upon model process times in hours

Microbial distribution	Transient lethality included	Transient lethality not considered
All at zone 1	41.4	53.3
All at zone 11	56.0	67.5
Number/ft^2 surface = K	53.6	68.8
Number/ft^3 = K	56.0	67.5

Note: Assuming a homogeneous population of 10^5 organisms with a $D_{125} = 3.5$ h, $Z = 25°C$, steady-state temperature = 125°C, initial temperature = 22°C, ΔT of the heating medium transient phases = 11°C/h and $F_T = 24.5$ h.

The marked reduction in process time noted when all of the organisms are on the outermost zone (zone 1) is due to the relatively short times of the transient phases.

When the lethality occurring during the transient phases is included in the process calculations, a relatively small reduction in total process time is noted between the most conservative approach (all organisms at zone 11) and a more probable distribution of the organisms, i.e., distributed uniformly over the total surface. For the latter calculation, P_s for each zone was taken as 9.1×10^{-5} since the P_s for the model was assumed to be 10^{-3}. In this case it was further assumed that the sterilization of each zone was an independent event and that the total probability of survival was equally distributed among the eleven zones of the model. In other words,

$$P_{s\,mod} = n\,P_{s\,zone} \tag{8}$$

and

$$P_{s\,zone} = P_{s\,mod}/n = 10^{-3}/11 = 9.1 \times 10^{-5} \tag{9}$$

When the lethality occurring during the transient phases is not included in the process calculations, a slightly more severe total process is required for the uniform-distribution situation than the most conservative situation. Although the N_o for any zone is less than 10^5, and a reduction in process time therefore would be expected, the decrease in P_s used in the calculations from 10^{-3} to 9.1×10^{-5} results in a net increase in the process time required to achieve sterility of the model ($P_{s\,mod} = 10^{-3}$).

As Schalkowsky (Ref. 7) pointed out, if the microorganisms are assumed to be uniformly distributed per unit volume of the model, then the process time is the same as when all of the organisms are assumed to be located at the most heat-resistant point (zone 11). In this case both the assumed N_o (10^5) and the P_s (10^{-3}) are divided by the n volumes into which the model is distributed, and therefore cancel out of the equation.

As can be seen from these illustrations, the distribution of microorganisms may significantly affect the calculation of process times, and therefore should be carefully determined.

The final process parameters are also greatly affected by the heat resistance parameters D and Z which are used in the lethality calculations.

As shown in Fig. 5, as the slope of the thermal death-time curve decreases (and Z therefore increases) the values of D_T, which is maintained at 3.5 h at 125°C, at any lower temperature also decrease. If D_T is reduced, so also is F_t, and $1/F_t$ increases with the result that a proportionally greater lethality occurs during the transient phases, and shorter process times result.

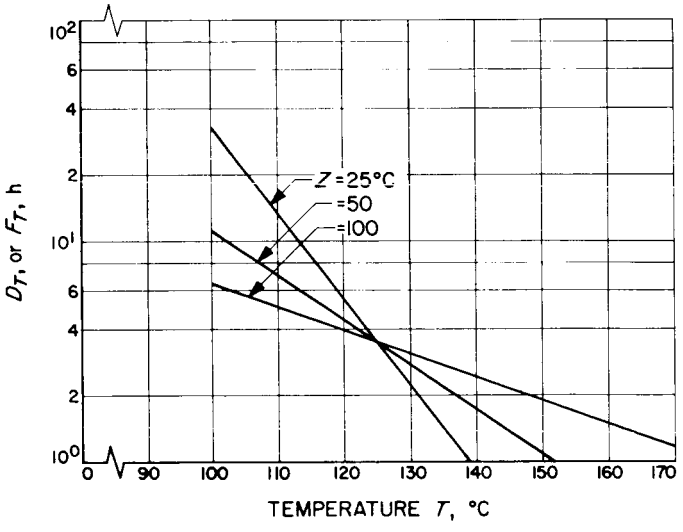

Fig. 5. Thermal destruction curves of different Z values, but with $D_{125} = 3.5$ h

The relationship between D, F_T and log N_o/P_s is an interesting one, as shown in Fig. 6. The curves of constant F_T value are hyperbolic in nature. At low D values such as are encountered in spacecraft surfaces, the relationship is insensitive to changes in population numbers. A very large change in the ratio of log N_o/P_s is necessary in order to change the F_T a relatively small amount. Even considering inaccuracies associated with microbial assays, it would appear that process times calculated for the sterilization of surfaces will be more than adequate since

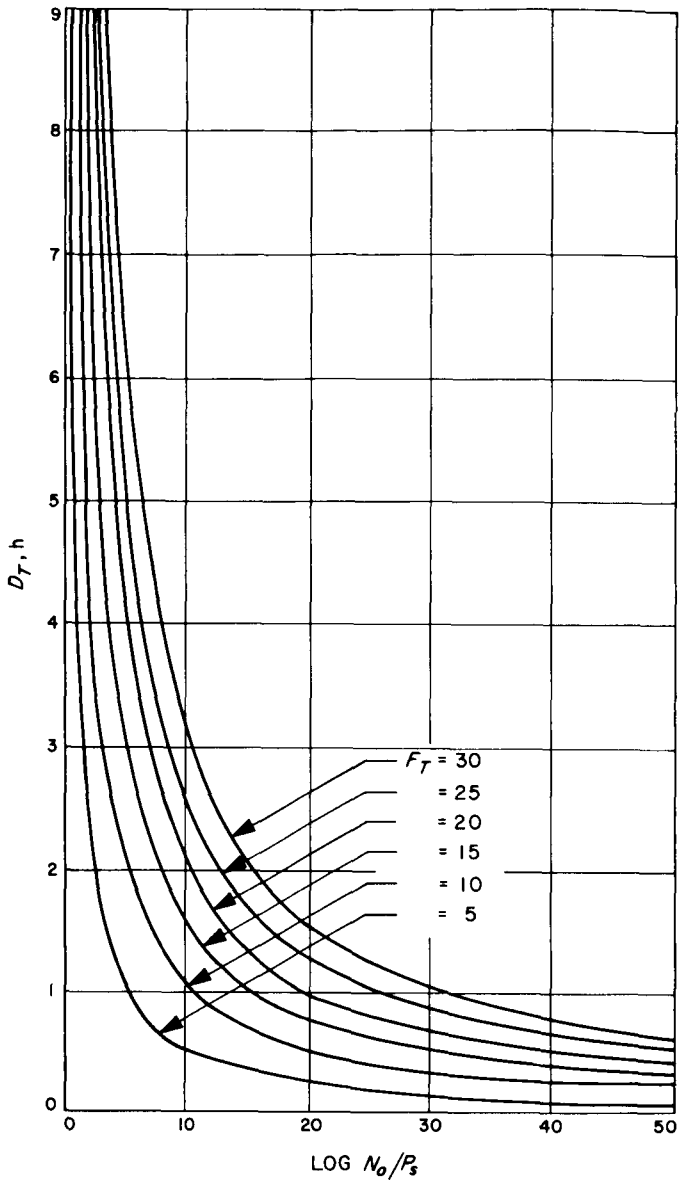

Fig. 6. Relationship between D_T, F_T and log N_o/P_s

relatively large safety factors can be incorporated in the estimation of N_o without significantly increasing the equivalent sterilizing process time.

Again, at high D values such as are encountered in certain matings of surfaces and in interiors, a small change in the term "log N_o/P_s" very significantly affects the equivalent process time and the model process time. Accordingly, extreme care must be used in making estimates of N_o in those situations where high D values may be encountered. In this situation the inaccuracies associated with microbial assays will result in errors of significant magnitude in the calculated process times.

Conversely, as can be seen from Fig. 6, errors in estimating D values, when the value is high, are of minor significance relative to the effect upon equivalent process time. However, when the D values are low, a relatively small change in the D value can result in a large change in the required equivalent process times.

As a result of these considerations, it would appear that considerable attention should be given to estimating the errors associated both with the assay techniques and with the establishment of D values in order to determine the controlling factors in the establishment of equivalent process times for use in calculating process parameters for spacecraft sterilization.

As mentioned earlier, the thermal characteristics of the spacecraft or its individual assemblies are also of considerable importance in establishing the terminal process parameters. A study was performed to ascertain the sensitivity of process-time determinations to heat-transfer characteristics. For this study each of the curves in Fig. 3 were assumed to represent a most heat-resistant situation in the model, and in each case all of the organisms were assumed to be located at the most heat-resistant point.

Approximate coefficients of heat transfer were then calculated for each curve. The respective lethalities during heating and cooling were determined and the total process times were calculated. Figure 7 presents the results. As expected, the curve is hyberbolic in nature since with a high conductivity the model should heat rapidly, and the resulting lethality during the heat application phases of the process should be high, resulting in

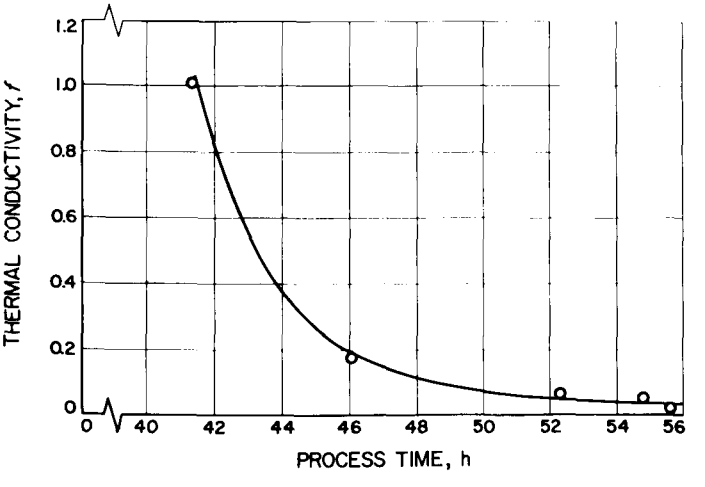

Fig. 7. Relationship between model thermal conductivity and required process time

Table 2. Process time calculations for various thermal conductivities assumed for model*

f (k)	L_H	L_C	L_S	t_H** (hours)	t_C (hours)	t_S (hours)	Process time (hours)
0.031	0.296	0.129	0.575	24.0	17.5	14.1	55.6
0.049	0.280	0.073	0.647	22.0	17.0	15.8	54.8
0.065	0.233	0.060	0.707	20.0	15.0	17.3	52.3
0.180	0.237	0.043	0.720	16.5	12.0	17.6	46.1
1.010	0.036	0.039	0.925	9.4	9.4	22.6	41.4

*F_{125} assumed equal to 24.5 h, i.e., $D_{125} = 3.5$ h, $N_0 = 10^5$, $P_s = 10^{-3}$; maximum temperature assumed to be 125°C.
**Time of heating equal time for shell to reach 124°C from initial temperature = 22°C.

a short process. Conversely, a model with low conductivity should heat slowly, resulting in a long process time. The data shown in Fig. 7 are the result of calculations presented in Table 2.

By considering the zone concept and utilizing the variable lethality effect encountered with varying conductivities as will occur in an actual spacecraft, a sterilization process can be developed that will achieve sterility with minimum heat-application time.

III. Summary

In summary, then, a simple geometric and thermal conceptual model has been developed to study the complex relationships existing during dry-heat sterilization between the characteristics of the microbial populations present and the thermal characteristics of the spacecraft and heating medium. The analytical concept can be used to establish sterilization process parameters which are compatible with any sterilization requirements such as variations in P_s, N_o, the microbial heat-resistance parameters, and the thermal behavior of the spacecraft. The process parameters which can be derived by use of the conceptual model may be for sterilization of subsystem interiors, spacecraft surface sterilization, or for sterilization of the entire spacecraft. Furthermore, the conceptual model can be coupled with a stochastic model to account for microbial accumulation during assembly.

The use of this model has indicated that:

(1) The integration of the lethal effects of the transient phase of the sterilization cycle will significantly reduce the severity of the process while attaining the desired sterility level.

(2) The distribution of microbial load upon the spacecraft may significantly affect the calculations of the required process parameters and therefore is necessary information for proper process calculation.

(3) If the D values used in process calculations are relatively low, the process calculations are relatively insensitive to errors in estimation of microbial load, but very sensitive to errors in estimation of D values.

(4) Conversely, if the D values are relatively high, the process calculations are very sensitive to small errors in estimating the initial microbial population and relatively insensitive to errors in estimation of D values.

(5) The process time calculations are inversely affected by changes in Z values.

(6) Since lethality occurs during both the heating and cooling phases of the sterilization cycle, the relationship between process time and spacecraft thermal behavior is a complex function but, in general, as the thermal conductivity increases, the required sterilizing process time will decrease.

(7) Consideration of all of the factors discussed is necessary to calculate the minimum process time to obtain the required sterility.

References

1. Stumbo, C. R., *Thermobacteriology in Food Processing,* Academic Press, New York and London, 1965.
2. *A Study of Design Guidelines for Sterilization of Spacecraft Structures,* Report No. 6450600, General Electric Co., Inc., Philadelphia, Pa., April 1964.
3. Schalkowsky, S., *Analytical Techniques in Planetary Quarantine and Spacecraft Sterilization,* Exotech, Inc., Washington, D.C., Final Report, NASA Contract 1340, November 1966.
4. Lorsch, H. G., "Biocontamination Control," *Space/Aeronautics,* Vol. 46, No. 6, pp. 82–91, November 1966.
5. Bigelow, W. D., Bohart, G. S., Richardson, A. C. and Ball, C. O., *Heat Penetration in Processing Canned Foods,* National Canners' Association, Bulletin No. 16L, Washington, D.C., 1920.
6. Hoffman, A. R., Stern, J. A., "Terminal Sterilization Process Calculation for Spacecraft," Presented at the *Society for Industrial Microbiology Meeting,* London, Ontario, Canada, August 21–24, 1967.
7. Schalkowsky, S., *Personal Communication,* 1967.