

DID YOU KNOW?

NO: 25

OCTOBER 19, 2009

F SUB ZERO - HEAT LETHALITY

There are two ways to control when the sterilize phase is done.

The method most people are familiar with is sterilizing at a constant known temperature for a known amount of time. The other method is formally known as Heat Lethality, but usually called “F Sub Zero” (F_0).

The F_0 way uses a load probe to monitor the temperature in the material being sterilized. The load probe temperature is used to calculate “Incremental F_0 ”. (IF_0 is sometimes called instantaneous F_0) and “Accumulated F_0 ” (AF_0). When this method is used, the sterilization phase is completed when the AF_0 has reached a set value. Typical AF_0 values used range from 10 to 16 and are determined during the normal Process Qualification (PQ).

The explanation of how Primus implements AF_0 is listed in the operator’s manual and is repeated below:

Heat Lethality (F_0)

Load probe(s) and/or F_0 control are sterilizer software options

F_0 has been adopted by the industry as a measure of heat lethality for sterilization

The following function is used in **pharmaceutical** sterilizers to provide a measure for heat lethality:

$$F_0 = F * 10^{((T-121.1)/10)}$$

F is the time in minutes and T is the temperature in Celsius. For instance, if F_0 is to be calculated for one second and the temperature is 121.1 °C the function becomes:

$$F_0 = 10^{((T-121.1)/10)} / 60$$

Load probe temperature is used to calculate F_0 . During a standard sterilization cycle, each new calculation is added to Accumulated F_0 (AF_0). This total is provided to the display.

Instantaneous F_0 (IF_0) provides the F_0 of the last minute and is updated every 10 seconds.

Resolution for IF_0 is in hundredths; resolution for AF_0 is in tenths.

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The standard for the PRIMUS Bio → Pharma® sterilizer Pri-Matic™ control system is to use one RTD load probe to perform F_0 functionality. The process variables that are displayed on the Operator Display relating to the RTD load probe are:

Temperature

IF_0

AF_0

If "End Sterilize Based on AF_0 " is selected and the corresponding set value for the Accumulated F_0 (AF_0) has been achieved, the sterilize phase will complete.

A more technical discussion follows:

F_0 is the equivalent exposure time at 121.11°C of the actual exposure time at a variable temperature, calculated for an ideal micro-organism with a temperature coefficient of destruction equal to 10.

Firstly introduced by the National Canners Association in 1968 (a), F_0 has become a topic in pharmaceutical production since the FDA used it extensively in the "Proposed rules" of June 1st, 1976 (b), with the following meaning (section 212.3): " F_0 means the equivalent amount of time, in minutes at 121°C or 250°F, which has been delivered to a product by the sterilization process".

For the calculation of it, "a z-value of 10°C or 18°F is assumed; the term z-value means the slope of the thermal death time curve and may be expressed as the number of degrees.... required to bring about a tenfold change in the death rate".

In practice, the knowledge of the temperature values as the continuous function of elapsing time is not available, and F_0 is calculated as follows:

$$F_0 = \Delta t \sum 10^{\frac{T-121}{z}}$$

where:

DELTA t = time interval between two following measurements of T

T = temperature of the sterilized product at time t

z = temperature coefficient, assumed to be equal to 10°C

If we assume a sterilization lasting 15 minutes, constantly at 121°C, we obtain:

$$F_0 = 15 * 10^{\frac{121-121}{10}} = 15 * 10^0 = 15 * 1 = 15 \text{ minutes}$$

indeed according to the definition of F_0 .

If we assume sterilization lasts 15 minutes, constantly at 111°C, we instead obtain:

$$F_0 = 15 * 10^{\frac{111-121}{10}} = 15 * 10^{\frac{-10}{10}} = 15^{-1} = 1.5 \text{ minutes}$$

Therefore, a 15 minutes sterilization at 111°C is equivalent, in terms of lethal effect, to 1.5 minutes at 121°C; this can be easily expected if $z = 10$.

Similarly, if we assume a 15 minutes sterilization constantly at 124°C, we have:

$$F_0 = 15 * 10^{\frac{124-121}{10}} = 15 * 10^{\frac{3}{10}} = 29 \text{ minutes}$$

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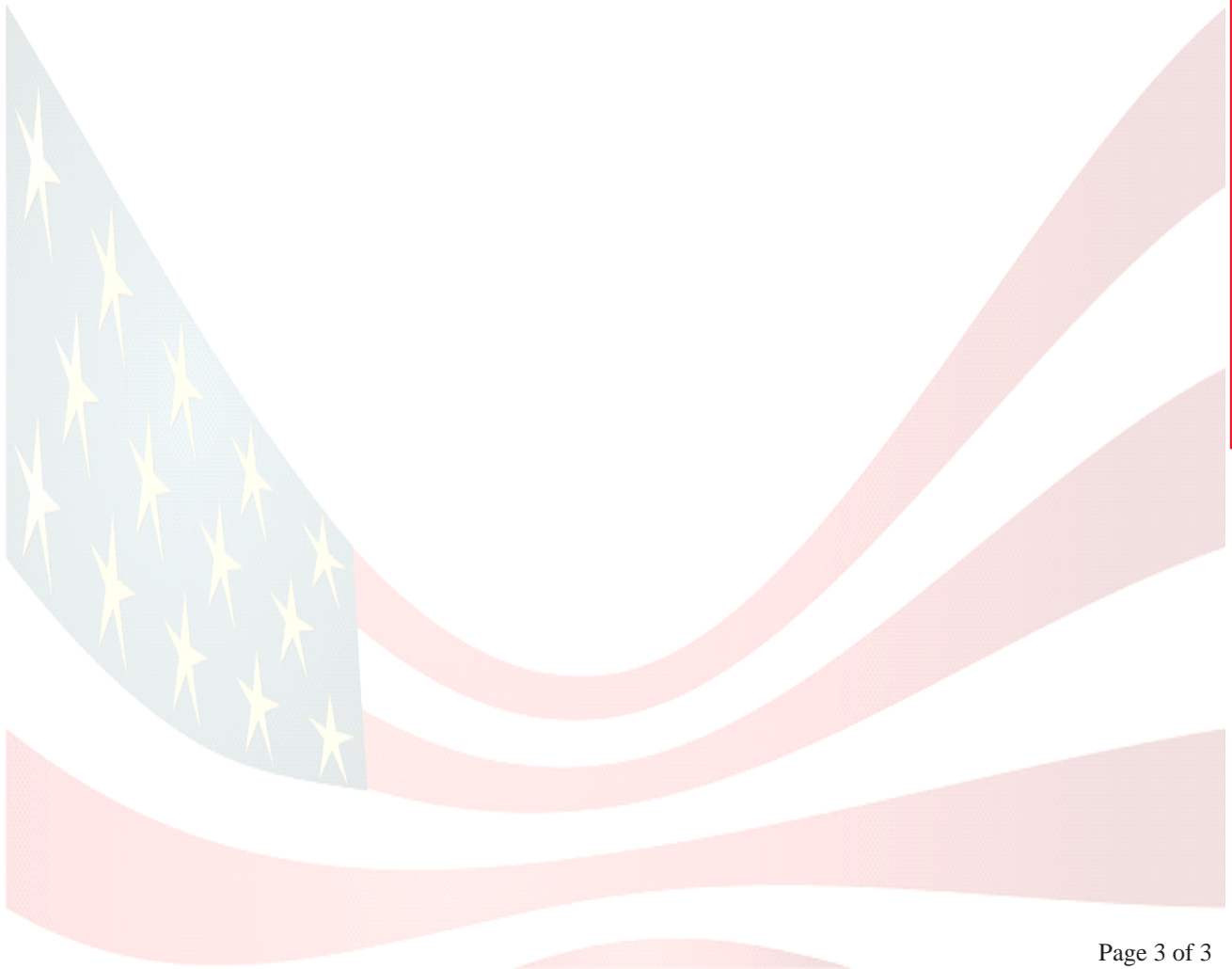
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It should be noted that although the Sterilize Phase ends when the Accumulated F_0 reaches the set point, Heat Lethality continues to be accumulated throughout the remaining phases. **Therefore, the final AF_0 will be higher than the set point.**



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