

January 2003 More on DEHT Issues

In October 2001, I wrote a Cleaning Memo on setting a Dirty Equipment Hold Time (DEHT). This month's memo provides additional reflections on the significance of challenging the cleaning process with the maximum DEHT. In addressing the maximum, one might ask, "Why challenge with the maximum time?" The answer is typically that the maximum time reflects the worst-case condition. As time passes, the soil (the manufactured product) on equipment surfaces may change its nature and become more difficult to clean. If the product has a volatile liquid, the residue may dry and become more difficult to clean. Other changes that may occur include microbial proliferation and degradation by mechanisms such as exposure to light or air.

As mentioned in the October 2001 Cleaning Memo, there are certain cases where time may have no effect on the difficulty of cleaning. An example might be cleaning of a tablet press. However, even in cases where the nature of the soil on the equipment changes over time, there may be a point at which no further change occurs in the soil (as least with respect to its difficulty of cleaning). If drying of an aqueous residue is the only factor in making it more difficult to clean, it is possible that once the residue becomes dried, any further increase in the time will have no effect on how difficult the residue is to clean. For example, in cleaning an aqueous based product, if the product becomes completely dry after 17 hours, then it may be possible to completely challenge the "worst-case" by making sure that in each validation run, the DEHT exceeds 17 hours.

If this approach is to be considered, what needs to be done? First, under conditions that simulate the amount of soil (manufactured product) and the drying of the soil on the equipment surfaces, the time of drying should be determined. This can be done by sampling the residue at intervals for moisture content or by measuring weight loss over time. If this is done, one should find that at a certain point the moisture content or weight becomes constant. The time at which this occurs defines the drying time (under specified conditions).

The next step should be some kind of laboratory simulation of the cleaning process to show no significant difference in cleanability between soils that have been dried at the simulated dry time (17 hours in the example cited above) and soils that have been dried for the maximum DEHT (which could be 36 hours, 48 hours or 72 hours). Note that suppliers of pharmaceutical quality detergents can assist in these types of cleaning evaluations.

Running these laboratory evaluations can provide a demonstration of when the residue becomes dry and of the fact that additional time does not significantly change the difficulty of cleaning. In utilizing this information, one might be tempted to just make sure that the DEHT in each of the three validation runs is at least as long as the drying time of the soil. While this can be defended, a better approach (at least until this has become more widely accepted) is to specify that one validation run be at the maximum DEHT (the maximum time specified in the cleaning procedure), with the other two validation runs being at times at least as long as the drying time of the soil. This latter approach prevents any potential problems that might arise in saying that once the drying time is exceeded, there is no maximum DEHT. While this might be the case, it is probably prudent still to specify a maximum DEHT and challenge at least one run of the three validation runs at that maximum time.

The purpose of this Cleaning Memo is not to specify what must be done for the DEHT in a cleaning validation protocol. Rather the intention is to present another alternative that might be applicable in given situations.