Environmental Monitoring and Investigations

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In both our own work and in discussions with other industry scientists, we have become aware of an escalation in the number of microbiological investigations being done in the event of so-called "excursions". We are of the opinion that when a process is outside its validated state of control as defined by a firm's process control efforts, investigations are absolutely necessary. However, we are finding that in too many cases events are being considered excursions when in reality they are nothing more than expected occurrences happening on a consistent background rate.

All industry microbiologists and aseptic processing experts understand very well that contamination will be observed at a low rate in even the most effectively controlled manned ISO 5 environments. This includes those areas of an aseptic process that are deemed "critical". Typically, a contamination rate (which is to say the observation of any contamination at all regardless of "level") is below 1% and in many cases below 0.5% in modern facilities. However, even at these low contamination rates this means that something like 1/100 to 1/200 samples will evidence growth. This could be termed the background recovery level, and it should be considered typical.

So, let's come right out and say it, the environments in which we aseptically process products labeled "sterile" are not sterile! Furthermore, as long as human operators including environmental samplers are working, they never can or will be sterile. Does it not then follow that if we define any contamination recovery as an "excursion" we are effectively investigating even when we are at or even below the normal background rate? It seems reasonable that we should investigate when we see more contamination than normal, but not when our results are within normal expectations. Investigating normal conditions it seems could be the very definition of busy work.

In our opinion the current situation arose when regulatory standards or "recommendations" began to imply that any contamination event above the level of zero within critical ISO 5 environments meant that an "action level" or "action limit" had been reached. There is general agreement among microbiologists that environmental sampling methods are simply not accurate, precise, sensitive or reliable enough to allow such fine distinctions to be made. In fact there is no real analytical difference between one colony forming unit (CFU), or say three CFUs. Also, zero growth does not mean that the environment is "sterile" it merely means that nothing grew. Really, we have no idea what the true sensitivity of microbial air or surface sampling is, but we do know that it is far less than 100% and that it is quite variable.

Perhaps the real issue is the idea that we can use environmental data to assess "sterility assurance". The belief that we can assess sterility assurance through monitoring leads to an absolutist approach to standard setting, which is

scientifically wrong. Long ago, industry and regulators agreed that it was not possible to test quality into products. Why can't we agree that monitoring the attribute of sterility into products is equally impossible? We urgently need dialogue among our competent regulatory authorities, compliance staff within firms and scientists to make sure that we are not investigating normal conditions. Doing is nothing more than a waste of quality assurance resources. We are fervent advocates of safe aseptic production, but safety is achieved through pragmatic scientific realism rather than busy work.

By all means we should be sure when our aseptic processing conditions are outside our normal range of control and when this occurs investigations are essential. However, investigating the normal is futile and wasteful. Since low level contamination is inevitable, an investigation into any recovery >0 is unreasonable. It should not surprise anyone that those required to conduct investigations of this kind struggle to find the hoped for "assignable cause". The reason for that is a simple one; there is no assignable cause for an expected and completely normal outcome. We humbly suggest that we reserve the excursion investigation for things that are not normal.