Striving for the highest Grade

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As a prototype for the future, is it possible to consider an energy efficient filter system that cost-effectively maintains airflow towards a reduced rate of change?

Michael Rodd, Chief Sales Officer at M+W Products (www.products.mwgroup.net) looks at elements of life sciences in the clean room and envisages how future practice can radically change the concept of clean room procedures.

It is common to expect the output of a clean room operation to end as a microprocessor in your phone, laptop or car, but in fact, the first measured effort to control an environment was used for medicinal purposes on a table in a hospital. British surgeon Joseph Lister in 1867, at a time when multiple surgeries were performed using the same contaminated equipment, sterilised his hand using carbolic acid and experimented implementing this technique on wounds and needles to discover the elimination of bacteria.

Although much has changed since, and both our efforts and realisations of scientific procedures have adapted, the dedication of modern life sciences was reinvigorated as a fairly new discipline of the clean room subdivision over the last century. This process encapsulates everything utilised by the way of clean room technologies in the production of medical substances, pharmaceuticals and biological compounds.

As the history of the pharma world displays, our requirement for a clean room stems from the need for contamination control. Whether that's using gloves during primitive operations or alcohol as an antiseptic to sterilise needles or creating paint and lacquer work out in uncontaminated air near the Pacific Ocean, our need to benefit from such processes has been fuelled by the requirement to control and clean our imminent environment.

This demonstrates something else too – that the clean room has developed from a permutation of science and engineering – assessing scientific processes that have worked and engineering them to deliver better results. This multidisciplinary approach has been encased by technological practices available at certain periods of time.

Fundamental to the field of life sciences and pharmaceutical micro biotechnology is contamination control. First and foremost, the apparatus used for pharmaceuticals in clean room laboratories should be dedicated and separated from other areas. Nailed down, this involves the classification between protecting the working environment and protecting the operator from any potential contamination. This is because humans remain the biggest cause of contamination; that may never change. To put this into perspective, the outer layer of human skin can host up to 1 million microorganisms per square cm, and equally, human saliva up to 1 billion per square ml.

The frenzy of microbes is difficult to keep on top of at every stage of the process. Basic negligence can cause the microorganisms from our clothes, mobile phones or bare skin to contaminate working stations. For instance, hands, whether gloved or un-gloved, are one of the main sources of spreading infection or transferring microbial contamination. Thus, an important part of good contamination control within a cleanroom requires the use of cleaning and disinfection agents. It goes without saying that just as personnel may be the biggest contaminants, they are also critical to the maintenance of asepsis in a controlled environment. Therefore diligence and training in clean room technology is essential throughout the entire process.

The improper analysis of microbiological inspections may cause inadvertent contamination. Therefore, thorough aseptic processing like product or microbial bioburden to calculate viable organisms is needed to prevent any sort of con-

tamination during the process stream. In some cases, even measuring total particulate count within a vessel does not cater for the continuous generation of organisms by individuals; therefore it does not always quantitate all contaminants and provide the whole picture of microbiological content. Microorganisms will associate with physical particulates and therefore it is necessary to include monitoring techniques that satisfy both the classification and regulatory requirements by differentiating the microbiological components of an operation. Stringent optimisation of tests will give assurance that bioburden of the environment is apt for *clean* laboratory practices.

In its simplest form, a product being operated within a clean room during a process line includes an enclosed vessel or large container that is sealed from external air temperature. Throughout this process, it is the aim of every operative to maintain conditions to a level where they can be declared sterile or aseptic.

A clean room is classified based on the cleanliness of its air so as far as clean rooms go, anyone wants to keep the environment as clean as possible. One of the trends we've seen across this spectrum (and it is a large spectrum) is on the lower end quality scale concerned with areas that are *Clean Not Classified* (CNC). These are areas that can be regarded *clean* within definitive purposes of the word in regards to the production area, but they are not actually *classified* because they work on a process we call Good Manufacturing Practice (GMP) or Current Good Manufacturing Practice (CGMP).

The ability to manufacture medical devices with consistent high quality relies on well implemented and well documented GMP. The GMP code sets out a guideline to achieve sterility assurance. Any business that delivers clean room technology requires constant monitoring and up-to-date certification.

The measurement most universally applied is the Grade A-D standard, whereby a cubic foot sample is taken of the environment and the number of particles greater than 0.5mm measured within it. Areas are classified on a graded system from A onwards, with A being the *cleanest*. So the purpose of a low quality CNC is to effectively get as close as possible to classification. D certified environments accept the inclusion of certain particles even in dynamic conditions (i.e. when people are operating within contained vessels) with turbulent airflow, whereas A certified environments deal with linear laminated airflow that is non-turbulent. Cleanliness is commonly achieved through the development of effective HEPA (High Efficiency Particulate Air) filtration and this is considered as clean as necessary for a GMP Grade A condition.

Let's complicate things a step further. Introduced here is the onion concept. Its name is derived from the idea that as you peel the onion, a processor must past through successive cleaner areas to reach the centre, non-turbulent, Grade A area. In essence, the onion concept caters for the disposal of multiple grade conditions within the same vessel or container.

Furthermore, the application of disinfectants on specimens reduces the microbial bioburden as we discussed earlier. Therefore, when collecting environmental monitoring samples, personnel should begin with Grade A locations and then move on to areas that are away from technical apparatus but still within the controlled zone.

This grade system is applicable in cases where processors and products are exposed during transportation, or operations that are required to be performed outside of sealed compartments. Grade B is commonly of high purity but does not necessarily involve laminate air flow. So the trick here lies in maintaining airflow to a certain speed. Essentially, imagine the onion concept: each time a layer of the onion is peeled, the amount of particulate or contaminated risk to the product is reduced.

For any sales or financial operative, however, this all costs money and clean rooms are an expensive market already. The integration of new technology and efficient solutions has ignited consid-

eration of future controlled environmental procedures to limit the number of air changes per hour. Can future systems be both more efficient and challenge the tradition of multiple air changes and still ensure constant clean air? This is a radical thought and not on the agenda yet, but with a global drive for efficiency and cost-saving mechanics already found within homes and our cars, is there a need for such ideas to be infused as part of the life science debate? A future model to strive for would be to find an energy efficient procedure of controlled environments that maintains the right quality and temperature at the lowest price possible. The future of pharmaceutical trends in the clean room is exciting.