Handy Helper

Application Note #07

Maintaining Sterility in Pharmaceutical Manufacturing How Digital Imaging with åCOLyte can Help

Introduction

At major pharmaceutical manufacturing facilities, microbiology Quality Control (QC) departments are responsible for testing tens of thousands of samples per month. These samples, often from several sites, are used to assess the sterility levels of, for example, the air in the plant or the water used to produce the pharmaceuticals. Most pharma companies operate an index system of acceptable levels of contamination, based on established international quality standards. This index ranges from 1 c.f.u (colony forming unit) /ml in critical samples such as the pharmaceutical products to 100 c.f.u/ml in the water used for production.

The reason plants producing pharmaceutical products have to be kept as clean as possible is the drugs they are manufacturing may be administered to patients suffering from life threatening conditions, such as cancer or heart disease. This means that many being treated could be immunocompromised, and accidentally introducing a simple, and in most cases harmless bacteria or fungi, could produce a serious infection in these people and may result in death.

Production facilities and the QC departments they serve are often geographically distant so communicating quality issues cannot be done in person but is a remote activity relying heavily on the use of email. Therefore, it is imperative that QC microbiologists generate images of culture plates clearly showing the microbial or fungal contaminant in question. These plate images are frequently the basis upon which decisions are taken to exclude certain personnel from the plant area, or in more serious cases, to shut down the plant for a total decontamination programme.

Capturing Images of Culture Plates

To record positive QC results many microbiology departments use either a standard or digital camera. Findings have to be recorded so that recommendations can be backed up and decisions on the appropriate course of action are available for discussion between production managers and QC department personnel.

The drawback of using either a standard or digital camera is that both require considerable skill to use them efficiently. Setting up the camera for optimum performance means users have to have knowledge of how a camera works to produce the highest quality images. Many microbiologists lack this type of photographic skill. Therefore, to resolve this problem many companies train a small number of members of the microbiology team in photographic techniques. They then produce the images for an entire department. This is not only time consuming but can result in positive plates not being photographed as they are generated but having to be stored or refrigerated until a suitable staff member is available to record the plate image. This batch type photography, although time efficient, can result in manufacturing plant staff not being alerted to contamination as rapidly as they could be and has the potential to allow minor problems to escalate.

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An additional difficulty QC microbiologists face with using standard or digital cameras is images need to be in a format which can be quickly and easily sent to the manufacturing facility. Production managers prefer to receive images via email, since posting them is too slow and faxing them does not produce a high enough quality image on which to base critical process decisions. Therefore, the problem which arises, is how to convert images into a format that is easy to email. This is simpler if a digital camera is used and software packages such as Adobe PhotoShop can help. However, the process is more time consuming if standard photography is used and involves using a scanner to produce a digital image.

Automating Image Capture

To overcome all the difficulties of capturing and storing images of culture plates, Synbiosis offers the åCOLyte system (Figure 1). Although primarily designed as an affordable colony counter, some major pharma companies are using åCOLyte as a quick and simple method of generating plate images. The reason for this is åCOLyte is easy to set up and requires no camera skills to be able to produce focused, full-colour on-screen images. The system's built-in LED illumination also offers optimised viewing of any plate type. Therefore, any microbiologist can use it with minimal training. The images can be automatically saved in a format, which is ready to email with a time and date stamp. Images are not only secure but are also GLP compliant and can be presented with confidence to external regulatory auditors. Some examples of the types of plate images åCOLyte can generate are shown in this application note.

Figure 1: A Synbiosis åCOLyte system

Monitoring Staff

Members of the teams involved in the manufacture and packaging of pharmaceutical products are asked to regularly place their finger tips and sections of their protective gowns on contact plates of an all purpose culture media such as Tryptone Soya Agar (TSA). The plates are incubated and if any fungi or bacterial appear, the most common being *Staphylococcus species* (Figure 2) staff are then encouraged to undertake a more rigorous programme of good hygiene practices. These include more regular gown changing and hand washing, as well as the use of antiseptic hand sprays.

Figure 2: Image generated by the åCOLyte system showing a TSA plate with Staphylococcus species colonies around the finger dab areas.
(Image kindly provided by AstraZeneca, Macclesfield, UK).

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Air Quality

TSA plates are placed open around the manufacturing areas to determine the sterility of the air circulating in the plant. The plates are incubated and if any contaminants such as mould or *Staphylococcus aureus* appear, a member of the production staff is alerted. In the case of moulds this often indicates a problem with the air filtration units resulting in contaminants not being filtered out quickly enough. In this case, the pressure of the filtration units is checked and a sporicidal clean-up process is initiated.

If the skin borne contaminant, *Staphylococcus aureus* is detected, it can often be linked to certain personnel. A corrective course of action with these staff is to encourage the use of antiseptic hand washes and antiseptic nasal sprays to prevent aerosols of these bacteria coming from their nasal passages. If these measures prove ineffective then these individuals have to be removed from critical aseptic areas.

Monitoring Water

Samples of water used in the production of pharmaceutical products are taken and mixed with molten R2A agar. This is poured into petri dishes, left to set and then incubated. If unacceptably high levels of bacteria, the most commonly seen being *E.coli*, are present then the filtration systems for the water have to be decontaminated.

Conclusions

åCOLyte is a versatile system and can capture images of contaminants growing on either pour, contact or spread plates. In addition, because the system has two arrays of LEDs for incident, transmitted and darkfield illumination, clear images of colonies can be acquired from a range of different coloured media types.

åCOLyte's software can be quickly installed on virtually any laboratory PC. The software's graphic interface is so intuitive to use that microbiologists can capture images in seconds with minimal training, making it easier for QC microbiologists to photograph their own results straight from the incubator. The image can also be emailed at the same time it is captured, thus rapidly alerting plant management to any potential issues and helping prevent the spread of more serious contamination.