



Handy Helper

Application Note #02

ProtoCOL Provides Accurate, GLP Compliant Results For Fast Assessment of Anti-microbial Therapies in Clinical Trials

Introduction

With the rush to get new anti-microbial therapies on the market to treat biological terrorism threats such as anthrax, methods of saving time at the clinical trial stage without compromising on accuracy are becoming increasingly important. Many new treatments for diseases caused by bacteria or yeasts concentrate on reducing or removing these micro-organisms from the affected area. Since colony enumeration provides the data on which product efficacy for most anti-microbial therapies is based, it is essential to obtain the most precise colony counts possible.

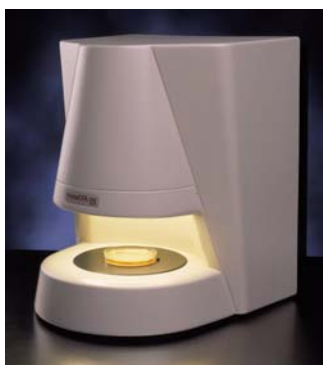
Manual Colony Counting – the Drawbacks

Manual methods of enumeration require users to count colonies using a light box and pen and then key the results into a computer. This is not only a time consuming and tedious task but leaves the way open for plate reading and computer keying errors to occur. In addition, because this method produces no computerised image of the plate alongside the colony count there is no means of carrying out an independent audit of the count (required for the approval of new therapies) to check the results for accuracy.

What's the Alternative?

To overcome the difficulties associated with manual counting and the lack of documentary evidence it produces, Synbiosis provides the ProtoCOL, a fully automated colony counter, (Figure 1). This fully integrated system combines a CCD camera with powerful software, which analyses plates, in accordance with published methods and automatically transfers the results to computer, thus preventing transcription errors.

Figure 1: ProtoCOL colony counting system



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The ProtoCOL is ideal for use in clinical trials because as well as being quality checked against validation standards it also provides a number of GLP compliant features that are essential when trial results are independently audited. These include automatic transfer of colony counting results into a table and storage in a secure database. The database is password protected and so ensures that, for instance, batches of results cannot easily be deleted. In addition, any editing of counts is recorded with a coded flag appearing next to the revised result. Every detail of the sample including pictures of the agar plates, system configuration, member of staff that read the plate, date and time are recorded in a professional report. This can be printed out and is of such a high standard that it can be presented to independent government auditors such as the Medicine's Control Agency (MCA).

Application of ProtoCOL in Clinical Trials

The ProtoCOL system is currently being used in clinical trials in the UK at the prestigious Skin Research Centre (SRC) part of the Microbiology Department at the University of Leeds. There the researchers are using the ProtoCOL to perform automated total viable counts of skin micro-organisms that have been spiral plated onto a range of selective media by a WASP spiral plater (Don Whitley Scientific Ltd, Shipley, West Yorkshire, UK).

The ProtoCOL at the SRC is being used to produce plate images and rapidly enumerate micro-organisms either implicated or directly associated with dermatological disorders such as acne, eczema, erysipelas, impetigo and folliculitis. These include propionibacteria on Reinforced Clostridial Agar (Oxoid, Basingstoke, UK) plus antibiotic supplements (Figure 2), coagulase-negative staphylococci on Iso-Sensitest Agar (Oxoid, Basingstoke, UK) (Figure 3), and the yeast, *Malassezia furfur* on a media, which has been formulated by the SRC and contains yeast extract, milk, lipid and cyclohexamide (Figure 4).

Figure 2: ProtoCOL generated image of propionibacteria growing on Reinforced Clostridial Agar containing the anti-staphylococcal antibiotic furazolidone

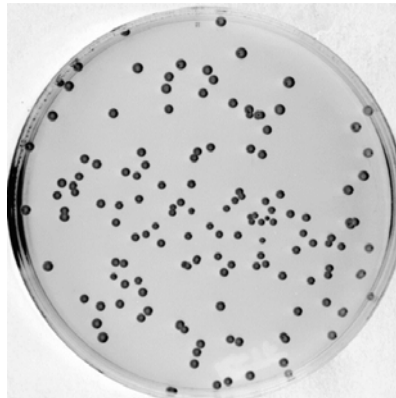
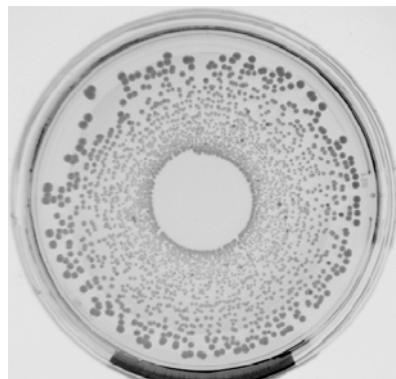
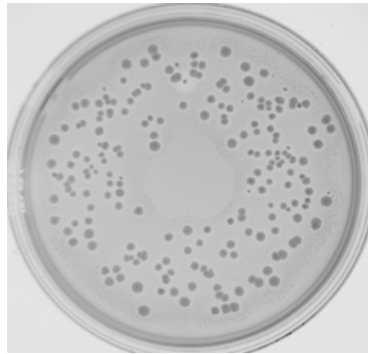


Figure 3: ProtoCOL generated image of coagulase-negative staphylococci on Iso-Sensitest Agar



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Figure 4: ProtoCOL generated image of Malassezia furfur on A1 medium containing yeast extract, milk, lipid, cyclohexamide and chloramphenicol.



Since the ProtoCOL uses software that automatically compensates for debris, bubbles, touching colonies, different sized colonies, coloured media and variations in agar thickness it produces highly accurate colony counts. The results of these counts are used to determine, which treatments are reducing the number of organisms on the skin of those on the trial, and is ultimately indicating the effectiveness of these new therapies.

The SRC has used the ProtoCOL system successfully for 18 months in conjunction with WASP spiral platers for all its clinical trials work based in Leeds. Recently, the SRC has diversified to provide mobile microbiology facilities for clinical trials. The ProtoCOL was used to enumerate organisms from a clinical trial of a new skin therapy carried out in GP and Primary Care Groups in Cornwall and at the University College Hospital Wales in Cardiff supplying microbiology services as part of a dermatology research study. Both studies have shown that using the ProtoCOL system, the SRC can complete a trial of 200 people in under two working weeks.

Conclusions

The use of the ProtoCOL colony counter in clinical trials at the SRC shows the system is flexible enough to generate precise, GLP compliant, automated plate counts of a range of different micro-organisms on a variety of selective media types and colours. This makes the ProtoCOL highly applicable for any pharmaceutical or biotechnology company which has to conform to GCP (Good Clinical Practice) guidelines on documenting and protecting data, yet is under pressure to produce potentially critical anti-microbial therapies that can be safely licensed and marketed in a reduced time scale.