

Article for *European Clinical Laboratory*

**Mobile Skin Microbiology Laboratory for Clinical Trials and Research
Offers Accurate Results and Alleviates Resource Shortages**

By

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Introduction

Abnormalities in the cutaneous microbial population of propionibacteria, coagulase-negative staphylococci and the yeast, *Malassezia furfur* are either implicated or directly associated with dermatological disorders such as acne, eczema, erysipelas, impetigo and folliculitis.

Therefore, most new treatments for these diseases concentrate on reducing or removing these micro-organisms from the skin's surface. Since most human dermatological conditions have unique features, animal models are not available and clinical trials of new treatments must be tested on human skin.

This presents a number of problems for those involved in clinical trials, particularly of acne therapies. Firstly, across Europe, it is becoming increasingly difficult to recruit enough affected subjects in one geographical area since at least 200 individuals per specific clinical trial are required. Consequently, there has been a recent shift towards multi-centre trials to ensure that a large enough population can be both recruited and tested because trial attendees then have greater accessibility to a local clinical centre.

One major difficulty with skin sampling is that once skin micro-organisms have been removed and put into a liquid storage medium their viability begins to drop very rapidly. For example, approximately 20 per cent of skin microbes stored at room temperature in phosphate buffered saline (PBS) die after 1 hour and if the sample is left for 24 hours less than five per cent of them will be viable. Since enumeration provides valuable data on product efficacy, it is essential that the most accurate count is obtained. Samples therefore, must be rapidly plated out and the best way to achieve this is to process them at the location they were taken.

However, many routine diagnostic microbiology facilities at multi-centre trial sites do not usually have the skill or expertise to provide specialist skin microbiology services, and are also unable to assign staff on a regular basis to process non-urgent samples for clinical trials.

To overcome all of these sample collection and quantitative processing problems the internationally recognised Skin Research Centre (SRC) at the University of Leeds has recently equipped and is using a Mobile Microbiology Laboratory Unit. The Unit provides specialist independent microbiological expertise and resources for clinical trials as well as *in vitro* evaluations of dermatological products using the wealth of knowledge that the SRC has built up in skin microbiology since 1975.

Microbiology on the Move

Since clinical trials to test the efficacy of products to treat for example, acne involve basic microbial techniques that do not require complicated equipment or space, it makes perfect sense to have a mobile laboratory for this purpose.

The SRC chose a 7.5 tonne truck (the largest vehicle that can be driven with a car licence in the UK) as its Mobile Microbiology Laboratory Unit so that it did not have to employ an HGV driver to move it from one trial site to another. Employing a driver would have added a considerable cost to the mobile service, making the venture economically non-viable.

The truck has an internal working space of 6 m x 2.5 m, which is divided into a waiting area, where skin sampling takes place and a laboratory where samples are processed. The truck also has its own generator to provide electricity and air conditioning and can be situated in any hospital or medical centre location that has a suitable car park.

Equipping a Mobile Microbiology Laboratory

The laboratory area is equipped with three cooled incubators, which saves on space since they can be used both for incubation or refrigeration as required. It also has three WASP spiral platers (Don Whitely, Shipley, West Yorkshire, UK), Bunsen burners and mixers. SRC staff chose the WASP for the Unit because it gives highly consistent results and is also robust enough to survive long journeys in a truck.

Running a Mobile Laboratory for Clinical Trials

Three staff members run the Unit, two to sample the skin, while the third member of the team simultaneously processes the samples. Only the microbiology division of the SRC at Leeds, which has six full-time and eight part-time microbiologists can support this level of activity because it can keep rotating the travelling staff around so that it does not cause too much pressure on human resources.

Sampling Skin Micro-organisms

Patients attending the clinic area of the Mobile Unit for sampling can have their cutaneous microflora sampled using a range of established techniques. These include techniques for sampling micro-organisms on the skin surface, in the pilosebaceous follicles, from skin squames and from scalp skin. Appropriate techniques are available for sampling from all areas of the body. Once the samples have been taken they are processed immediately using the on-board facilities.

The microbial suspension is spiral plated using the WASP system onto a range of media that are selective for skin micro-organisms. To culture propionibacteria SRC staff use Reinforced Clostridial Agar (Oxoid, Basingstoke, UK) plus antibiotic supplements, for coagulase-negative staphylococci they use Iso-Sensitest Agar (Oxoid, Basingstoke, UK) and for the yeast, *Malassezia furfur* a media, which has been formulated in-house and contains yeast extract, milk, lipid and cyclohexamide is used.

The plates are incubated for an appropriate time *Malassezia furfur* (14 days), propionibacteria (7 days) and coagulase-negative staphylococci (48 hours). After incubation, the plates are refrigerated on-board if required so that total viable count can be carried out back at the central SRC laboratories in Leeds using a ProtoCOL, automated colony counter (Synbiosis, Cambridge, UK). (Figure 1)



Figure 1: ProtoCOL colony counting system used by the SRC at Leeds University.

The SRC chose the ProtoCOL system for colony counting because as well as being quality checked against validation standards it also offers a number of GLP compliance features that are essential when the SRC's clinical trials results are MCA 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, staff member, date and time are recorded in a professional report, which is printed out and presented for the MCA audit.

The Mobile Microbiology Unit does not have a ProtoCOL installed inside it as standard operating procedures allow for short-term refrigerated storage of plates after incubation and transfer of the plates back to the SRC in Leeds for counting. However, if the Mobile Unit were to travel to places outside the UK and be away from base for extended periods of time, then it may become necessary to install a ProtoCOL in the Unit so that counting can be done whilst on the road.

An alternative method for remote plate counting that the SRC is currently piloting is to store and send digital images of the plates from the Mobile Unit. These images are taken in the Unit with a digital camera system and emailed to the central laboratory in Leeds for colony counting with the ProtoCOL system. If this proves successful then the Mobile Unit will only need to install a digital camera to be able to enumerate trial results from samples taken anywhere in the world.

Results

The SRC's Mobile Microbiology Laboratory Unit was commissioned in August 2001. To date the Unit has been successfully used by a multi-national company for a clinical trial of a new skin therapy based 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 demonstrated that the Mobile Unit manned by three experienced staff is functionally and logistically capable of collecting and processing up to 80 samples per day and could process up to 18 samples per hour with additional manpower. This level of sustained workload is only possible because of the speed and reliability of the WASP spiral platers compared to manual methods. The

consistency of the plating system is complemented by the automated ProtoCOL colony counting system, which produces accurate, consistent and traceable results with greatly reduced operator fatigue.

Conclusions

Using a Mobile Microbiology Laboratory Unit in multi-centre studies allows accurate counting of viable microbial numbers, as well as consistent data collection without the need to establish specialised microbiological facilities at each participating site. The use of a Mobile Unit in conjunction with GLP compliant equipment such as the WASP spiral plater and the ProtoCOL colony counter in the SRC's central laboratory ensures compliance with GCP guidelines on protecting data quality and documenting results. This now makes it possible to offer rapid on-site testing of potential new treatments for skin disease, which would otherwise have only been available at specialist hospitals or major clinical centres.

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