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Content and Abstracts

Science and Technology Feature

The current state of PCR approach in detection and identification of carbapanem hydrolysis β-lactamases genes

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Antibiotic resistance is arguably the most serious health-related issue of the current time. This is even more so with carbapenem-resistant Enterobacteriaceae, for such microorganisms are resistant to the carbapenems (the 'antibiotics of last resort'). One of the most important considerations is in the detection of bacteria that carry the carbapenem-resistant gene. For this, molecular-based phenotypic and genetic-based polymerase chain reaction (PCR) methods are available. In contrast to phenotypic methods, molecular-genetic techniques, such as PCR, are considered to have the potential for improved detection of carbapenem-resistant genes by virtue of specificity, accuracy and rapidity. The tendency in PCR techniques is to develop

towards the real-time systems equipped with multiplexing functionality. However, as shown in our study, standard PCR with electrophoresis detection continues widely to be used for the detection and identification of the carbapenemase gene. Therefore, despite progress in PCR technology, methods deployed for the detection of serious hospital-acquired infections around the world are arguably neither the most accurate nor the most efficient. This issue is of concern for pharmaceutical scientists in relation to the use and development of PCR technology and in relation to new drug development.

Key words: PCR, carbapenemases genes, electrophoresis detection, antibiotics, antibiotic resistance, hospital infection, Enterobacteriaceae.

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Science and Technology Feature

Shifting liability from the pharmaceutical company to the supplier

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Shifting liability from the pharmaceutical company to the supplier saves money and efforts of testing. It requires a transfer of the duties to take care to that party within the chain, where the risks arise in the manufacturing process. Adopted by suppliers, this reduces the risk of product defects. For the remaining risks, sufficient insurance coverage should be put in place by the supplier.

Key words: Tortious liability, strict liability, EU Directive for product liability, warranty, fault, quality assurance agreement, transfer of obligations, General Conditions and Terms of Business, GMP, inspection of incoming goods, verification of suppliers, contracted-out services.

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Science and Technology Feature

Review of core principles and best practice in the teaching of aseptic manufacturing in UK Schools of Pharmacy

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As a Level 7 MPharm project, a study was carried out on how the Schools of Pharmacy within the United Kingdom teach aseptic technique to undergraduate students. A questionnaire with open questions was sent to all the schools offering a validated Master of Pharmacy degree in the academic year 2010–2011. The data were then used to design a second questionnaire with closed questions. The responses were analysed and areas of good practice identified. How these areas may be incorporated into the Liverpool John Moores University programmes is discussed.

Key words: Aseptic Manufacture, Cleanroom, Education, Clothing, School of Pharmacy, Environmental Monitoring.

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Content and Abstracts

Determining incubation regime and time to results for automated rapid microbiology EM methods

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The use of growth-based rapid microbiology methods (RMMs) requires a time to result (TTR) to be determined with a defined incubation regime in order to obtain accurate results and take full advantage of potential time-savings provided by the RMM. A case study involving an environmental monitoring (EM) application to illustrate the simple process was performed using the automated Growth Direct™ System. Recovery of a suite of in-house bacterial and mould isolates was examined at different incubation profiles to define the optimal regime to obtain the best recovery. Of the three, serial incubation at 22.5°C followed by 32.5°C was identified as optimal for the recovery of both the bacteria and mould. A TTR of 72 h for this incubation profile was calculated, and the accuracy of the TTR was confirmed by comparison of the Growth Direct result with spread controls of the test organisms followed by equivalence testing versus the standard method using EM samples. An alternative regime of a single temperature of 28°C was subsequently examined, and resulted in a 60 h TTR, and comparable recovery versus the control spread plates indicating that this may be a viable alternative to serial incubation.

Key words: Time to results, TTR, rapid microbiology methods, growth-based detection, Growth Direct System.

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Factors influencing the HEPA filter leak test result: assessing the risk of a pass

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The High Efficiency Particulate Air (HEPA) filter installation leak test checks HEPA and Ultra Low Penetration Air (ULPA) filters for leaks in situ. The test is designed as an on-site test to check HEPA/ULPA filter cells for integrity and seals for tightness after installation. The test is undertaken because HEPA filter media and seals are easily damaged if they are not handled correctly during transport and installation. The test can be performed either with an aerosol photometer or with a discrete particle counter (airborne particle counter). This article is confined to the more widely used test performed with an aerosol photometer and associated artificial aerosol challenge.

In the pharmaceutical industry, the desired result of the test is a well-defined "PASS" or "FAIL". However, a number of factors which influence the result of the test are not routinely accounted for and filters which have met the acceptance criteria may, in fact, fall short of the requirements. Those filters which meet the requirements of the test performed may still have significant defects.

Key words: HEPA, Photometer, Aerosol, Scan, Leak, 0.01%.

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Clothing systems evaluated in a dispersal chamber

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A dispersal chamber or "body-box" has been used for studying the protective efficacy of different types of clothing systems for cleanrooms and associated controlled environments, such as operating rooms. Measurements were carried out in order to relate airborne dispersal of particles and bacteria-carrying particles to the quality of fabrics and the design of clothing systems. The results show the relevance of dispersal chamber testing in the evaluation of clothing systems.

Key words: Dispersal chamber, body-box test, airborne contamination, clothing systems, contamination sources, source strength.

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Content and Abstracts

Assessment of the suitability of R3A agar for the subculture of microorganisms isolated from pharmaceutical water systems

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Microbiological quality control of pharmaceutical water systems is of importance in ensuring that trends in contamination are detected and responded to. This is not least because water is a niche environment for many types of microorganisms and a vector for their transfer. Trending relates to actual microbial counts recorded, incidents and the types of species recovered. To facilitate species identification, microorganisms need to be subcultured from the isolation medium (Reasoner's 2A (R2A) agar in Europe). Transfer onto the wrong media can result in the microorganism not growing. This paper describes research into three different media for subculturing: low nutrient (R2A); highly nutritious (tryptone soya agar) and medium nutrient (R3A) and concludes that a higher recovery is obtained where R3A agar is used

Key words: Airborne bacteria-carrying particles, air flows, clothing systems, source strength, ongoing surgery.

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Performance of clothing systems in the context of operating rooms

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The number of airborne bacteria-carrying particles in the operating room is considered an indicator of the risk of infections to the patients undergoing surgery susceptible to infections. The filtration efficacy of the fabric and the design of the clothing systems affect the number of bacteria-carrying particles in the air during ongoing surgery. Results from different clothing systems evaluated in the operating room during ongoing surgery will be discussed.

Key words: Airborne bacteria-carrying particles, air flows, clothing systems, source strength, ongoing surgery.

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Science and Technology Feature

The critical factors and the potential impact of temperature excursions on biotechnology products in frozen storage

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There are no papers specifically dealing with temperature excursions in the cold storage of biotechnological products, particularly those in early-stage clinical trials where the optimal stability and storage conditions may not be fully known or understood. This paper gathers together available information to provide a framework for risk assessment when defined low temperature storage conditions have been breached. In particular, this paper draws attention to the various transition temperatures which may alter product stability or quality.

Key words: Biotechnology, investigational medicinal products, freezing, thawing, crystallisation, glass transition, storage, stability, risk assessment.

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Calculation of air supply rates for non-unidirectional airflow cleanrooms

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This article describes a method for estimating the air supply rate required in non-unidirectional airflow cleanrooms to obtain a required concentration of airborne particles and microbe-carrying particles. The variables considered are: surface deposition, emission rates of airborne contamination from personnel and machinery, filter removal efficiency, effectiveness of cleanroom garments, effectiveness of air supply distribution, and the contribution of filtered air from clean air devices. Consideration is also given to the variability of airborne contamination in cleanrooms, and the air supply rate required to ensure that the required airborne concentration will be rarely exceeded.

Key words: Calculation of air supply rates; airborne contamination; non-unidirectional airflow cleanrooms; airborne particles; microbe-carrying particles.

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Assessing airborne contamination using a novel rapid microbiological method

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The cleanliness of changing rooms used to access pharmaceutical cleanroom facilities is of considerable importance. This ensures that the changing environment and the act of putting on cleanroom suits do not generate high levels of contamination; for such contamination might be carried on personnel leaving changing areas and into the process areas. Furthermore, it is important to avoid the transfer of contamination to the outside of the garment during the gowning process. A study was undertaken to assess the levels of airborne contamination in a changing room during use. To assess this, a changing room was examined under different conditions: at-rest; occupied (with different numbers of personnel); and post-use. For the assessment, a novel rapid microbiological method was used. The assessment of microbiological air quality within changing rooms is conventionally undertaken using methods which rely upon microbial growth media. Due to incubation times, several days are required to ascertain the contamination level risk. This paper describes the use of an alternative real-time continuous monitoring system (the BioVigilant IMD-A® System), based on optical spectroscopy. The paper concludes that increasing the numbers of personnel going through a changing room increases the level of airborne biological activity and increases the length of time required for the room to recover. The study also demonstrates the usefulness of the rapid microbiological method.

Key words: Environmental monitoring, microbiology, rapid microbiological methods, particle counting, microbiological agar, spectrophotometric, real time monitoring, IMD-A®, viable but non-culturable microorganisms, cleanrooms, changing rooms.

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Science and Technology Feature

Development and current state of installed HEPA filter leak testing

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For the leak testing of installed HEPA filters in cleanroom environments, two testing procedures are available: aerosol photometers and discrete particle counters. This paper provides a short outline on the historic development, current state and characteristics of both procedures.

Key words: Installed HEPA filter leak testing, ePTFE membrane media, aerosol photometer, discrete particle counter.

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