The methodology for this research project followed those adopted by Lorcheim, Lorcheim and Czarneski (2009) and again by Lorcheim (2011). The three chemical indicator coupons for each of the two beta-lactams were removed and returned to the laboratory for analysis. All other equipment was then removed from the site.

Chemical indicators (CI) of various materials (316L Stainless Steel, Aluminium and Perspex (Acrylic) were used to validate successful inactivation. The CIs were impregnated with two strains of beta-lactams manufactured in the facility (1 ml of 500 ppb Amoxicillin and Penicillin V (each) in methanol). The three carrier materials were selected for testing based on their prevalence in the manufacturing workplace. The carriers were approximately 100 mm long by 100mm wide by 5-mm thick. Validation of recovery was completed on control samples (n=8). Prior to deploying the CIs into the facility, each sample was labelled with a location number and material number. The site locations for each set of chemical indicators are shown in Figure 1. In total, there were 80 samples of each material used with a total number of 240 samples.

The following results were obtained from the chemical indicator data and concentration of chlorine dioxide (CD) gas from the study. Table 2a shows the mean post-decontamination concentrations of the two beta-lactams. Figure 2a shows the concentration of chlorine dioxide (CD) gas from each of the twenty sampling points and it can be seen that in all locations that the minimum exposure of 7200 ppm-hrs was achieved. The mean post-decontamination concentrations for both Amoxicillin and Penicillin V in all samples was well below the adopted EEC level of acceptance of 50ppb. The post-decontamination results, it is feasible to assume that the decontamination of the Pharmaceutical Facility was successful and may now be reprocessed, reused or demolished.

ACKNOWLEDGEMENTS

The author would like to acknowledge the assistance of Mr. Mark Czarneski from Geobiology, Takushima for technical advice and all others who assisted with this project. We would also like to acknowledge Prof. Joseph Cole from Edith Cowan University for advice on statistical methods and interpretation.

REFERENCES


Figure 2a shows statistical analysis from results for the three materials

<table>
<thead>
<tr>
<th>Test Material</th>
<th>Penicillin Type –</th>
<th>Amoxicillin –</th>
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</thead>
<tbody>
<tr>
<td>aluminium</td>
<td>0.761</td>
<td>1.831</td>
</tr>
<tr>
<td>Stainless Steel</td>
<td>2.287</td>
<td>5.085</td>
</tr>
<tr>
<td>Perspex (Acrylic)</td>
<td>0.761</td>
<td>1.831</td>
</tr>
</tbody>
</table>

Table 2a – Concentration of chemical indicator coupons at each of the twenty sampling points

Site remediation of a penicillin production facility using Chlorine dioxide gas as a sterilant

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This health risk to both workers at Beta-lactam production facilities and the public at large has led to Pharmaceutical companies having purpose built reaction caused by the release of mediators from certain types of white blood cells and organs which are often dedicated to Beta-Lactam production for the life of the facility and equipment therein to levels of less than 50ppb Maximum Residual Level (MRL) (50 ug/kg) (EEC, 1990) was required for re-purposing facilities, the European Regulation Standards EEC (1990) which covered the facility and equipment using liquid disinfectants and sterilants, however re-use or re-purposing either the building or the equipment is often dedicated to Beta-Lactam production for the life of the facility and equipment therein to levels of less than 50 ppb Maximum Residual Level (MRL) (50 ug/kg) (EEC, 1990) was required for re-purposing facilities, the European Regulation Standards EEC (1990) which covered the facility and equipment using liquid disinfectants and sterilants, however re-use or re-purposing either the building or the equipment inside (Lorcheim, 2011) and again by Lorcheim (2011). This project was adopted for this project.

As there is no International Standard prescribing the minimum beta-lactam residue for re-processing facilities, the European Regulation Standards EEC 2377/90 of beta-lactam residue in dairy products for safe consumption of less than 50ppb Maximum Residual Level (MRL) (50 ug/kg) (EEC, 1990) was adopted as the equivalent safe level for the purposes of this project.

The air of this research project was to decontaminate the facility and all equipment therein to levels of less than 50ppb Maximum Residual Level (MRL) (50 ug/kg) (European Regulation Standards EEC 2377/90) was safe for re-use or reprocessing; for both Penicillin strains, Penicillin-V and Amoxicillin and to determine if there has been a significant reduction in residual penicillin concentration for both strains pre- and post-decontamination.

ABSTRACT

The methodology for this research project followed those adopted by Lorcheim, Lorcheim and Czarneski (2009) and again by Lorcheim (2011). The two strains were Penicillin-V and Amoxicillin. Successful decontamination was achieved with concentration levels of Chlorine dioxide of 7200 ppm-hrs (5mg/l, for 10 hours) and the chemical indicator coupon analysis penicillin concentration was below 50ppb (EEC, 1990). The facility has been re-used for a different application.

INTRODUCTION

Penicillin and other beta-lactams (the core structure of many antibiotic families) have been used in clinical treatment of virus and other infections in patients for over half a century (Alderman, 1991). However, the use of penicillin and other beta-lactam strains has been limited in the clinical treatment of infectious diseases by the number of cases of allergy or hypersensitivity to these antibiotics (Chang et al, 2013). In some case studies, hypersensitivity has been observed in 10-20% of cases resulting in diarrhea, rash, urticaria, and superinfection such as candidiasis (Chang et al, 2013). Inflammation and pain at the injection site are also common for intravenously administered penicillin with less common adverse reactions such as fever, vomiting, erythema, dermatitis, angioedema and seizures (Romano et al, 2001). In some case studies, 0.01-0.04% of patients displayed anaphylaxis, a severe allergic reaction or caused by the release of mediators from certain types of white blood cells triggered either by immunologic or non-immunologic mechanisms (Chang et al, 2013) and can be fatal 0.0015% of cases or in 1 of 50,000 (Chandra et al, 1988).

This health risk to both workers at Beta-lactam production facilities and the public at large has led to Pharmaceutical companies having purpose built facilities for the manufacture of Beta-lactam products separate to their main manufacturing plant during remediation.

There was a statistically significant difference between the pre- and post-decontamination swabs (p<0.05 – t-test Excel) for both penicillin strains. The reduction in concentration to low levels (<50ppb) was significant from a pre-decontamination control mean of 129.82 and 317.24ppb for Amoxicillin and Penicillin-V respectively to a mean range of 0.05-1.47ppb for both which suggests that the Chlorine dioxide is effective at inactivating these two strains. An area of further investigation may be to determine if there is any statistical difference between the three materials used as the carrier for the penicillin strains and to determine if there are any material compatibility differences on Chlorine dioxide’s ability to inactivate on different materials.

Methods

The three chemical indicator coupons for each of the twenty sampling points (80 locations x 3 materials; 316L Stainless Steel, Perspex (Acrylic) and Aluminium. RESULTS

The following results were obtained from the chemical indicator data and concentration of chlorine dioxide (CD) gas from the study. Table 2a shows the mean post-decontamination concentrations of the two beta-lactams. Figure 2a shows the concentration of chlorine dioxide (CD) gas from each of the twenty sampling points and it can be seen that in all locations that the minimum exposure of 7200 ppm-hrs was achieved and for both strains were below 50ppb which would suggest that the decontamination using Chlorine dioxide was successful. This is synonymous with Lorcheim (2011) who showed a similar level of inactivation of penicillin strains.

At all gas sample locations, a minimum of 7200 ppm-hrs exposure to Chlorine dioxide gas was achieved. In fact, in most locations, the exposure of Chlorine dioxide gas was greater than 10,000 ppm-hrs. In all chemical indicator samples, the post-decontamination penicillin concentration was well below the 50ppb adopted EEC standard level for acceptance. Whilst there was variability in the data, all individuals and mean concentrations for both strains were well below 50ppb which would suggest that the decontamination using Chlorine dioxide was successful. This is synonymous with Lorcheim (2011) who showed a similar level of inactivation of penicillin strains.