Scrubbing up the environment: The beneficial impact with reduced cleanroom environmental contamination following an upgrade to change facilities and procedures

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Introduction

The Pharmacy Production unit at University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) is a Medicines and Healthcare Products Agency (MHRA) licenced facility holding a Manufacturers Specials (MS) licence and Manufacture/Importation Authorisation for Investigational Medicinal Products (MIA (IMP)). The unit carries out aseptic preparation of injectable doses and eye drops as well as non-sterile production of oral and topical dose forms.

At an MHRA inspection in April 2017 it was reported that the changing facilities required improvement, as employees had to pass through an unclassified area straight into a grade C area with only one change. As a result outdoor clothing, along with environmental contaminants, were being bought into changing areas that lead to grade B and C cleanrooms. This was in direct contradiction to the current recommendations within the EU Good Manufacturing Practice (GMP) Annex 1. To address the deficiency a business case and a bid for capital funding was submitted to fund a refurbishment of the department to build improved changing facilities. The improved changing facilities would enable the staff to wear dedicated clothing within the department instead of their own “outside” clothes. The refurbishment would also provide improved hand washing facilities at the point of entry to the department and a new assembly area for aseptic products to improve the process flow for aseptic work. The business case and bid for capital funding, supported by evidence of deficiencies reported in the inspection, was successful and a budget was allocated for the refurbishment work.

In addition, the Quality Assurance team (responsible for assessing environmental monitoring plates and creating action reports for any out of specification (OOS) results) had reported concerns regarding the number of action reports being issued for certain locations. Areas of key concern were cleanroom 4 and its associated change and the initial change room 1 used for entry to the aseptic suite.

In early 2020 the refurbishment of the department was completed and focus was turned towards dedicated clothing for staff to wear within the department. It was decided that the staff would change in to scrubs on arrival, that these would be worn for the day and then sent for laundering at the end of each working day. Feedback received from staff regarding practicalities and working processes led to a suggestion of having 2 sets of scrubs. Light pink scrubs would be worn by the staff under their cleanroom garments when working in the grade B cleanrooms, while burgundy ones would be worn in the rest of the department. This decision was adopted on the provision that supplies of scrubs be readily available within the hospital, that there was a supply of scrubs that could be separated from the scrubs in general use around the hospital and processed separately, and that the scrubs could be laundered on a daily basis using the trust linen contract and following procedures that were already in place for the hospital. It was possible to introduce the scrubs at a relatively low cost, particularly when compared to the cost that would have been incurred had we obtained clothing from our cleanroom garment supplier. The wearing of scrubs was introduced on 1st July 2020 following a change control process and this was well received by the staff.

Changes in environmental monitoring results

As expected, following the introduction of wearing scrubs, we noticed an immediate and significant reduction in the number of colony forming units (CFUs) being grown on the department passive settle plates. **Figure 1** illustrates the number of CFU’s detected on passive plates within the aseptic unit, dramatically decreasing by 68% in the first month. After the intervention, the mean number of CFU’s seen reduced from 2036 (Jan –Jun) to 624 (July- Jan). The reduction in CFU numbers has been maintained and we now have data for the three years following the change confirming the decrease.

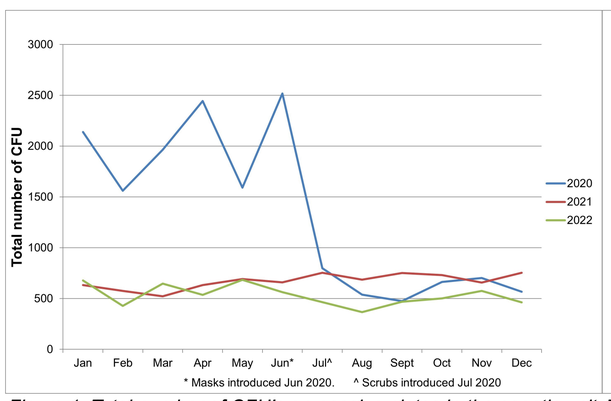

Figure 1: Total number of CFU’s on passive plates in the aseptic unit

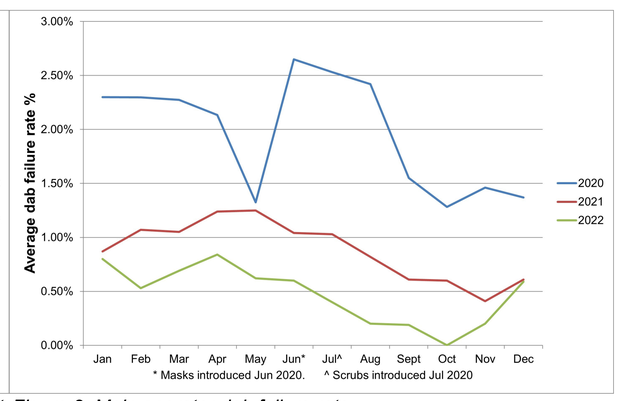

Figure 2: Main operator dab failure rate

Another positive and immediate result, along with observing a reduced number of CFUs on passive settle plates, was a decrease in operator finger dab failure rates (as shown by **Figure 2**). The finger dab failure rate reduction (along with other measured quality assurance controls) provides continued confidence in the preparation and supply of safe injectable medicines.

Coincidentally, the numbers of recorded moulds detected across passive and active air sampling plates have remained relatively stable (**Figure 3**), suggesting the new gowning procedure has had less of an impact on reducing mould and fungi contamination within the production unit. A high level investigation into the anomaly result seen in November 2020 established a deficiency associated with tray cleaning — specifically those used to transfer stock to and from the department — and was noted as the probable root cause.

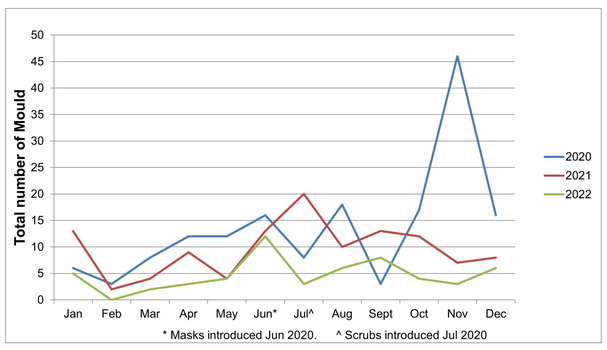

Figure 3: Total number of mould on passive and active plates

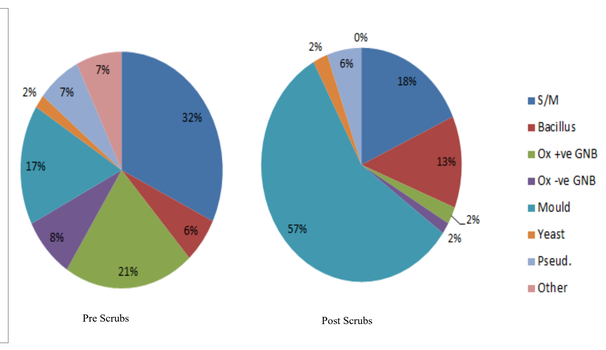

Figure 4: CFUs identified on passive plates between January to June 2020 (Pre scrubs) and July to December 2021 (Post scrubs)

From July 2019 to July 2020, 261 colonies were identified as Staphylococcus/Micrococcus sp. This dropped to 56 colonies for the same time period between 2020 and 2021.The predominant organisms previously grown in the department have been skin commensals (Staphylococcus epidermidis, Staphylococcus haemolyticus, Micrococcus luteus, Kocuria rhizophilia) and this is one area where a reduction in CFU’s has been greatest (**Figure 4**).

Additionally in June 2020 wearing surgical face masks became compulsory in healthcare settings as part of the UK response to the COVID-19 pandemic and so this was also considered when assessing if this had an impact on the number of CFU’s being grown on settle plates. As an immediate reduction in CFU’s in June was not seen (i.e. when face masks were worn), this change was considered less significant than the immediate reduction seen in July 2020 following the introduction of scrubs.

The most significant reduction in passive plate CFU’s has been seen in the cleanroom changing rooms (**Figure 5 and Figure 6**).

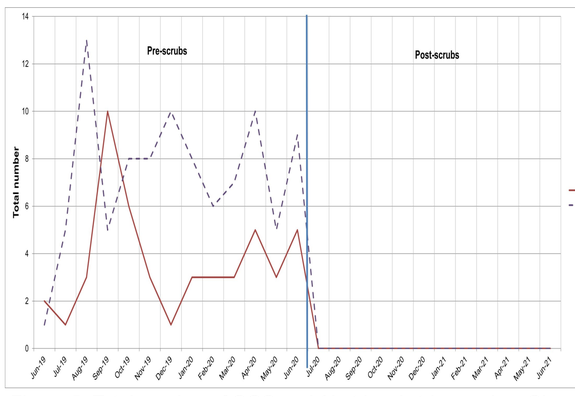

Figure 5: Total number of OOS and Alert levels triggered on Change 1 plates between Jun 2019 and Jun 2021

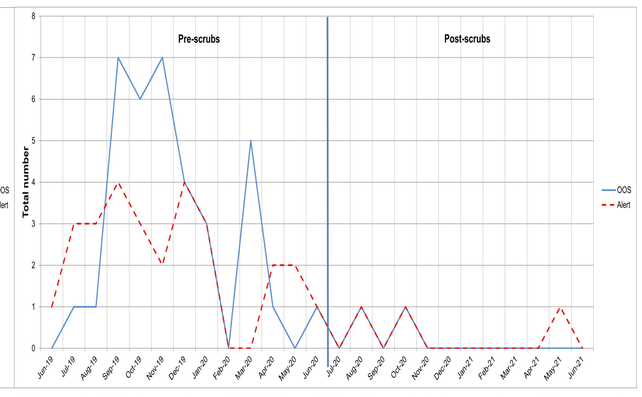

Figure 6: Total number of OOS and Alert levels triggered on Change 4 plates between Jun 2019 and Jun 2021

Prior to the introduction of scrubs, staff were required to remove their outside clothing in the changing room adjacent to clean rooms and strip down to their underwear before donning their sterile cleanroom suits. The new change procedure, which requires the addition of a cleanroom suit over the cleanroom specific scrubs (rather than removal of clothes), is likely to have reduced the shedding of particles and skin cells associated with the removal of outside clothing in the changing rooms, as shown in **Figure 7**.

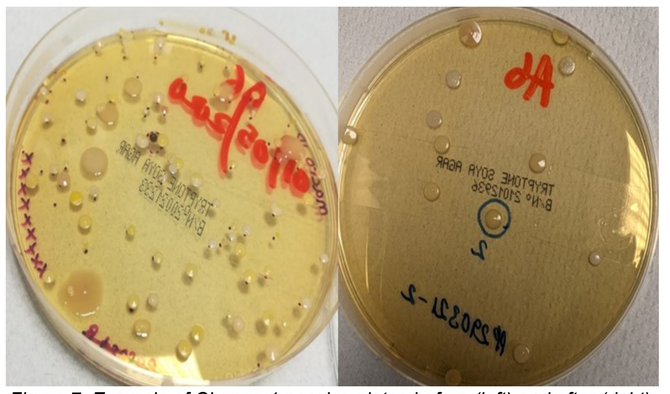

Figure 7: Example of Change 1 passive plates before (left) and after (right) the introduction of cleanroom scrubs.

Conclusion

The combination of the newly reconfigured change facility and the introduction of scrubs were demonstrated to have a profound beneficial impact upon environmental contamination detected within the hospital aseptic cleanroom facility. Observations of trended growth media sampling results from the routine environmental monitoring program showed a significant reduction in the quantity of micro-organisms detected following the introduction of scrubs. Importantly this is indicative of a general decrease in the overall bioburden in the cleanrooms and a reduction in the risks of contamination of the aseptic products with bacteria, which could pose a clinical risk to the patients receiving them.

The improvement has addressed the major GMP non-compliance regarding changing. The department was inspected by the MHRA again in June 2022 and the inspector was reassured by the changes that have been implemented and the improvements in environmental monitoring results. Additional benefits have been associated with capacity and cost savings. Reductions in OOS plates has meant less time spent compiling and completing OOS reports. These savings have been made as fewer plates have required further identification services.

Acknowledgements:

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References

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