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A comparison of three different cleaning methods for reducing contaminants on contact surfaces – a preliminary study

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ABSTRACT

The aim of this study was to evaluate three different cleaning procedures routinely applied in processes to prevent microbiological product contamination. The evaluation was done in the context of their hygienic suitability and cleaning effectiveness according to defined surface hygiene standards. Furthermore, the suitability of a generic testing method to monitor cleaning effectiveness was investigated. The results of this preliminary study revealed discrepancies between the results acquired with a generic method compared to the conventional microbiological surface examination in the context of surface hygiene monitoring. The results demonstrate the higher efficiency of the semi-automatic system in comparison to the mechanical system on surfaces with the same characteristics. The results also indicate that in both of applied the semi-automatic systems, cleaning effectiveness depends on the surface accessibility and cleaning direction. Based on the results presented, we can conclude that for maximum benefit, visual, non-microbiological, and microbiological methods should be combined as an integrated cleaning monitoring strategy.

Key words: cleaning, two-bucket system, box system, mechanical cleaning, visual inspection, microbiological control, hygiene

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INTRODUCTION

The environment of the processes with high hygiene control to prevent product contamination is an important factor in determining the quality and safety of the final products. Sandle [1] noted that cleaning and disinfection are necessary in order to prevent microorganisms surviving in cleanrooms and for maintaining a level of hygiene in laboratories. Cleaning is needed to remove soil (such as protein and grease) from surfaces, and disinfection, if necessary, to inactivate or to kill microorganisms. As Moore and Griffith [2] stated, 'cleanliness' is, however, a relative concept: what is acceptable as being 'clean' in one situation may be unacceptable in another. Lelièvre et al. [3] asserted that cleaning is a complex phenomenon whose efficiency depends on production conditions and the design of equipment, and on operating conditions. Indeed, soils generated during production are often complex, containing microorganisms as well as organic material, which could modify both the microorganisms and the solid surface properties [3]. Prabu et al. [4] pointed out that pharmaceutical products and active pharmaceutical ingredients (APIs) can be contaminated by other pharmaceutical products or APIs by cleaning agents, by microorganisms, or by other materials (e.g., airborne particles, dust, lubricants, raw materials, intermediates, and auxiliaries). Adequate cleaning procedures are essential in order to avoid product contamination especially microbiological contamination. Documented standard cleaning procedures for each piece of equipment should be prepared for a comprehensive infection prevention strategy and an important step in the manufacture of pharmaceutical products [5, 6]. It is vital that the equipment design is evaluated in detail in conjunction with the product residues that are to be removed, the available cleaning agents and cleaning techniques when determining the optimum cleaning procedure for the equipment. Cleaning procedures should be sufficiently detailed to remove the possibility of any inconsistencies during the cleaning process. The following parameters are to be considered during cleaning procedures [5]. Shi and Zhu (2009) indicated that biofilms were often established by various microorganisms on the equipment surfaces of the production line. *L. monocytogenes* became one of the major causes of contamination of food products or transmission of diseases. Therefore, it is very important to develop cleaning and disinfection methods and control systems in food-processing plants and environments. Prabu et al. [4] indicated that cleaning has recently attained a position of increasing importance in the pharmaceutical industry. Virtually every aspect of manufacturing involves cleaning, from the initial stages of bulk production to the final dosage form to ensure the safety, identity, strength, quality, or purity of the drug product. Modern pharmaceutical manufacturing involves highly technically trained personnel, complex equipment, sophisticated facilities, and complex processes. Akl et al. [7] indicated that the cleaning procedures for the equipment must be validated according to good manufacturing practice (GMP) rules and guidelines. Cleaning validation is, however, a significant analytical challenge for the pharmaceutical industry [8]. The pur-

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pose of cleaning validation is to prevent contamination and cross-contamination in pharmaceutical dosage forms [4]. Cleaning validation is a documented process that proves the effectiveness and consistency of cleaning pharmaceutical production equipment. Cleaning validation consists of two separate activities: the first is the development and validation of the cleaning procedure used to remove drug residues from manufacturing surfaces and the second involves the development and validation of methods for quantifying residuals from the surfaces of manufacturing equipment. Furthermore, many sampling points of the manufacturing facility and the manufacturing equipment have to be tested to verify the occurrence of contamination [7]. Peles et al. [9] stated that the typical residual acceptance limits (RAL) used to verify the cleanliness of pharmaceutical manufacturing equipment are selected for residuals that are deemed to be a risk to subsequent products based on potency and toxicity. The limits are defined as residual mass/surface area ($\mu g/cm^2$) and fall well below the accepted "visibly clean" limit of 100 μg per 25 cm^2 [10, 11]. The residual mass on the manufacturing equipment surface is quantified with a validated analytical methodology from swab extracts or rinse, the products of swab or rinse sampling [9].

Griffith et al. [12] demonstrated that the effectiveness of sanitation procedures has traditionally been evaluated using different methods, such as visual inspection, swabs, dipslides and contact plates. Visual inspection is insufficient for defining cleanliness [13] or for objectively evaluating the microbial contamination of all surfaces [14], although this method is still widely used to assess the level of cleanliness [15]. ATP bioluminescence is a widely used technique for the rapid validation about cleaning effectiveness. Compared with traditional microbiological testing, ATP bioluminescence has advantages including the rapidity of its results, which can be obtained within 2 min [15].

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Among the rapid tests, Oberyszyn and Robertson [15] developed a method to examine aerosol containment using a modified, commercially available product called Glo Germ® (Glo Germ, Moab, UT). This product is used for teaching aseptic techniques in hospitals, industry, restaurants, and schools and is visualized with ultraviolet (UV) or black light. Glo Germ® is available in three forms: a white powder, an orange oil-based suspension, and a white lotion based suspension of a melamine copolymer resin. Carrascosa et al. [16] summarised the results of some studies, which considered rapid techniques to be particularly useful in large manufacturing plants where regular and frequent monitoring can provide management with data on trends. In the case of ATP, it also provides rapid results of the amount of organic remains and microbial contamination on the surfaces of establishments. Calvert et al. [17] pointed out that this method does not identify the quantity of the microorganisms or contaminant species; it can be used as a medium for monitoring hygiene and verifying cleanliness. Consequently, to monitor the efficacy of disinfection procedures, some microbiological testing (using dip slides, contact plates, or swabs) may be required [16].

The aim of this study is to analyse three different cleaning procedures, applying their specific protocols (the double bucket system, the box system, and the mechanical cleaning) in order to determine the differences between them and to examine their hygienically suitability when used in processes of high hygiene control. To perform this study holistically, we also included cleaning verification with a generic test.

MATERIALS AND METHODS

Surface cleaning techniques

The three different cleaning techniques described in Table 1 were evaluated.

Table 1: Description of cleaning techniques

Cleaning type	Cleaning procedure
Box system	The box system provides prepared cleaning wipes impregnated with 1% cleaning solution* ready to use and stored in a box fixed on the handcart. The excess cleaning solution is strained off and stored in the separate compartment under the box. Wipes are used via the telescoping stick and changed after approximately every 2 m^2 or more often if cleaning effectiveness is not sufficient. There is no wring-out step. Used wipes are collected in a separate compartment also fixed on the handcart.
Double bucket system	Two buckets fixed in the handcart are filled with 1% cleaning solution*. The first (blue) bucket contains 15L and the second (red) bucket contains 2L of prepared cleaning solutions. A cleaning wipes wringer is located above the red bucket. The wipe is first soaked in the red bucket, wring out and used for cleaning. After that, approximately every 2m^2 the wipe is soaked again into the red bucket, rinsed and wrung out, followed by soaking it in the blue bucket and wringing it out. After the cleaning procedure in one room is finished, the cleaning solution in both buckets is replaced with a new one.
Mechanical cleaning	The cleaning machine is composed of a reservoir for clean water (filled in before the cleaning procedure) and the dosage compartment containing a 1% cleaning solution*. The cleaning procedure is executed with the round horizontal wheel in the bottom of the cleaning machine. After the cleaning procedure is finished, the wastewater is removed from the reservoir, followed by rinsing and drying the equipment. Also, the cleaning wheel coming into contact with the surface is rinsed under running water and dried.

Legend: *Alcohol-based cleaner suitable for use on all water-resistant surfaces, objects, and floor coverings as well as on coated floors. Ingredients according to 648/2004/EC [18] Non-ionic surfactants < 5%, water-soluble solvents, fragrances (linalool), preservatives (methyl-/methylchloroisothiazolinone). pH value (concentrate): approx. 7 pH value (ready-to-use solution): approx. 7.5

The box and double bucket system were evaluated in two separate but comparable areas. Mechanical cleaning was evaluated in the area typical for that type cleaning. The surface material evaluated was the same in all three areas.

Sampling points

Sampling points (20 cm^2 each) were systematically selected regardless of the area and cleaning type investigated (Table 2). When selecting the sampling points, accessibility and workload in the area as criteria were considered. Sampling points 1 to 6 were equally distant from each other (50 cm) and, in the case of sampling points 1 to 4, equally distant from the walls and corners (15 cm). To assure that a sampling point was always on the same spot, the centre of the sampling point was marked with a small black dot resistant to the cleaning procedures evaluated.

Table 2: Description of sampling points

Sampling point	Sampling point criteria
1	Right corner area close to the room entrance.
2	Right corner area opposite to the room entrance.
3	Left corner area opposite the room entrance.
4	Left corner area close to the room entrance.
5	Area in the middle of the room opposite to the room entrance.
6	Area in the middle of the room close to the room entrance.

Surface visual control with Glo Germ®

On each sampling point from 1 to 6 (Table 2), different kits (lotion-based, oil-based, and powder) were deposited before the cleaning procedure. Each kit was first deposited on the sampling point in the size of a pea and then distributed with a cotton swab on a surface of 20 cm^2. There was no cleaning of the surface for at least 20 minutes after deposition. After the cleaning procedure had been completed, each sampling point was checked in detail under the UV light. If there were no kit residual left on the surface, the sampling point was evaluated with a mark of 1 during evaluation. If there were any remains left on the surface the sampling point was evaluated with a mark of 0.

Surface sampling and microbiological analysis

Systematic unannounced surface sampling was executed in three sequences in the case of each type of cleaning. During each sequence, two sampling intervals were done. Before the first surface sample (BC) was taken, the surface cleaning was not done for at least 24 h. The second sample (AC) was taken 25 minutes after the cleaning procedure to assure that the sampling point was completely dry. To exclude cleaning accessories as a possible cause of contamination cleaning solutions and wipes were also sampled before the cleaning procedure and analysed in each sampling sequence.

Surface samples and samples from cleaning wipes (Box and double bucket system) were taken with sterile swabs (cotton swab in 9 mL sterile physiological solution). The surface sampling technique was applied according to the ISO18593 standard [19]. The cleaning solution was collected in sterile 100 mL containers prior to the cleaning procedure starting.

Surface samples and samples from cleaning wipes were taken with sterile swabs.

Microbiological analysis was performed in an internal microbiological laboratory of a company with processes of high hygiene control. According to the internal company standards of environmental microbiological quality, Gram+ bacteria were determined. Surface samples were incubated on Soybean Casein Digest Agar Medium for 5 days at 30 ± 2 °C. Before incubation on agar media, samples of cleaning solutions were treated with aseptic membrane filtration (0,46 μ) in a laminar flow cabin. Because internally determined warning and action limits for Gram+ bacteria were not exceeded in AC samples, no further specific

Microbiological analysis was performed in an internal microbiological laboratory of a company with processes of high hygiene control.

analysis were done. Standards of environmental microbiological quality (warning limit and action limit) are internal in their nature and therefore not published in this paper.

RESULTS

Simple visual inspection of the sampling points after cleaning was in all cases evaluated as visually clean because there were no kit residues on the surfaces that would be visible to the naked eye. However, based on the results presented in Table 3, we can determine that based on the GloGerm® method there are differences visible under UV light. The results in Table 3 demonstrate that the most effective way of cleaning is mechanical cleaning, which successfully removed all three kit types from the surface in all sampling points except 1st and 6th. Monitoring of cleaning effectiveness after applying the system and the two-bucket system has revealed that the test kit applied on the surface was often smudged (especially when sampling points are more difficult to reach) and, therefore, evaluated as not being sufficiently clean. Comparison of the box system and the two-bucket system also reveals that the oil-based kit is more successfully removed from the surface with the box system, while efficiency in case of other two kits applied is comparable and related more to the sampling point. We can see that situation at sampling point 1 and 6 is generally, at least, satisfying (Table 3).

Table 3: Evaluation of surface cleanliness after cleaning according to cleaning type and the sampling point using Glo Germ® method

Cleaning type	Kit type	Sampling point					
		1	2	3	4	5	6
Box system	Lotion-based	0	1	1	0	1	0
	Oil-based	1	1	1	1	1	1
	Powder	0	1	0	0	1	0
Double bucket system	Lotion-based	0	1	1	1	1	0
	Oil-based	0	1	0	0	0	0
	Powder	1	0	1	1	0	0
Mechanical cleaning	Lotion-based	0	1	1	1	1	0
	Oil-based	0	1	1	1	1	0
	Powder	0	1	1	1	1	1

Legend: 1 – Complete absence of the kit under UV light; 0 – remains of the kit visible under UV light

A microbiological investigation was also conducted. In most of the cases presented in Table 4, the number of CFU is already low before cleaning. The internally defined surface hygiene standard defined as action limit of 200 CFU is not crossed, indicating good hygiene practice about the surfaces investigated. After cleaning, the degree of purity significantly improves in all cases, demonstrated as lower microbiological counts. Only in one case of mechanical cleaning is the internally defined surface hygiene standard, with the minimal limit of 50 CFU, not reached after the cleaning (Table 4).

Table 4: Microbiological situation (CFU/mL) before and after cleaning at the surface after microbiological examination of surface sampling in three sequences of (two samples in one sequence) according to the cleaning type and the sampling point

Cleaning type	Sampling sequence	Sampling interval	CFU/mL at each sampling point					
			1	2	3	4	5	6
Box system	1st	BC	41	4	13	15	22	97
		AC	0	0	0	3	0	2
	2nd	BC	13	4	11	13	2	8
		AC	0	2	0	0	0	0
	3rd	BC	16	6	2	3	3	10
		AC	0	2	0	0	0	1
Double bucket system	1st	BC	9	12	18	9	1	2
		AC	2	0	0	0	0	0
	2nd	BC	6	3	5	72	15	5
		AC	0	0	0	2	0	0
	3rd	BC	21	30	7	3	19	4
		AC	0	1	2	1	0	0
Mechanical cleaning	1st	BC	53	67	91	107	59	44
		AC	7	23	1	3	2	0
	2nd	BC	45	47	68	58	23	6
		AC	6	46	7	39	13	1
	3rd	BC	93	31	120	55	31	29
		AC	3	1	69	21	10	2

Legend: BC – Before cleaning; AC – After cleaning

The microbiological investigation of cleaning solutions was on average between 8 and 11 CFU/mL, which is lower than the internally defined action limit (100 CFU/mL). The microbiological investigation of swabs taken from cleaning wipes yielded no microbiological counts (CFU).

Calculating the results from Table 4 into an average cleaning effectiveness according to the cleaning type, we can observe the higher efficiency of box system and two-bucket system at all sampling points when compared to the mechanical cleaning (Figure 1), which is contrary to the results obtained with the GloGerm® method. However, we have to consider that the microbiological counts before cleaning were higher in the case of mechanical cleaning (Table 4). This could be related to the greater frequency of workload in comparison to the other two areas evaluated. Another reason for the lower efficiency of mechanical cleaning could be related to the fact that after the mechanical cleaning procedure is accomplished more water is still present on the surface in comparison to the box system and two-bucket system.

Closer examination of the cleaning performance according to the sampling point indicates that effectiveness is also related to the accessibility of the cleaning area during the cleaning procedure. Sampling point 6, located in the middle of the room, has the lowest discrepancy in the cleaning efficiency when all three cleaning methods are compared (Figure 1). In addition, the cleaning efficiency in the case of sampling point 1 (not considering the cleaning type) is generally better compared to

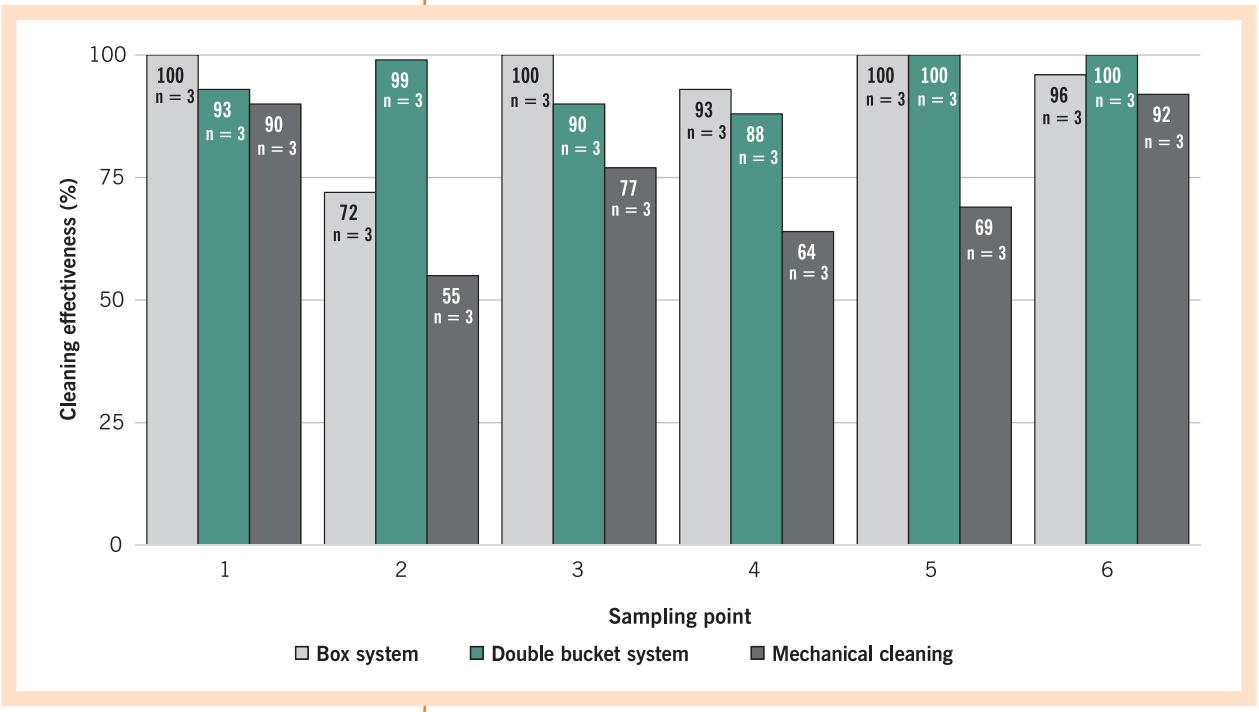

Figure 1:
Average cleaning effectiveness (%) according to the cleaning type expressed as a reduction in the number of CFU/mL after cleaning; n – number of sampling sequences

sampling points 2–4 in spite of their locations, which are quite similar. This also indicates that the cleaning direction is important. The area of sampling point 1 was cleaned first in the case of all three cleaning types, which is again contrary to the results gained with GloGerm® method (Table 3) where sampling point 1 was (other than sampling point 6) evaluated as at the least effectively cleaned.

DISCUSSION

The scarcity of advanced and recent publications in the area of general hygiene management is obvious in scientific literature. If the publications exist, they are focused on particular types of interests, which are frequently about pathogens. Consequently, we lack data that would enable a comparison of the state of the art in general, and we cannot determine the microbial population dynamic in this area of activity. The main focus of each cleaning procedure is to ensure the required levels of cleanliness of different places, the workspace, equipment and other accessories, which all influence the safety, quality, and effectiveness of the final products. This is not only the elimination of particular pathogenic species. Cleaning does not entail the end of a productive procedure but the beginning of the procedure of a new product. Therefore, if cleaning is not also taking into account general hygiene, it easily brings the system into a situation in which certain spoilage microflora or even potentially pathogenic flora are accumulating resistance and slowly begin to predominate. Therefore, it is of crucial importance to screen this aspect of cleaning efficiency as well. For that reason, we performed this study.

Al-Hamad and Maxwell [20] determined that the risk of acquiring infection from environmental surfaces, such as floors, walls, or the surfaces

of medical equipment or furniture, is probably small. However, there is a large body of clinical evidence, derived from case reports and outbreak investigations, which does identify links between poor environmental hygiene and the transmission of micro-organisms causing hospital-acquired infection. Srey et al. [21] emphasized that pathogenic microorganisms in biofilms formed in different food industries settings are a source of food contamination. As the demand for fresh, ready-to-eat and processed foods increases, many studies are needed to address biofilm removal and disinfectant efficacy in food industries. Sinsheimer et al. [22] showed that professional wet cleaning has been determined as an energy efficient, nontoxic, zero-emission technology, and it can be used to process previously dry cleaned garments. In our study, the monitoring of cleaning effectiveness after applying the box system and the two-bucket system has revealed that test kits applied on the surface were often smudged and therefore evaluated as not being sufficiently clean. This demonstrates that the cleaning effect is largely dependent on the cleaning type applied and cleaning technique applied by the cleaning staff. Sinsheimer et al. [22] also concluded that the cleaners they studied in California who switched to professional wet cleaning were able to maintain their level of service and customer base while lowering operating costs. They also found that the cleaners were able to transition to professional wet cleaning without a great degree of difficulty and were highly satisfied with the new technology [22, 23].

Cleaning effect is largely dependent on the cleaning type applied and cleaning technique applied by the cleaning staff.

In this preliminary study, according to the GloGerm® method the results indicate that the most effective way of cleaning is mechanical cleaning (Table 3), which is not the case when the microbiological evaluation is done (Table 4) revealing the discrepancy between the results gained with the generic method compared to conventional microbiological examination. The results of average cleaning effectiveness according to the cleaning type demonstrated the box system to be the most efficient followed by the two-bucket system and the mechanical method (Figure 1). In the case of mechanical cleaning, it should be noted that workload was higher compared to other two areas when this cleaning method was used as intended (Table 4). Another reason for the lower efficiency of mechanical cleaning could be related to the fact that, in comparison to the box and two-bucket systems, after the cleaning procedure is accomplished more water remains present on the surface. Although both methods applied for surface hygiene monitoring cannot be directly compared, the contrast between the results of the GloGerm® method and microbiological analysis indicates the need for the validation of generic methods before being applied as a standard way of monitoring of surface cleanliness. The absence of a test kit does not necessarily also mean a better microbiological situation and vice versa. Moreover, one can observe that the tests applied might be linked to the cleaning process (Table 3). It seems that mechanical cleaning can be handled well with all three test kits, which was not the case with the other two cleaning protocols. Closer examination in other industrial circumstances would also be beneficial to clarify this inconsistency in test reliability. The results of our preliminary study support the conclusions of Griffith et al. [24], who demonstrated that for maximum benefit, vis-

It was ascertained that the accessibility of sampling points is correlated with the effectiveness of the cleaning procedure.

ual, non-microbiological and microbiological methods should be combined, resulting in the production of an integrated cleaning monitoring strategy. Moore and Griffith [2] indicated that conventional microbiological techniques would detect only the microbial component of any residual surface contamination. Furthermore, despite the use of hygiene swabs enabling the detection of relatively low levels of bacteria on a wet surface, previous studies have indicated that the recovery of microorganisms is severely compromised when the sampled surface is dry.

It was ascertained that the accessibility of sampling points is correlated with the effectiveness of the cleaning procedure. An important step in the manufacture of pharmaceutical products, demonstrated by Akl et al. [7], is the cleaning of equipment and surfaces. The cleaning procedures for the equipment must be validated according to GMP rules and guidelines. The main objective of cleaning validation is to avoid contamination between different productions or cross-contamination [7]. Resto et al. [25] indicated the main requirements for the validation of cleaning processes in the pharmaceutical industry, specifying that no detergent should remain after the cleaning process, what is similar for processes for high hygiene control. The accessibility of sampling points during the cleaning procedure and cleaning direction defined the effectiveness of cleaning performance (Table 4, Figure 1) according to the sampling point (e.g. sampling points 5 and 6 located in the middle of the room in case of the double bucket system have higher cleaning efficiency in comparison to other sampling points). We estimated good hygiene practise considering the surfaces investigated before cleaning (e.g. in most cases the number of CFU is low under the internally defined action limit (200 CFU)) and after cleaning (e.g. the degree of purity in all cases except one improves, demonstrated as lower microbiological counts) (Table 4). For validation of the cleaning process and for continuously educating cleaning staff, quick and objective feedback on the surface cleanliness is of paramount importance [26].

Luick et al. [27] found that subjective and objective measures of cleanliness based on visual inspection, ATP assay, or aerobic culture were all able to demonstrate significant increases in the proportion of surfaces considered clean if analysed before and after the routine terminal cleaning protocol described in this paper. However, if visual inspection were used alone, a significantly higher proportion of surfaces would be considered clean before terminal cleaning.

CONCLUSION

The evaluation of three different cleaning procedures revealed that cleaning effectiveness depends on the surface accessibility and cleaning direction. Discrepancies between results acquired with a generic method compared to conventional microbiological surface examination in the context of surface hygiene monitoring were discovered. The semi-automatic system has shown higher efficiency in comparison to the mechanical system on surfaces with the same characteristics. We can conclude that an integrated cleaning monitoring strategy should be

The evaluation of three different cleaning procedures revealed that cleaning effectiveness depends on the surface accessibility and cleaning direction.

based on a combination of visual, non-microbiological and microbiological methods for optimal cleaning results.

This preliminary study provides vital information in the context of the very small number of publications in the field of general basic hygiene management. Assessing all interactions within cleaning procedures in different hygiene processes, it seems that many issues do not have the attention they deserve. However these kinds of research are internal in its nature and have often a confidential status. Despite of lack of published studies in this field, this kind of research is constantly underway in processes of high hygiene control including the one participating in current study, as this is one way of ensuring adequate product quality. This is of particular importance, as results of our preliminary study might serve as a basis for further professional and scientific research. This preliminary study's findings suggest that future research should explore these themes in greater depth.

Assessing all interactions within cleaning procedures in different hygiene processes, it seems that many issues do not have the attention they deserve.

LIMITATIONS OF THE STUDY

The reader of this paper should take into consideration a few limitations of the current study, which is of a preliminary nature. The study was conducted in a single institution for the processes of high hygiene control with a modest sample size and minimal sampling sequences. There was no intention to validate a generic method for surface hygiene evaluation. Smaller surfaces were evaluated under semi-controlled circumcentres with regards to the cleaning solution, surface characteristics and location of sampling points. The possible effect of the cleaning staff was not considered.

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