Automation by cleanroom robots is clever GMP

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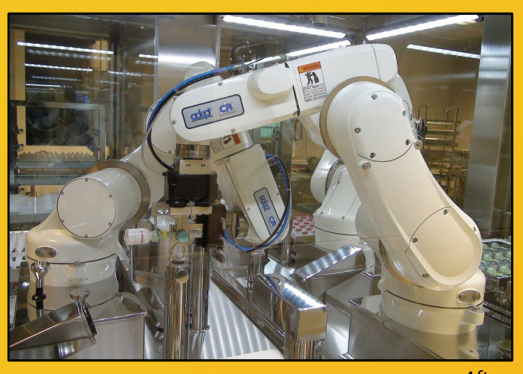
Is automation the key to success?

Before



After

Background

The traditional process in preparing ready-to-use antibiotics imposes the following challenges:

1) Limited capacity leading to shortage problems
2) Monotonous repetitive work
3) High risk human involvement in large scale aseptic processing

To address these issues, two collaborating Danish hospital pharmacies have automated the process by introducing cleanroom robots.

Objective

To evaluate the implementation of cleanroom robots in preparing ready-to-use antibiotics.

Method

In 2007, the hospital pharmacies from the Capital Region of Denmark and Odense University Hospital decided to automate the process of preparing ready-to-use antibiotics. Technical possibilities were utilized to maximize compliance to GMP. All qualification and validation was completed by the first product release in June 2011.

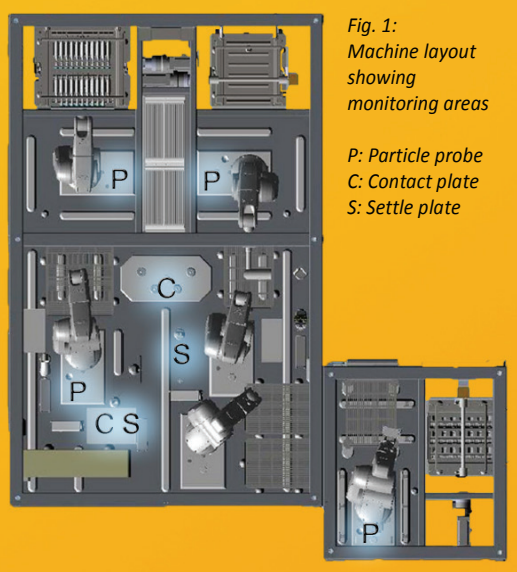


Fig. 1:
Machine layout showing monitoring areas

P: Particle probe
C: Contact plate
S: Settle plate

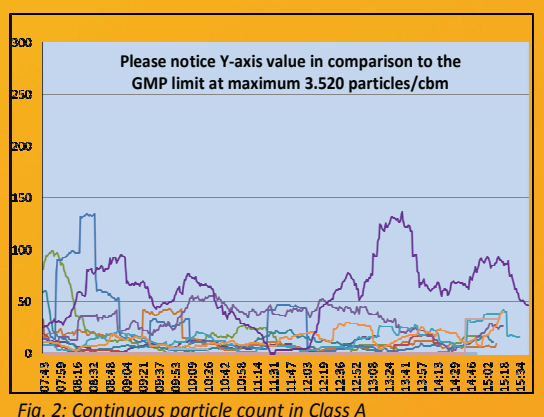


Fig. 2: Continuous particle count in Class A
Counted particles size 0,5 µm/cbm versus time of day

Results

We discovered that:

1) Production capacity increased from 150 products per hour to 350 products per hour with equivalent man-hours
2) The payback period is estimated to be 4 years based on the increased capacity and the initial financial investment of approximately 1 million €
3) The monotonous repetitive work was reduced to a minimum
4) Compliance to GMP was optimized by:
   - Excluding human interference in Class A
   - Using cleanroom robots
   - Qualifying robot movement and UDF (unidirectional airflow)
   - Manufacturing machine parts in polished 316 steel
   - Using vision and image processing for continuous process monitoring
   - Fitting probes for particle count
5) Microbiological monitoring by settle plates and contact plates in Class A (Fig. 1) shows full compliance to GMP stating < 1 cfu/4 hours respectively < 1 cfu/plate
6) Continuous particle monitoring in Class A shows full compliance to GMP stating a maximum permitted number of particles/cubic meter of 3.520 particles size 0,5 µm (Fig. 2) and 20 particles size 5 µm.

Load Class C

Automated load Class A

Automated load Class A

Discussion

We achieved a convincing outcome with fully operational production lines.
A criterion for a realistic payback time is to make full use of the production capacity. This depends on the customer's willingness to choose the ready-to-use system in the calculated volume and accordingly pay the added price for ready-for-use antibiotics compared to traditional antibiotics. An additional challenge is the competing ready-to-use systems being introduced to the marked. Furthermore the EU tendering procedures concerning the active drug may cause changes in production methods as well as potentially increase the cost of the automated production.

Conclusions

The implementation of cleanroom robots in preparing ready-to-use antibiotics has proven to be clever GMP.

Automation requires initial investments and time, but automating the process has increased production capacity and facilitates a healthy work environment. Concurrently, automation made it possible to optimize compliance to GMP on several important and critical aspects of a large scale aseptic processing.

The product produced Ready-to-use i.v. antibiotics

Acknowledgement

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