DIGITAL INDUSTRIES SOFTWARE

Next-generation clean room management

Achieving a comprehensive contamination control strategy using a digital twin for simulation and smart infrastructure

Executive summary

Clean room operators are facing challenges like high operational costs, unexpected down-times and frequent delays in introducing new or revised products. Building and verifying the digital twin of the infrastructure and performing 3D simulations for particles, air flow and energy helps create and restructure production and laboratory environments faster and at lower costs. This supports contamination control strategies as the European Union Good Manufacturing Practice (EU GMP) Annex 1 requires, reduces equipment use for experiments and tests, supports predicting contamination sources and accelerates time-to-market for new or changed products.

Introduction

To keep the level of aerosols and other particles in the air low, clean rooms are necessary for scientific research and industrial products that uses nanoscale processes, like manufacturing semiconductors or pharmaceuticals. American physicist Willis Whitfield invented clean rooms in 1960, which he designed to keep everything from dust to airborne organisms or vaporized particles away from the materials technicians or engineers were handling inside of them. They can also prevent the escape of hazardous materials.

The number of particles of a defined size per cubic meter of air quantifies the clean room's cleanliness level. Although the air in urban areas typically contains 35 million particles of 0.5 micrometers (µm) and bigger per cubic meter, an ISO 14644-1 level 4 certified clean room, which is commonly used in the pharmaceutical industry, permits only 352 particles of that size.

To achieve this, clean rooms require strict control of airborne particulates, usually by filtering outside air before entering using progressively finer filters. Clean room designers use special materials for walls and appliances to minimize generating airborne particles, while high-efficiency filters constantly renew and recirculate the air, removing internally generated contaminants. To warrant high effectiveness, operators tightly control air temperature and humidity levels inside a clean room. Clean rooms are usually kept at a positive pressure to prevent cross contamination.

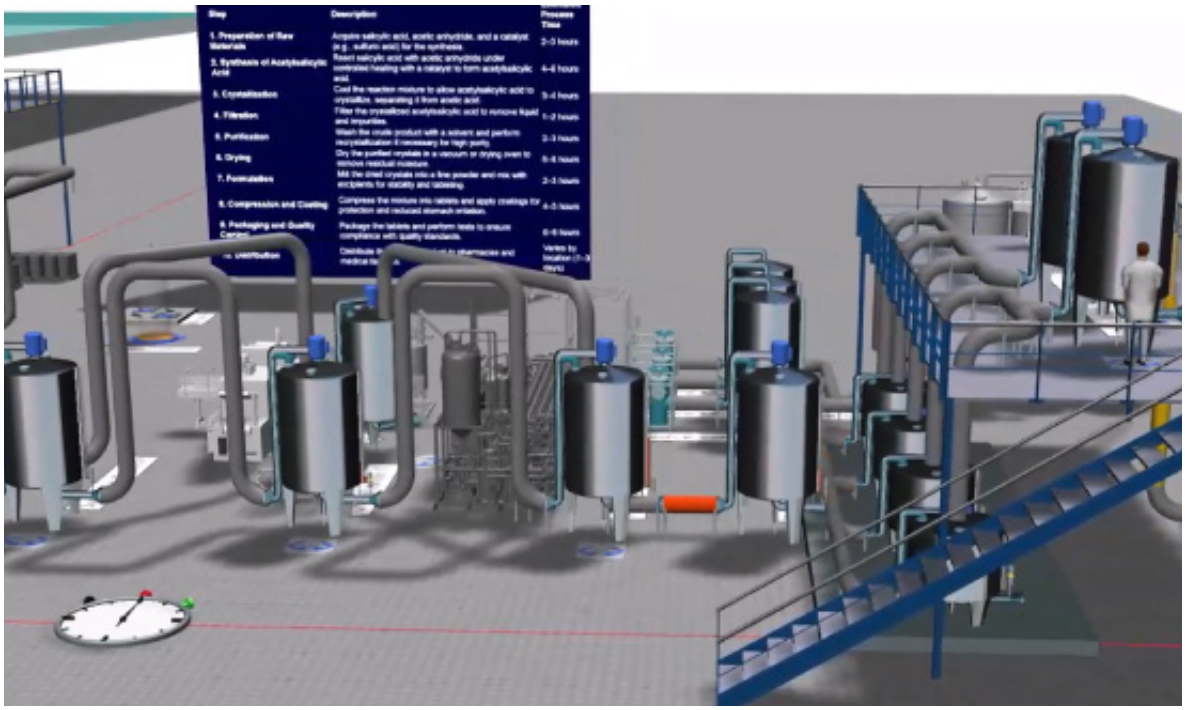


Figure 1. Building the digital twin of a clean room starts with creating a static model of the room using existing CAD data, followed by optimizing the equipment location and material flow.

Changing requirements

Clean rooms are generally expensive to operate and not pleasant to work in. To a certain extent, this is due to the widespread practice of operating heating, ventilation and air conditioning (HVAC) systems at a maximum level to be on the safe side. Previously, designers built a clean room used for aseptic processing and its installations by rule of thumb and hoped to achieve the desired category. However, EU GMP Annex 1 guidelines are more stringent than others, requiring clean rooms to meet particle counts at operation and at rest.

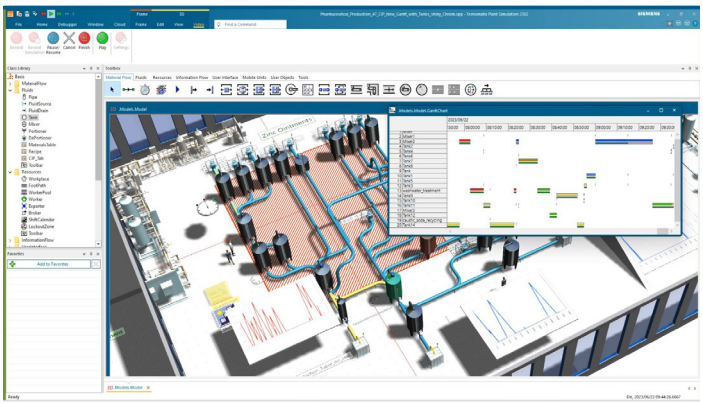


Figure 2. Simulating a clean room using a digital twin can be used to optimize operations.

In close cooperation with the World Health Organization (WHO), the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and the Food and Drug Administration (FDA), the annex was revised to align with similar regulations outside the EU. It requires a specific contamination control strategy encompassing biologically active and auxiliary substances as well as primary packaging products throughout the entire manufacturing process. This impacts and includes facility and equipment design.

A contamination control strategy should have the simulation of material and users in the production or lab as well as the fluid behavior of particles as part of the design phase to improve the understanding of the process and contamination behavior. It needs to be in place prior to introducing new products, modifying existing ones, replacing equipment or altering processes. With a typical 25 percent annual product modification rate, updating and validating production facilities using traditional, experimental methods implies long implementation periods and high costs.

Designing a digital twin

Although the pharmaceutical industry still shows potential for significant improvement in its leveraging of digital technologies, everything it requires is there. Software products can be used to build and verify a comprehensive digital twin of a clean room, generating immediate improvements and savings. Since all building and plant planning is usually carried out using 3D computer-aided design (CAD) software and vendors provide information on structures and materials, all this information is available, and operators can apply it to design verification via computer simulation.

This starts with creating a static model of the room. Although state-of-the-art simulation software provides CAD functionality, using CAD data from architectural design or building information management (BIM) systems greatly reduces the time clean room designers require. Additionally, manufacturers usually provide CAD data for the equipment. This information can then be used in plant software like Plant Simulation in the Tecnomatix® portfolio to optimize the equipment location and material flow based on the customer's recipes. This also offers opportunities to introduce representations of the people working and moving in a clean room.

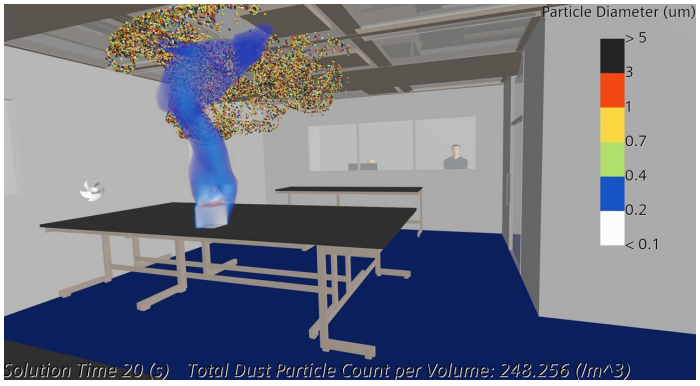
In the plant simulation model, users can easily make and test changes before implementing them. The simulation identifies bottlenecks in the flow of materials or resources and shows the production key performance indicators (KPIs) based on the changes. By changing the simulation setup, users can optimize the digital twin of the plant, which provides a basis for the real-world building and equipment infrastructure. The benefits of using simulation lead to better process understanding, reduce documentation and testing efforts, optimize operations and facilitate a faster time-to-market.

Optimizing dust, air and temperature flow

The greatest potential for fulfilling the requirements of Annex 1 while reducing energy consumption, improving the clean room's working environment and speeding up new or modified pharmaceutical products' time-to-market is by using computational fluid dynamics (CFD) simulation. Using Simcenter™ STAR-CCM+™ software for digitalizing all stages of product creation makes it easy to simulate, analyze and optimize the flow of air, energy use and contaminant removal.

Set up from scratch within a few hours, these simulations come with easily comprehensible graphic representations of particle clouds or temperature and pressure distributions and include variations in particle emissions by humans. This enables planners to optimally place the processing equipment, air holes, windows and doors in a clean room as well as dimension the room's HVAC equipment. It also allows operators to compare results they achieved under various boundary conditions, thus facilitating an airborne contamination control strategy.

Due to the short turnaround time of CFD simulations, this virtual clean room test and assessment is not only feasible for new products and productions but also for all changes. Operators can model worst-case scenarios in a short time frame to improve process understanding in aseptic productions and reduce smoke tests. This reduces documentation and testing efforts, optimizes operations and facilitates a faster time-to-market.



Figures 3a and 3b. Set up from scratch within a few hours, these simulations come with easily comprehensible graphic representations of particle clouds or temperature and pressure distributions.

Aligning the real and digital worlds

Upfront simulations enable clean room operators to design the physical clean room to comply with Annex 1 by providing them with a better understanding of contamination processes, identifying critical areas and facilitating virtual training. Using a flexible smart infrastructure system allows them to have identified requirements guide operations rather than react to passive monitoring.

Building X is a Siemens platform that includes smart, energy-efficient solutions for building management. For instance, it allows for monitoring and steering clean room equipment. Plant Simulation, Simcenter and Building X are part of the Siemens Xcelerator business platform of software, hardware and services, which can cover the entire process chain.

To predict fluid behavior, the system uses the proper orthogonal decomposition (POD) method to collect data from different CFD simulations with various contamination source locations in a clean room and the fixed sensor locations. In case of a contamination alert from a sensor in the production facility or lab, it can immediately identify the location of the contamination source.

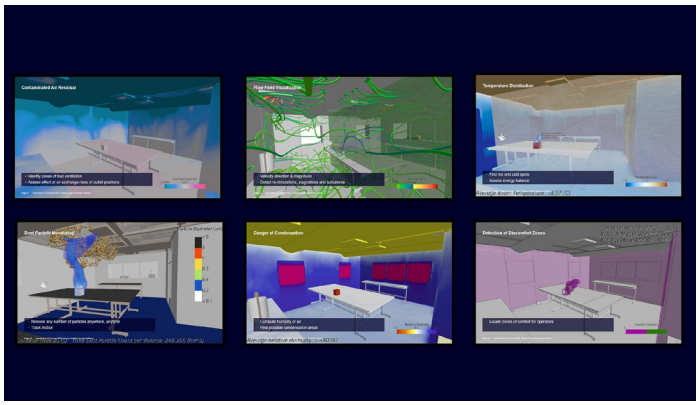


Figure 4. CFD simulation can be used to predict and optimize various criteria, including air contamination, air and particle flows, temperature and pressure distribution, danger of condensation and discomfort zones.

Integrated with locally installed control systems, this helps ensure compliance, improve energy efficiency, reduce the carbon footprint and prevent unplanned standstills.

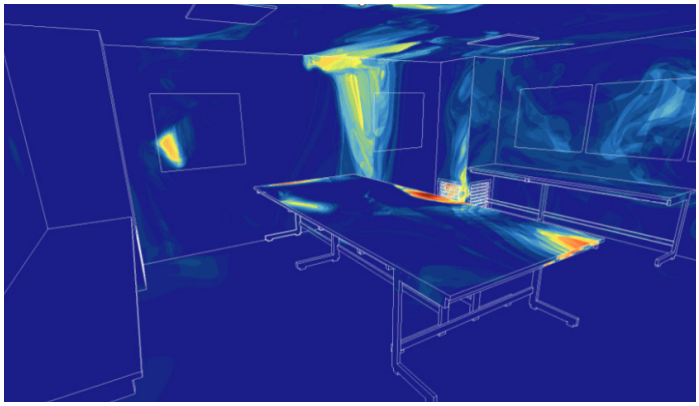


Figure 5. Predict contaminations with the help of POD based on CFD simulation correlated to sensors.

Conclusion

Aligning the physical and digital worlds, comprehensively using the clean room digital twin for design and operation helps replace the traditional, costly practice of over-specifying equipment and treating symptoms by proactive root cause recognition. Operators can reuse the resulting data during operations under changing ambient conditions as well as in case of clean room modifications.

Clean room planning and operating using a digital twin for up-front material flow and particle distribution simulation, smart operation and lifecycle management makes developing and employing a contamination control strategy much more predictable and helps reduce the carbon footprint and time-to-market of new or modified products.

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