

## Reduce Machine Stops for a Safer Aseptic Production

*If aseptic production lines had none or very few stops, staff would not have to interfere with the automated process and risk spreading microscopic particles in the high-risk zone where the medicine is fully exposed.*

The lines are non-isolated “Filling Lines” where the exposed glass vials move through the line in order to be filled with medicine and sealed with a cap before leaving the area as finished products. When humans intervene, they must open one or more transparent doors around the line protecting the exposed vial and even with full protective gowning align with proper management practice they constitute a contamination risk. Production and patient safety requirements are very high in pharmaceutical industries and rules and standards are set accordingly and controlled by e.g. the FDA. It is crucial that these standards are met without compromising the fact that production must run as effectively as possible, i.e. the OEE, for the pharmaceutical companies to deliver the expected number of batches with finished products to their retailers around the globe.

*Stops on these production lines are interrupting the production flow efficiency and human interventions following them are disturbing the sensitive aseptic production environment.*

If the root causes of these stops can be reduced significantly, there is also a very high potential of reducing their consequences as well with both a larger effectivity, OEE, and better patient safety as result. In order to reduce these root causes, they first need to be determined from a huge variety and volume of unstructured data. A methodical strategy is outlined:

1. The data is sorted in stop time stamps, but there are too many different stages of logged information for each time stamp, so a vast data preparation procedure in excel is necessary.
2. An innovative mapping system using the alphabet is invented using the data preparation information to give each unique stop reason derived from the data a one to four letter code.
3. The codes are used in appropriate mathematical statistics; Principal Component Analysis (PCA) and Robust Regression are used to find the major stop cause(s) causing human intervention vs. no human intervention measured in door openings. Simplified, a door opening means human intervention close to the exposed vials and microscopical particle contamination risk.

It turns out that the by far most common stop cause can be interpreted as “Tipped Vials” followed by “Crushed Glass”. Line knowledge sharing further implies the severity of these, where e.g. a crushed glass situation results in a two-hour clean-up and hundreds of wasted vials, a serious impact on the OEE as well as an additional glass particle contamination risk into the open vials. The focus turns therefore towards preventing these stop types, and preferably to a degree that would eliminate them almost completely. Two main proposals for solving the suggested root causes of these major stops are presented, and these must be implemented by following correct company procedures.

Proposal 1. Stabilize the lines and synchronize the belts to reduce sudden movements when starting and stopping areas, that would result in vials tipping and/or pushing too hard against each other causing cracks.

Proposal 2. Changing the vial material by looking into the actual glass properties being used today, i.e. the Borosilicate Glass, and establish why a new glass material currently popular on the market is a better choice.

The future of aseptic production is constantly changing, being modernized and moving forward in various ways. Artificial Intelligence (AI) and Machine Learning are used in fantastic ways, often with the purpose of preventing problems by finding them in advance. This only works when enough data has been gathered and sorted and the correct algorithms developed and taught accordingly. In the meantime, we need solutions built on years of studies in the fields of math, physics and chemistry to make aseptic production standards in every pharmaceutical company even more efficient, safe and as always with the interest of the patients coming first.