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Batch Traceability for a Chemical Production Process

A project of AICOS Technologies

Problem setting

In the context of a GMP validation procedure, a chemical plant wanted to analyze the production process of a chemical active substance from the point of view of the batch traceability. Using mathematical computation and a simulation study carried out with the software package SIMBAX, it has been proved that the reverse batch traceability of the end product batches can be guaranteed. This analysis has been performed not only for the usual recipe from the process control system but also for two extreme variants, in order to make statements which are robust against possible production disturbances.

Modeling the process

The production process considered consists of ten processing and six buffering stages. A single device is available for each stage. The process starts with a batch stage, then the material is stored in a buffer tank and from there it is processed further in a continuous manner. After another buffering stage, a second stage working in batch mode is carried out, followed by several consecutive continuous operations with intermediate buffering. Finally, the process terminates with four batch stages.

In order to be able to understand thoroughly the production process and to perform the batch identification study, the *recipe* (model of the process) and the *layout* (model of the plant) have been represented using the material flow simulation software package SIMBAX. Since the mixing of different batches is only possible in buffer tanks and none of the last three batch stages constituted the bottleneck of the production process, these stages did not need to be integrated into the simulation model. Thus,

starting batches – i.e., those from the first process stage – were represented identically in an end product batch and in a batch of the last model stage.
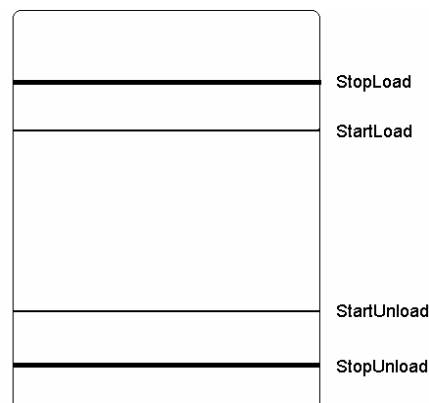

Figure 1. — *Model of a buffer tank.*

The buffer tanks, which play an essential role for the mixing of batches, were modeled as follows. A buffer tank is controlled by the four parameters *StopLoad, StartLoad, StartUnload* and *StopUnload* defined in Figure 1. These parameters correspond to limit quantities and determine from or until which level it is allowed to fill or to empty a buffer tank. Hence, they have in general different values for each buffer tank.

The starting situation is an empty tank which it is only allowed to fill until its contents amount to at least *StartUnload*. From this time onwards, the contents of the tank may vary only between the two thick lines defined by *StopLoad* and *StopUnload*. The buffer tank can therefore be filled and emptied (eventually at the same time) as long as the amount of material in the tank is between these limits. If the contents reach the upper limit *StopLoad*, then the tank may not receive

material any more until its contents have decreased to the level *StartLoad*. Analogously, the tank may not deliver material any more as soon as its contents have reached *StopUnload* and as long as they have not increased again to the level *StartUnload*.

The three process variants mentioned above differ only in these four values for the single buffer tanks. The two extreme variants correspond to situations in which the tanks are always driven with minimum, respectively maximum, contents.

Simulation methodology

The results are based on the composition of the end product batches that represents which starting batches are present in each final batch and in which proportion (in per cent). This composition was computed using an adapted version of SIMBAX, for each process variant considered and for about 200 end product batches.

The simulation methodology used made it possible to recompute the composition of the contents of each buffer tank – i.e., their distribution over starting batches in per cent – after each transfer operation to or from a tank and hence to always keep it up-to-date. For this computation, three cases had to be distinguished depending on whether the buffer tank was

(a) only filled,

(b) only emptied or

(c) at the same time filled and emptied.

On this basis, the composition of the end product batches could be easily derived.

Results

For all three process variants considered, the batch composition showed a high level of regularity, which led to the conclusion that the batch traceability could be guaranteed in spite of the many continuous process stages. In case of the usual production process, 12 starting batches were represented in a proportion exceeding 0.1% in any final batch (except during a short production starting phase). The maximum proportion of a starting batch in an end product batch amounted to about 16.8% (see Figure 2 which represents the starting batch composition of seven different end product batches).
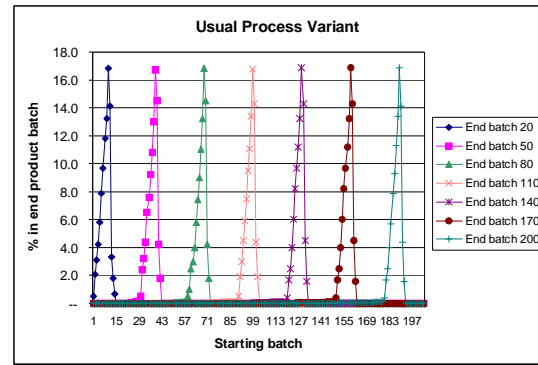

Figure 2. — *Composition of end product batches 20, 50, 80, 110, 140, 170 and 200.*

In case of a production process with almost empty buffer tanks, the number of starting batches which were significantly (i.e., with a proportion of at least 0.1%) represented in an end product batch reduced to 5, while in the case with rather full tanks, it reached 14. The maximum proportion amounted to about 50%, respectively 16%, for these process variants. Hence, the value of 14, as the number of starting batches significantly represented (with a significance level of 0.1%) in an end product batch, constituted a result that was on the safe side on the one hand and not too far from the reality of the normal process variant on the other hand.

The consideration of other significance levels led to similar conclusions – although with different numerical values – thanks to the high level of regularity of the batch composition results. This definitively established the batch traceability for the process considered.