

Up-scaling of Fluid Bed Processes

Introduction

As a result of the FDA PAT initiative an increased interest in process understanding is seen in the pharmaceutical industry. Also a rising interest in “consistent” processes is noticed. Aim is that during pharmaceutical processing each particle should undergo the same experience independent of equipment or scale of operation. This paper reviews the consequences of transferring a fluid bed process from scale 1 to a larger scale 2.

Set up

Assume two fluid beds (1 and 2, 2 being larger than 1) of similar geometry. Be:

A1, A2 fluidisation areas (m²)

V1, V2 air flow (m³/h)

v1, v2 fluidisation velocity (m/sec)

h1, h2 (static) height of product bed (m)

M1, M2 Batch weight (kg)

T1, T2 Inlet air temperature (°C)

S1, S2 Amount of process gas per mass unit of product and time

Out of the A and V the fluidisation velocity v (m/sec) can be calculated as:

$$v = c * V / A \quad c \text{ being a conversion factor}$$

Predicting the parameters for process transfer

A) Drying

Fluid bed 1 with a fluidisation area A1 is filled up to a height h1 with wet material. The batch weight M1 can be calculated as

$M1 = A1 * h1 * d1 * k1$ d1 (kg/m³) being the bulk density and k1 being a shape factor taking into account the non cylindrical shape of the fluid bed processor.

For the characterisation of the drying performance of the system the amount of process gas per mass unit (kg) of product and time S1 is calculated as

$$S1 = V1 / M1 = V1 / (A1 * h1 * d1 * k1) = v1 * A1 / c * (A1 * h1 * d1 * k1) = v1 / c * (h1 * d1 * k1)$$

Fluid bed 2 with a fluidisation area A_2 is filled up to a height h_2 with wet material. The batch weight M_2 can be calculated as

$M_2 = A_2 * h_2 * d_2 * k_2$ d_2 (kg/m³) being the bulk density and k_2 being a shape factor taking into account the non cylindrical shape of the fluid bed processor.

Task is now that particles in process 2 should undergo the same experience as in process 1. This means mainly

- the same mechanical stress (characterised by the fluidisation velocity v)
- the same exposure to temperature and humidity for the same time

For a given material with an identical bulk density $d_1 = d_2$ the situation is easy as long as the shape factors k_1 and k_2 of the 2 fluid beds are identical and if bed height h_2 is identical to bed height h_1 . The process gas volume V_2 in the larger fluid bed can be predicted as $V_2 = V_1 * A_2 / A_1$ This equation is a result of the demand for an equal fluidisation velocity.

A second consequence is that S_1 is equal to S_2 which means, if the same inlet temperature is selected $T_2 = T_1$, overall drying time and exposure of the material to heat and moisture are identical. Only correction which may be necessary is a little lower inlet temperature operating the large fluid bed as due to the "better" surface/ volume ratio less heat losses occur,

In most real fluid bed systems the situation is different. Typically the bed height h_2 in larger processors will be bigger than the bed height h_1 in a smaller processor. This already means that there is more mechanical stress to the materials due to the increased product bed height, which might for delicate granules lead to a certain degree of breakage and therefore to an increased amount of fines. As a second consequence it is no longer possible to maintain both the identical mechanical and thermodynamic conditions. Therefore it has to be decided what is more critical to a particular product.

1) Keep the exposure to humidity and temperature constant. This means $S_1 = S_2$. This can only be realised if the amount of process air in the fluid bed can be set as $V_2 = V_1 * A_2 * h_2 / (A_1 * h_1)$. As a consequence the fluidisation velocity in fluid bed processor will be larger. $v_2 = v_1 * h_2/h_1$ as can be shown by simple mathematics. If this option is selected the overall drying time and the exposure of the product to temperature and moisture will be kept the same. Downside of this option is that there is not only an increased mechanical stress by the increased height of the product bed but additionally by the higher fluidisation velocity. For most granules this will lead to a finer particle size distribution and especially to an increased amount of fines. This option is attractive if the granules are very robust or if the particle size distribution is not critical for the downstream processing.

2) Keep the mechanical stress for the particles constant. This means the fluidisation velocity should be identical: $v_1 = v_2$

As a result the amount of process gas per mass unit and time S_2 is compared to S_1 reduced by the factor h_2/h_1
 $\Leftrightarrow S_2 = S_1 * h_1/h_2$

This has two effects: Drying phase 1 (Zero Order drying) during which the process air is saturated is prolonged by the factor h_2/h_1 . The end of drying phase 1 is reached when a rise in product/outlet temperature can be detected. One can try to compensate for this by selecting a higher inlet air temperature. Is selected properly for example using data from an h-x-Mollier Diagram the duration of drying phase 1 can be kept but it will happen at

a higher product temperature. Which of these strategies is the more appropriate one is of course product dependent.

Under the same circumstances ($h_2 > h_1$; $v_1 = v_2$ and $T_1 = T_2$) Drying Phase 2 (First Order Drying) will be affected in 2 ways. As there is more material (moisture) per amount of process air the product temperature will be lower and the absolute humidity of the process air will be higher (and of course also the relative humidity). Second the duration of drying phase 1 will be prolonged. Which of these 2 effects will be how significant is product dependent. How much the characteristics (dissolution, tablet hardness, chemical stability...) of the final product will be effected is also product dependent.