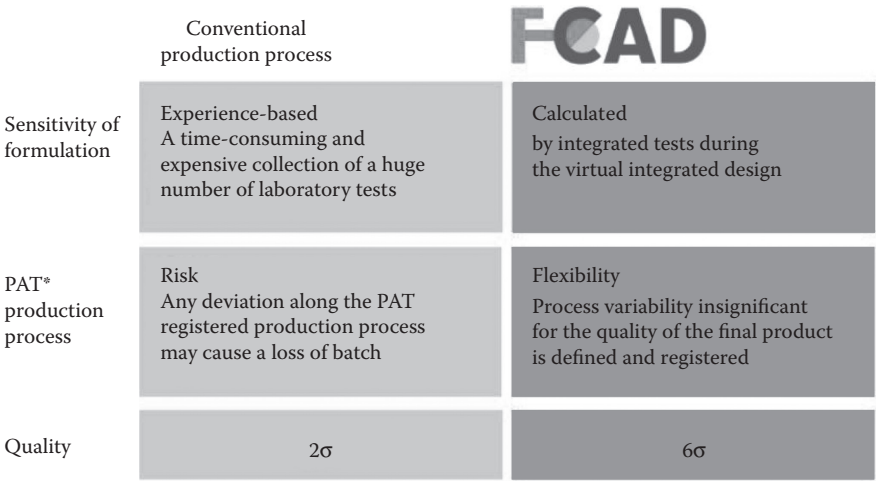

FIGURE 20.11 F-CAD approach based on the workflow of the automotive and aircraft industries compared with the current workflow, which leads to a mean quality of 2σ of the final marketed dosage form. Due to a rigorous application of the Right, First Time concept it is possible to achieve a 6σ quality. (From Leuenberger, H. et al., Virtual Design of Tablets, Lörrach 2014). *PAT production process involves a scientific approach and process analytical technology (PAT) tools for process optimization. (From Leuenberger, H. and Lanz, M., *Adv. Powder Technol.*, 16, 1–36, 2005.)

parameters describing the physico-chemical properties of API and excipients—the results of further *in-silico* batches within the defined formulation design space can be trusted. Thus, it is not necessary to explore and validate with lab experiments all cornerstones of its formulation design space.

For simplicity, only the three most important types of physico-chemical behavior of ingredients involved are discussed, that is, API dissolution, excipients which hinder dissolution by their swelling capacity, and hydrophilic excipients such as MCC, which show after a lag time a fast wicking of water similar to disperse SiO_2. Interestingly, for a physico-chemical description of a component such as a water soluble API, a single dimensionless parameter c_1 is needed, which depends on the dynamic API solubility (slope of intrinsic dissolution rate). The parameter c_1 is an estimate at time zero for the number of iterations needed to dissolve an API cell using the CA approach. Thus, a high c_1 value means a low water-soluble drug. For an excipient with swelling capacity, an additional parameter c_2 is needed to describe the swelling process. In general, no more than two parameters are needed per component. Pores of a tablet, that is, the void space, also need a c_1 value, which for a hydrophilic one is equal to zero. For a more refined *in-silico* calculation it is recommended to take care, in addition, of hydrophobic pores of a tablet formulation with poor wettability with c_1 values > 0.

The Diffusion Equation Governing the Dissolution Process

For simplicity the following discussion is limited to the 1D case concerning the differential equation describing the dissolution, which is identical with Fick's law, respectively the 1D heat equation:

$$\frac{\partial}{\partial t}T(\mathbf{r},t) = \kappa \frac{\partial^2}{\partial x^2}T(\mathbf{r},t) \tag{20.1}$$

Row 1 with columns $(i-1),(i),(i+1)$

T_{i-1}	T_i	T_{i+1}

Just imagine a sheet with rows numbered 1, 2, …… 25 and with columns from A to Q. Row number 1 may represent a thin metallic rod consisting of equally sized cubes A to Q, which can be put into a close contact, that heat is easily conducted. At time $t = 0$ the cube (i), which has the