World Wide Journal of Multidisciplinary Research and Development

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WWJMRD 2016; 2(12): 59-61
www.wwjmrd.com
Impact Factor MJIF: 4.25
e-ISSN: 2454-6615

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Using computational fluid dynamics modelling to study continuous manufacturing process of drug substance ingredient

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Abstract
Pharmaceutical industries faces increasing problems related to manufacture of drug substance which also called as *active pharmaceutical ingredient* or API. To eliminate or minimize such risks and problems, applying of an innovation for product manufacture at all phases should be done by industries. CFD is one such an innovation that has enormous capacities to lead pharmaceutical industries into the future and solve the problems and optimizes exciting process, gain high efficiency, minimize cost and time of production, reduce energy requirement and shorten cycles of process-product development. Integration of the CFD into manufacture process has great benefits for industries and all research and manufacturing staff should be aware of this technology in order to increase efficacy and quality of product manufacture.

Keywords: Computational fluid dynamics, Pharmaceutical industry,, Manufacture of active pharmaceutical ingredient

1. Introduction
Computational fluid dynamics (CFD) as a branch of fluid dynamics is a highly sophisticated integration of applied computer science, chemistry, physics and engineering sciences that utilizes numerical methods and algorithms in order to solve and analyse problems involving fluid flows and relevant phenomena.CFD has great potential to apply in pharmaceutical industries for improvement of quality and process efficiency in manufacturing of drug substance (API) of interest. Unlike experimental methods CFD provides full-field data and various parameters such as temperature, density, velocity, pressure and others of interest can be obtained at each point in the simulated flow domain using CFD technology. Thus CFD has enormous capabilities in order to implement in design, analysis and rapid prototyping at various stages of drug substance manufacturing (.H.S.Pordal and et al, 2002).

CFD for mixing: CFD technology can be used to examine the performance of the mixers and to predict the degree of mixing obtained thus determining whether more mixing elements are required.CFD is a viable approach to analyze and optimize stirred tank performance, to predict impeller performance and flow –field characteristics. CFD also is capable to predict shear stress distribution within a stirred vessel. Shear stress evaluation is important for dissolution, emulsification, and dispersion applications. It also is important during the processing of biochemical products, when excessive shear may lead to damage of bio-cells and loss of product efficacy. (Kumaresan T, Joshi JB 2006)

CFD for emulsification: Emulsification deals with the dispersion of one liquid into another as small droplets. Ultrasonic homogenizer is used for emulsification process. During operation of ultrasonic homogenizer, high frequency vibrations of the blade create cavitations which in turn produce high quality emulsion and dispersions Cavitation intensity may affected by several parameters such as fluid viscosity, temperature and amount of dissolved gas. Caviation intensity also is related to ultrasonic frequency and ultrasonic power. Hence cavitation intensity should be controlled well otherwise uncontrolled cavitation intensity can be dangerous because it can be lead to the pitting and erosion of material. Industries can enhance the performance of ultrasonic emulsifiers by obtaining information about size,density, speed of collapse, and intensity of implosion of cavitation

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bubbles. Identification of cavitation bubbles regions can be done by flow field study around ultrasonic actuators. In this way CFD methods can be used for simulation of fluid flow and obtaining a detailed understanding of the flow physics.CFD technology also can study influence of actuator frequency and amplitude cavitation bubble region formation as well as the transport of cavitation bubble regions.

CFD for solids handling: CFD can be successfully applied to analyze, minimize and eliminate the risk of erosion generated from particle impact on the walls of the transport equipment. CFD also can be applied to analyze the unsteady and chaotic flow behavior in fluidized beds.

CFD for separation: CFD methods can be applied for analyzing and prediction of performance separation devices such as cyclones and
scrubbers.

CFD for dryers: CFD is a beneficial method for analysis of the performance of an industrial dryer before making major structural changes to the dryer.

CFD for packaging: CFD can be applied to conduct virtual experiments before changes are made to the filling lines or to the package geometry. This method allows a wide range of conditions to be tested and leads to an optimized filling process.

CFD for energy generation and energy-transfer devices: Deficiency in heat-transfer equipments can lead to downtime and a significant loss of revenue. Hence failures associated with such equipments directly affect production cost. So Proper performance of this type of equipment should be analyzed well. CFD methods can be applied to analyze thermal and flow fields within such devices. Through the use and design guidance of CFD simulations, we can reduce the formation of pollutants such as NOx. CFD also is able to understand flame characteristics such as stability and burner efficiency, maintaining of which are very important to the appropriate performance of a process heater. (.H.S.Pordal and et al, 2002) (S.V. Patankar,1983), (D.A. Anderson and J.C. Tannehill 1984), (Zhiwu (David) Fang 2010).

2. Materials and Methods

The basis of the CFD methods is on the first principles
of mass, momentum, and energy conservation,
CFD contains solution of conservation equations for mass, momentum, and energy at numerous locations within the flow domain (can be thousands of locations). These locations are designed by generation of a mesh. The applications of equations are done at various mesh locations using discretization techniques. The computed solution provides flow variables such as temperature, pressure, density, velocity, concentration, and so on at thousands of locations within the domain. The wrapped user friendly CFD software packages can be implemented to simulate fluid flow,, chemical species transport, heat transfer, and reactions for a large variety of applications. CFD software packages may differ in look, performance and accuracy but they are the same in the basic principles and steps; however, the basic principles and steps concerned in implementing a CFD analysis are the same. The selection of CFD packages for conducting project is based on the application and process of interest.
Manufacture of API or active pharmaceutical ingredient of interest can be improved in all steps of development processes using CFD technology. For this purpose CFD is applied generally in the following steps during manufacturing.CFD analysis can be grouped into three major steps: preprocessing, solution, and post processing:

Preprocessing: It involves several steps such as recognition of the flow region of interest, geometrical representation of the region, definition of a relevant mesh and the implementation of the principles of flow physics. The appropriate selection of the region of interest and proper simplifications are essential keys for conducting a prosperous calculation. In the first step when the region of interest defined, then generation of a computer model is done. Most commercial CFD packages provide a computer-aided design–like geometry generation engine. The second step is mesh definition. The governing equations are solved at various locations in the flow domain. These locations depend on the mesh resolution which itself is an essential key for CFD calculation accuracy and the required time for a solution. The essential factors for selection of suitable mesh are user experience and skill. Proper boundary conditions are applied for definition of regions of inflow, outflow, walls, and other important characteristics. Physical models within the software are activated to simulate flow physics relating to the application. For instance, simulation of turbulent flow is done by activation of a turbulence model. Critical factors for the overall accuracy of a CFD solution are selection of proper physical models and their applicability to the flow physics. (.H.S.Pordal and et al, 2002) (Zhiwu (David) Fang 2010)

Solution: After completion of problem definition, next step which is submission of the problem to the solver is done for computation of a solution hence it is called solution step. Although the solution method is automated, user intervention frequently is required to obtain a stable converged solution.

Post processing: Analysis of CFD results are performed in the post processing step. A CFD solution provides full-field data; flow variables at thousands of locations are available. A representation of the flow field is generated by plotting flow variables in space on a plane, in a line, or in a three-dimensional region of interest. Analysis of the spatial plots for analysts gives a look inside the unit, which is not available experimentally. However, the actual value of CFD simulation often present in its capabilities to provide exact predictions of integrated quantities such as mass transfer rates, heat-transfer rates,, and forces imposed on the inside of equipments.
Although these steps are main principles of the CFD applications, for various steps of manufacturing such as mixing, emulsification, handling, separation, centrifugation, heat generation and so on, depending on the purpose of CFD application and the type of procedure, different types of CFD software &analysis are required. (.H.S.Pordal and et al, 2002) (Hörmann, T, Suzzi, D, Adam, S. et al)

3. Discussion

CFD technology overcome many disadvantages of product manufacturing and can achieve following approaches Examination of mixer performance and prediction of mixing degree which both have great influence on product quality &process efficiency during mixing process, Proper placing of impellers at various locations which accomplished by mixing efficiency, Prediction of flow-filed characteristics, Prediction of shear stress distribution within a stirred vessel, Identification of cavitation bubble regions around ultrasonic emulsifiers and control cavitation intensity during emulsification, Study of influence of actuator frequency and amplitude cavitation bubble region formation as well as the transport of cavitation bubble regions during emulsification, Analysis, minimization and elimination of erosion risks during handling

,Analysis and prediction of performance of separation devices such as cyclones and scrubbers, Analysis of the performance of an industrial dryer and optimization of equipment configuration, Optimization of filling process of packaging, and analysis of thermal and flow fields within heat transfer devices. So this technology can be used in order to take its advantages in manufacturing of drug substance to shorten the time and cost and increases the quality and control.

4. Conclusion

Application of CFD methods into manufacturing pharmaceutical substances can cause shortening in time of production, optimization of existing processes, reduction of energy requirement, high quality and efficiency of production and process and high efficiency in cost saving.

5. References

1. D.A. Anderson, J.C. Tannehill, and R.H. Pletcher, *Computational Fluid Mechanics and Heat Transfer* (McGraw-Hill,New York,NY,1984).
2. H.S.Pordal,* C.J.Matice, and T.J. Fry, The role of CFD in pharmaceutical industry, *Pharmaceutical Technology FEBRUARY 2002*, 72-79.
3. Hörmann, T, Suzzi, D, Adam, S. et al. J Pharm Innov (2012) 7: 181. doi: 10.1007/s12247-012-9142-x.
4. Kumaresan T, Joshi JB. Effect of impeller design on the flow pattern and mixing in stirred tanks. Chem Eng J. 2006;115 (Issue 3):173–93.
5. S.V. Patankar, Numerical Heat Transfer and Fluid Flow (Hemisphere Publishing Corp, Bristol, PA, 1983).
6. Zhiwu (David) Fang, Computational fluid dynamics is a powerful tool to optimize processes. BioPharm International, 010 Volume 23, Issue 4.