IJPSR (2023), Volume 14, Issue 6 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 06 September 2022; received in revised form, 14 December 2022; accepted, 20 May 2023; published 01 June 2023

UPCOMING TRENDS OF PHARMACEUTICAL MANUFACTURING SCIENCES

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Keywords:

DOE (design of experiments), QBD (quality by design), CFD (computational fluid dynamics), ICH (International Conference on Harmonization)

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ABSTRACT: The global pharmaceutical sector is in vital need of both Innovative technology for solutions and basic science, allowing the production of highly engineered drug products. Commercial-level manufacturing of Complex drug delivery systems utilizing current technologies is challenging. Work within the pharmaceutical trade has been restricted for an extended time to the analysis and development of the latest active compounds; in the meantime, the structure of the assembly, dominated by batch-wise technologies, has not been modified until now. This review covers vital components of producing sciences, starting with risk management ways and design of experiments (DoE) techniques. Experimental techniques ought to, wherever attainable, be supported by process approaches. Thereupon regard, state-of-art mechanistic method modeling techniques square measure represented intimately. Implementing materials science tools paves the thanks for the molecular-based process of future Drug delivery systems. A pic of a number of the prevailing tools is bestowed. This review addresses fundamental tools for increased process understanding and perspective on future process philosophy.

INTRODUCTION: Traditionally, the biopharmaceutical and pharmaceutical industries were not the forerunner of innovative engineering solutions and new chemical engineering principles. Drug product manufacturing was controlled by a regulatory framework that safeguarded the quality of the final product and performed batch-based operations testing, raw material and characteristics of end-product, fixed process conditions, and in-process material [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(6).2695-04

This article can be accessed online on www.ijpsr.com

DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(6).2695-04

And some Limitations related to this quality by testing thinking have broadly been confessed for small molecule and biopharmaceutical products [2, 3]. In contrast, processing of other fields and related manufacturing sciences have accomplished sophisticated technologies that help increase our current process and product understanding.

Although there has been growing interest in the safety and quality of medications while simultaneously cutting the cost of manufacturing pharmaceuticals by implementing more structured pharmaceutical development and manufacturing approaches. The science-based approaches are rapidly spreading, and acceptance has created a more flexible environment for implementing existing and well-established chemical engineering knowledge [4, 5].

Taking recent example is the introduction of the United States Food and Drug Administration (US FDA) process analytical technology (PAT) guidance and the quality by design (QbD) approach by the International Conference on Harmonization (ICH). QbD-based thinking is a perfect opportunity for the pharmaceutical community to take the manufacturing sciences into the new millennium. It has to be, although it is pointed up that the concept of PAT is not entirely new, as process analysis/control has been an important area of chemical engineering for decades [6, 7]. However, PAT introduces the idea of real-time process control, and real-time quality assurance (QA) in pharmaceutical manufacturing is the basis for modern process engineering. Novel manufacturing methods is the example (e.g., based on continuous flow chemistry) that are now being introduced by industry, academia, and regulators. The recently published white paper series on continuous manufacturing (CM) from the MIT-Strathclyde symposium in 2014 highlights the current thinking state. Also, the ICH is developing a new guideline (ICH Q12) that can serve as the basis for implementing CM across the industry in a widespread manner. The present article rather intends to cover the underlying science, introduce the main techniques involved in the QbD approach, and provide an overview of these tools together with future perspectives.

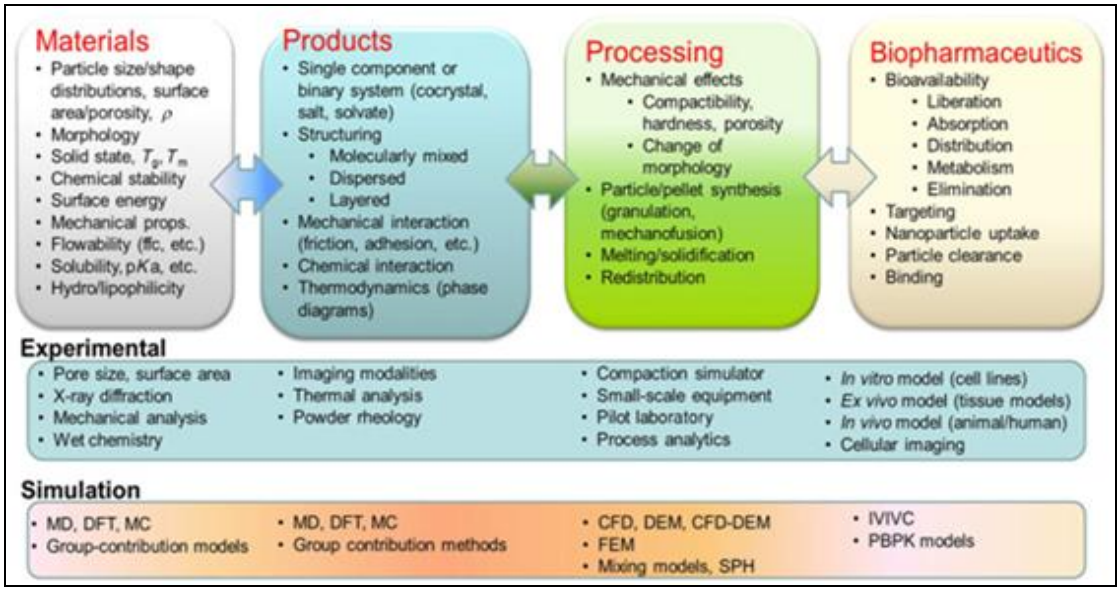

FIG. 1: VIEW OF PHARMACEUTICAL DEVELOPMENT

During the past decades, one visible part of all PAT and QbD activities has been sensor development [6]; near-infrared (NIR) spectroscopy has been used almost as a synonym for PAT in many cases. It needs to note that science-based manufacturing of pharmaceuticals involves not only the application of novel process analytical sensors and measurement solutions but also the other fundamental tools utilization for increasing our understanding by the implementation of risk management strategy, formalized design of experiments (DoE), advanced data analysis techniques, first-principles based process modeling and control, and fundamental material characterization together with molecular modelling. With engineering principles and product design, we are recently observing a change in the paradigm change, becoming the guiding principle of pharmaceutical development. We are adopting a way of thinking in which pharmaceutical ingredients, pharmaceutical products, and related manufacturing processes. We must understand the compounds and materials that predict and/or measure compound properties and define and characterize their constitutive behaviour. Furthermore, we have to understand ingredients interaction (thermodynamics vs. kinetics) and how the delivery requirements determine the ingredients and the corresponding processing and by considering the process, we must understand and identify the critical variables and their effect on the quality and develop and validate mathematical models, which contributed to the successful operation of chemical and Petro-chemical plants in

the large amount. Most importantly, the patient has to be the center of focus [7] **Fig. 1.**

The present study covers the recent developments in the manufacturing sciences related to QbD-based thinking. It outlines the future direction of scientific research in this field, which supports further development of the regulatory framework.

Fundamental Tools for Increased Process Understanding:

Risk Management and DoE:

Risk Management: Quality risk management (QRM) is defined as an integrated action aiming at, first, identifying, assessing, and prioritizing risks and, second, minimizing, monitoring, and controlling the related undesired event. QRM is most effective when applied throughout the entire life cycle of the bio-pharmaceutical or pharmaceutical product. In various industries, RM is widely utilized, and several approaches exist. In the QbD, QRM related to the development and manufacturing of pharmaceuticals with a focus especially on customer (i.e., patient) health and safety is important. All risk management activities should be performed by a team with enough background to examine the given product and related processing. This multidisciplinary team should have participants with experience in dosage form design, process engineering, manufacturing, and quality functions and a moderator who can formally lead the risk management process. Risk management is a continuous process and, in many cases, a constant operation. Based on the existing supporting standards and guidelines, using risk assessment tools and methods is a daily routine [8, 9]. Risk is defined as a combination of the probability of occurrence and the severity of harm [10]. The QRM workflow consists of (1) initiation, (2) assessment, (3) control, (4) review and (5) communication of risks **Fig. 2.**

The estimation involves the identification of hazards based on a systematic use of information. Then, an analysis links the probability of occurrence and detectability with the severity of harm during a qualitative or quantitative process as shown in Fig. And risks are evaluated finally and ranked according to defined criteria. At last, the risk must be reduced to an acceptable level (control). Here, suggested actions are defined to decrease the severity, probability and detectability of harm. The goal is to reduce the quality risk to a non-critical level or implement decision loops that ensure keeping the risk under control. Mechanisms that monitor its output in the review phase consider the QRM workflow.

The frequency depends on the level of risk. Finally, the risk must be communicated to stakeholders (*i.e.,* executive company representatives, authorities, doctors and patients).

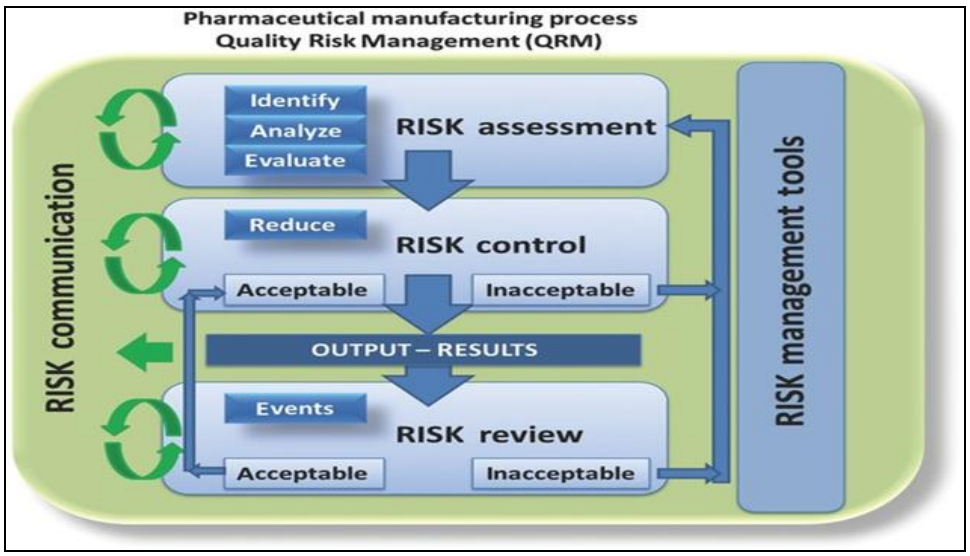

FIG. 2: PHARMACEUTICAL MANUFACTURING PROCESS

Ishikawa (fishbone) diagram may be a sensible place to begin; that provides an outline of the system beneath investigation and often minimizes potential misunderstandings in an exceedingly multidisciplinary risk management team. Succeeding level of risk management may be an

additional careful risk assessment instrument. There's a range of typically accepted tools, and also the choice relies on the formal in-house risk management experience. It's necessary to notice that the depth of a risk assessment depends on the state of development; that is, approaches to the first-in-man formulation are completely different from those applied to industrial production. Within the pharmaceutical producing setting, chiefly tabular risk analysis ways are accustomed support plant or instrumentality qualification, process, method, computerized system or clean up, validation, service, and maintenance. These QRM tools additionally support {the sensible the great the nice} producing observe (GMP) or good engineering observe. Ways and tools in risk management that are most typically used are counselled by the ICH within the Q9 "QRM" guideline are:

- Risk ranking and filtering.
- Preliminary hazard analysis-criticality assessment.
- Fault tree analysis.
- Failure mode and effects analysis.
- Hazard analysis and critical control points.
- Hazard and operability analysis.

Successful implementation of risk management comprises the risk-based specification of qualification measures and the definition of means to control the risks relating to product quality and process performance.

Design of Experiments: Investigation of the variables that affect the process will be performed using a formal experimental style. Risk analysis should be the place to begin allocating the resources for this activity. While not knowledge-based exclusion of variables, the quantity of experiments will increase dramatically.

It's conjointly vital to use previous information to outline the vary within that the experiments square measure performed and to exclude experimental areas during which it'd be not possible to work. Utilization of previous information is crucial for guaranteeing that solely an affordable range of experiments square measure performed.

A simple set of screening experiments provides a decent experimental summary of the system under investigation. A choice on the range amount, the quantity} of variables to be enclosed, and the variety of levels at which they're to be investigated can confirm the ultimate number of experiments performed. In an exceedingly simplified case, once 2 variables are investigated at 2 levels, a comparatively low variety of experiments are needed (four). After applying a full factorial style at 2 levels, a variety of experiments will be generalized into a straightforward equation 2k, wherever k is the variety of variables. However, four experiments are seldom enough for screening functions, and experimental activities will expand (three/four/five variables on 2 levels can end in 23/24/25 = 8/16/32 experiments, respectively). Full factorial style permits the investigation of each main and interaction effect; however, as mentioned higher than, with AN exponential increase within the price of experimental activities.

The number of experiments is often reduced consistently by implementing the third factorial style, with the experimental load calculated as 2k-p, wherever 1/p is the fraction's size. For instance, Andersson *et al.* aimed to optimize early drug development pill formulation by making a model with high prognosticative power and playacting as few experiments as doable. The authors highlighted the importance of considering the quantity of experimental points once the provision of a drug substance may be a limitation. They utilized a third factorial style to reduce the quantity of experimental runs in their study.

The experiment design will be used more for optimization and strength testing of the operational variables. Factorial style on 2 experimental levels doesn't enable modeling of quadratic terms (i.e., potential non-linear relationships), which might be resolved by consistently adding experimental points to the planning. Adding a middle purpose (or points, just in case of continual experiments) to the middle purpose and axial points will resolve this drawback, and a lot of advanced interactions will be sculptural by implementing a central composite style. As with factorial design, however, the number of investigated factors is often redoubled at the value of the redoubled experimental load. This

may be solved by victimization fractional factorial style as a start line for CCD.

Mechanistic Process Modeling: In the last years, the mechanical modeling of pharmaceutical unit operations has made significant progress. Many groups, both in industry and academia, have recognized the potential of modern process modeling, including the ability.

- To improve the elemental scientific understanding of a method. In this case, models don't have to be compelled to give associate correct description of the method. Often, qualitative data of the result of parameters on the system behaviour (i.e., via a "learning model") will satisfy.
- To optimize, scale up or transfer a method from one instrumentation to another. In this case, models must be compelled to accurately represent the truth.
- To give quantitative measures within the context of QRM (e.g., FMEA) by playing sensitivity studies (e.g., that parameter may be a CPP).
- To study the result of uncertainty and variability of the fabric parameters on the method performance.
- To replace experiments throughout a method characterization part.
- To study the result of method disturbance or start-up and shut-down phases on the method performance. During this case, transient models are needed to capture the method dynamics. Such models can even be utilized in management systems, as an example, for model-predictive management.

Because of a larger number of simulation tools currently in use, only a limited overview is provided here that only focuses on modeling and simulation of

a. Fluidic systems, including multiphase flows (e.g., bioreactors, synthesis processes, crystallizers, *etc*.)

b. Particle-based processes (e.g., particle handling, powder mixing, etc.)

c. Fluid-particle systems (e.g., fluidized beds, suspensions, and particle transport)

d. Pharmaceutical flow sheet or process modeling (e.g., for continuous processes, control models, and global optimization.

Fluidic Systems and Multiphase Flows: Computational fluid dynamics (CFD) are well-established tools for the simulation of pharmaceutical unit operations that involve fluidic and multiphase systems, including stirred tanks, crystallizers, gassed batch reactors, bubble columns, and bioreactors. Generally, the goal is to grasp the blending dynamics intimately, the result of blending on the property of competitive reactions, the influence of gassing and stirring on the element distribution, the identification of dead zones, or the characterization of the shear rate distribution for shear-sensitive merchandise.

Typical CFD strategies embody Reynolds-Averaged Navier– Stokes (RANS) solvers with turbulence modeling of varied levels of detail. For example, the impact of agitation and shear stress in numerous kinds of laboratory instrumentality (rotator, orbital shaker, magnetic stirrer, and vortex mixer) on the soundness of proteins was investigated via RANS CFD strategies by Tibeto-Burman *et al*.

Similarly to single-phase simulations, a spread of ways is wont to describe flows in point reactors that square measure generally supported RANS or LES descriptions of the continual section. Currently, the foremost careful ways permit the analysis of the deformation of individual bubbles that during this square text measure mentioned as point DNS (MDNS) as they generally involve DNS of all the phases.

These techniques embody the quantity of fluid, Lagrangian ways (where the grid follows the gas-liquid interface, and, therefore the front-tracking methodology introduced by Unverdi and Tryggvason. Another approach is the Euler–Euler (EE) methodology, which treats the concerned phases as interpenetrating continua. Its advantage is that there are no particles or bubbles, so the number of particles isn't a limiting issue.

The last major methodology is that the Lagrangian particle pursuit tracks the dispersed particles, for instance, the individual bubbles or droplets, within the flow field as purpose sources. Because the motion of the continual part is solved on an associate Eulerian frame of reference, it's usually noted as Euler–Lagrange (EL) approach.

Particle-Based Systems: Many pharmaceutical-producing operations cope with particles, particularly in secondary (drug product) production. Examples embody powder mixing, granulation, milling, roller compaction, tableting, and pill coating. Reckoning on the properties of the fabric, the granular flows will be extremely advanced, containing indiscriminately formed particles of assorted sizes, mechanical attributes, and concentrations. Though for several years solely time approaches prevailed (based on soil mechanics for quasi-static flows or on scientific theory for granular flows within the collisional regime), recently new modeling techniques became obtainable to a wider community, which permit a mechanistic simulation of particulate flows [10]. In these strategies, particles are considered individual components and collision forces; therefore, the ensuing particle trajectories are determined for every collision or time step. There are 2 main methods: the hard-sphere approach (assuming binary, fast collisions) and, therefore, the soft-sphere approach (allowing multiple and enduring contacts that are sculptural by the forward overlap of particles) that's ordinarily named because of the separate component methodology (DEM). Though the previous is appropriate for dilute flows (such as powder conveying) with few collisions, the latter is applied to dense powder flows, usually encountered in pharmaceutical production. These strategies don't contemplate the gas section and filling inter-particle voids.

Fluid–Solid-Particle Systems: Solid particles that are fluidized or suspended in an exceedingly liquid are of times utilized in pharmaceutical producing, as example, in fluid bed drying, agglomeration and coating processes, wet edge, dissolution, suspension production, also as within the transport of solids. Liquid-particle systems (e.g., suspensions) and gas-particle systems behave otherwise and need different simulation approaches. We specialize in dense fluid (liquid and gas) particle suspensions. A recent review of simulation methodologies for dilute suspensions (where particle collisions are comparatively rare; however, turbulence is vital, which is mostly the case for pp. zero.01), is found in Toschi and Bodenschatz. Most of the ways mentioned below are applied solely to mono-disperse spherical particles. Studies on irregular particles are scarce and restricted to easy shear flow simulations of particles, not ECF [11, 12].

Process Simulation: For many years, simulation of the plant-wide system behaviour, via either static or dynamic simulators has been a typical tool employed by method engineers to review and optimize the performance of chemical and organic compound plants. Within the pharmaceutical field, however, it's seldom been used as

CM continues to be solely within the adoption part, and Method simulators for solid materials have solely recently reached the amount of sophistication needed for routine applications.

For example, Parsival, SolidSim and gSolids are flow-sheet simulation tools particularly designed for solid process operations, which provide a comprehensive set of further options (e.g., unit operations libraries, custom modeling, dynamic simulation, property libraries) and permit the implementation of kinetic models and coupling with different classical simulation tools (e.g., CFD, DEM, and Matlab). They will model size fractions via supposed PBE models.

Using population balance models to review particle-population dynamics (i.e., the amendment in particle size distributions) has become progressively common in recent decades. Hulburt and Katz were the primary ones to gift PBEs for a category of issues in particle technology. Many attempts have since been made to use population balance modeling in particulate processes. Many numerical techniques exist for finding PBEs. Ramakrishna and Mahoney, and Kraftpaper reviewed them. In recent years, varied studies have been performed with the special target of understanding the dynamics of the process: time to steady state, the interaction of unit operations, the impact of method upsets, start-up, and shut sequences, and method optimization. Application

examples embody crystallization, granulation pill producing, and mixing. Modeling of continuous method plants was dispensed likewise, as an example, by. Flow-sheet-based management models for plant-wide management via model prophetic management (MPC) were recently enforced.

In the future, method improvement and management *via* dynamic flow textile will be of skyrocketing importance, particularly within the context of CM, wherever these model's area unit is crucial for method management and improvement. However, additional strong simulation tools are needed to permit the quality use of multi-dimensional PBE and dynamic simulation area unit. Additionally, fashionable tools to characterize the dynamics of non-steady-state systems, like bifurcation analysis, should be used.

Final Remarks on Method Simulation: Clearly, models area unit simply associate degree approximate illustration of reality and area unit valid solely among explicit conditions. Materials and method parameters got to be established victimization refined experimental strategies. Accuracy, responsibility and prediction ability got to be established for each model and for each simulation technique. This method (termed model validation) is vital, particularly for style and scale-up models. Validation is best performed via

1. Simplified setups that analytical or actual solutions area unit identified.
2. Comparison with existing well-established solutions within the literature.
3. Predictions by well-established simulations tools or experiments allotted at varied scales.

With that regard, it's necessary to notice that experiments area unit erring likewise. In engineering, associate degree agreement within the range of 100 percent between experiment and simulation is considered sufficiently correct for many applications. Finally, it should be noted that the field of modeling and simulation is advancing. Not solely simulation codes have become additional subtle each year, and mechanistic models are improved endlessly; however, conjointly, the hardware is developing as an example, a brief, whereas past, several hundred-thousand particles were thought of as the higher limit for DEM simulations. Currently, advanced GPU codes (running on graphic cards) may be wont to simulate within the order of a hundred million particles. Several years from currently, even particle numbers higher than one billion could also be achieved. Though the world is apace developing, ways to mix method models with molecular simulation tools (not reviewed here) and ways to simulate/predict material properties and organic relationships have to be compelled to be known. Thus, vital analysis efforts are needed in the future.

Materials Science: The chemical compounds used for medication functions have become additional advanced, and, at the same time, the demand for extremely built innovative formulations is growing [17, 18, 19]. As such, the role of materials science is gaining vital Material characterization is going to be {progressively increasingly more and additional} more vital, as explaining the processability of advanced systems needs an in-depth characterization of the structure of matter.

Development of product-supported, well-defined solid forms (polymorph, solvate, salt, co-crystal, and amorphous) of a given low-molecular-weight compounds, additionally because the advanced nature of biopharmaceutical medication, like organism antibodies and recombinant proteins, are underpinning the importance of basic materials science. Understanding the fabric properties could be a key to winning commercial-scale production of prescribed drugs. Future-producing solutions for innovative drug delivery systems (DDSs) will be supported by advanced and non-traditional pharmaceutical engineering principles, for instance, microfluidics and lithography. At the identical time, innovative therapies' success will be investigated by exploiting nano-level diagnostics with progressively powerful imaging modalities, like resonance imaging (MRI), optical imaging, ultrasound, antilepton emission picturing, laptop picturing, and single gauge boson emission X-raying. This review doesn't give a full summary of all offered techniques. However, we tend to gift a couple of samples of solid-state analytical tools and connected screening approaches. Techniques that have not been thought of as a primary alternative

once analyzing solid pharmaceutical dose forms are getting routine: the structure of matter and unit interactions is explored through victimization solid-state nuclear resonance (NMR) and cyclotron radiation. *Via* cyclotron radiation, a photograph of changes within the solid-type composition of the sample is provided in but a second. Through particular sample holder styles, structural changes throughout dissolution testing are evaluated. A lot of careful illustration of the solid-type composition throughout the process is achieved by mimicking the strain conditions occurring at varied method steps. Implementing assorted tools for visualizing the inner 3D structure of dose types and novel imaging modalities offers a whole image of the complete dose form and not solely the surface info. microscope techniques as well as elemental analysis to supply an outline of the spatial distribution of assorted components within the sample.

Problems Associated with Sample Preparation (Cutting) is Avoided by Utilizing a Number of the Imaging Modalities as Mentioned Above: X-ray computed micro-tomography, MRI, imaging at rate frequencies and optical coherence pictorial representation (OCT). Innovative thermal analysis and physical science analysis of melted polymer–API mixtures will facilitate style process conditions for the preparation of solid dispersions, as an example, with extrusion and 3D printing principles. Surface-sensitive techniques searching surface energetics are equally important once exploring bulk powder behaviour. Their square measure many strategies of measurement of bulk powder behaviour and powder rheometer may be a usually used approach for troubleshooting within the production setting. Detailed analysis of fabric properties on a nanoscale is associated with the processability of this material. Single crystal level observation with AN atomic force magnifier (AFM) was directly associated with the packing of molecules within the crystal and used to justify the particle level behavior.

Perspective to Future Process Philosophy:

Future Manufacturing Technologies [14, 15]: Over the last years, decade-old paradigms of pharmaceutical and bio-pharmaceutical production have modified dramatically as regulators, industry, and pharmaceutical scientists began to understand that new product generations couldn't be created exploitation of superannuated technology. Future product area unit a lot of complicated. They're structured on several levels and nano-structures, usually involving (combinations of) extremely active substances at low concentrations and area unit administered in novel ways. At a similar time, higher and better-quality demands and an ever-increasing price awareness need effective and strong solutions. Thus, new production technologies can augment classical routes a lot of and a lot of. Most drivers of the latest technology embrace

1. CM, as well as QA in period *via* PAT,
2. Processes appropriate for nano-structured DDSs and
3. Producing technology for personal and on-demand drug products.

Future Healthcare System [21, 22, 23]: The aid sector is facing many major challenges: the aging population and, therefore, the inflated value of medicines for society need basic changes during this business space. The fields of genetic science and private nosology have undergone quick development. The Human Order Project has created an enormous information facultative of the additional tailormade drug merchandise event and faded the worth of sequencing a median human order to the $1,000 (Illumina, the leading maker of polymer sequencers, proclaimed the $1,000 early 2014). However, all this information has not been translated into industrial success nevertheless. At the instant, the medical specialty is the sickness space with the most late-stage development. The recently introduced PMI emphasizes the importance of development during this space, and producing strategies for future prescription drugs ought to be modernized to make this development doable. There is a niche between the investments in order analysis and the final drug product. The analysis in producing of extremely designed prescription drugs has not been acknowledged. There's a transparent would like for brand spanking new producing solutions for the twenty-first-century drug merchandise. Closing the gap between progressive biology and, therefore, the final drug product needs focusing additional on the innovative pharmaceutical product style.

The key facultative issue for cost-efficient customized therapies is the development of recent producing principles. Additional versatile process solutions supported by continuous operations can alter customized DDSs with custom-made doses, drug unharness characteristics and a combination of multiple drug compounds supported by individual desires. These developments ought to occur in parallel with the event of genetic science and, especially, technological innovations within the field of IT, diagnostic tools, and miniaturized analytical devices.

CONCLUSION: This review introduces the tool case required for the future production of prescribed drugs. It demonstrates that important progress has been created in recent years driven by changes within the regulative framework and a stronger interaction between pharmaceutical and engineering sciences.

Moreover, existing gaps about the rational development of drug products and, therefore, the associated producing processes became a lot of apparent, starting from the requirement to mix molecular, materials, and method models in a very comprehensive machine framework to the demand for a lot of advanced PAT tools sure as shooting applications. Though abundant elemental data may be complete and, therefore, the technical tools for implementing innovative pharmaceutical producing principles do exist, a lot of work is required.

ACKNOWLEDGEMENT: The Authors are thankful to Principal Dharashive V. M. for providing the laboratory facility and for her persistent, creative encouragement and valuable guidance throughout the research work. Also, I would like to thank my supervisor for all his help, guidance, and assistance throughout the work. Working under his supervision has been a great pleasure and wonderful learning experience.

CONFLICTS OF INTEREST: The authors declare no conflict of interest.

REFERENCES:

1. Jukka R and Johannes K: The future of Pharmaceutical manufacturing sciences. Journal of P'ceutical science. 2015; 104: 3612-3638.
2. Yu L: Pharmaceutical quality by design: Product and process development, understanding, and control. Pharm Res 2008; 25(4): 781–791.
3. Rathore AS and Winkle H: Quality by design for biopharmaceuticals. Nat Biotechnol 2009; 27(1): 26–34
4. Oksanen CA and Garc´ıa Munoz S: Process modeling and control in ˜ drug development and manufacturing. Comput Chem Eng 2010; 34(7): 1007– 1008.
5. Reklaitis GV, Khinast J and Muzzio F: Pharmaceutical engineering science—New approaches to pharmaceutical development and manufacturing. Chem Eng Sci 2010; 65(21): 4-5.
6. Simon LL, Pataki H, Marosi G, Meemken F, Hungerbuhler K, Baiker A, Tummala S, Glennon B and Chiu MS: Assessment of recent process analytical technology (PAT) trends: A multiauthor review. Org Process Res Dev 2015; 19(1): 3–62.
7. Selen A, Dickinson PA, Mullertz A, Crison JR, Mistry HB and Dressman JB: The biopharmaceutics risk assessment roadmap for optimizing clinical drug product performance. J Pharm Sci 2014; 103(11): 3377–3397.
8. Pharmaceutical Quality System Q10. International conference on harmonization of technical requirements for registration of pharmaceuticals for human use, ICH Harmonised Tritpartite Guideline 2008.
9. WHO Guideline on Quality Risk Management, working document QAS/10.376/Rev.2. Geneva, Switzerland 2010.
10. Ketterhagen WR, Ende MT and Hancock BC: Process modeling in the pharmaceutical industry using the discrete element method. J Pharm Sci 2009; 98(2): 442–470.
11. Katagiri J, Matsushima T and Yamada Y: Simple shear simulation of 3D irregularly-shaped particles by image-based DEM. Granul Matter 2010; 12(5): 491–497.
12. Matsushima T and Chang C: Quantitative evaluation of the effect of irregularly shaped particles in sheared granular assemblies. Granul Matter 2011; 13(3): 269–276.
13. Ramkrishna D and Mahoney AW: Population balance modeling. Promise for the future. Chem Eng Sci 2002; 57(4): 595–606.
14. Kraft M: Modelling of particulate processes. KONA Powder Particle J 2005; 23: 18–35.
15. Wulkow M, Gerstlauer A and Nieken U: Modeling and simulation of crystallization processes using parsival. Chem Eng Sci 2001; 56(7): 2575–2588.
16. Ramachandran R, Arjunan J, Chaudhury A and Ierapetritou M: Model-based control-loop performance of a continuous direct compaction process. J Pharm Innov 2011; 6(4): 249–26.
17. Boukouvala F, Chaudhury A, Sen M, Zhou R, Mioduszewski L, Ierapetritou M and Ramachandran R: Computer-aided flow-sheet simulation of a pharmaceutical tablet manufacturing process incorporating wet granulation. J Pharm Innov 2013; 8(1): 11–27.
18. Laitinen R, Lobmann K, Strachan CJ, Grohganz H and Rades T: ¨ Emerging trends in the stabilization of amorphous drugs. Int J Pharm 2013; 453(1): 65–79.
19. Mitragotri S, Burke PA and Langer R: Overcoming the challenges in administering biopharmaceuticals: Formulation and delivery strategies. Nat Rev Drug Discov 2014; 13(9): 655–672.
20. Hartman RL, McMullen JP and Jensen KF: Deciding whether to go with the flow: Evaluating the merits of flow reactors for synthesis. Angew Chem Int Ed 2011; 50(33): 7502–7519.
21. Editorial. The human genome at ten. Nature 2010; 464(7289): 649– 650.
22. Editorial. What happened to personalized medicine. Nat Biotech 2012; 30(1): 1–1.
23. Collins FS and Varmus H: A new initiative on precision medicine. New Engl J Med 2015; 372(9): 793–795.

24. Aksu B, Beer TD, Folestad S, Ketolainen J, Linden H, Lopes ´ JA, Matas Md, Oostra W, Rantanen J and Weimer M: Strategic funding priorities in the pharmaceutical sciences allied to Quality by Design (QbD) and Process Analytical Technology (PAT). Eur J Pharm Sci 2012; 47(2): 402–405.
25. Wening K and Breitkreutz J: Novel delivery device for monolithical solid oral dosage forms for personalized medicine. Int J Pharm 2010; 395(1): 174–181.
26. Miriam Sarkis and Andrea Bernardi: Emerging Challenges and Opportunities in Pharmaceutical Manufacturing and Distribution 2021.
27. European Medicines Agency (EMA). Biological Medicine European Medicines Agency. Available online: https://www.ema. europa.eu/en/glossary/biological-medicine (accessed on 28 December 2020).
28. Warren, G. Quality by Design (QbD) Overview. 2015. Available online: https://www.pda.org/docs/default-source/websitedocument-library/chapters/presentations/australia/quality-by-design-(qbd)-overview.pdf?sfvrsn=f022b28e_6 (accessed on 1 February 2021)
29. Taylor P: Outsourcing PharmA GSK and Pfizer Team up on Continuous Manufacturing Project. Available online: https://www. outsourcing-pharma.com/Article/2015/11/03/GSK-and-Pfizer-team-up-on-continuous-manufacturing-project (accessed on 25 December 2020)
30. Li MY, Ebel B, Paris C, Chauchard F, Guedon E and Marc A: Real-time monitoring of antibody glycosylation site occupancy by in situ Raman spectroscopy during bioreactor CHO cell cultures. Biotechnol Prog 2018; 34: 486–493.
31. Chiaccio F, D'Urso D, Compagno L, Chiarenza M and Velardita L: Towards a Blockchain Based Traceability Process: A Case Study from Pharma Industry. IFIP Adv Inf Commun Technol 2019; 566: 451–457.
32. Markarian J: Supply Chain Challenges for Single-Use Systems. Biopharm Int 2019; 32: 16–19.
33. Böhl OJ, Schellenberg J, Bahnemann J, Hitzmann B, Scheper T and Solle D: Implementation of QbD strategies in the inoculum expansion of a mAb production process. Eng. Life Sci 2020.
34. Bano G, Wang Z, Facco P, Bezzo F, Barolo M and Ierapetritou M: A novel and systematic approach to identify the design space of pharmaceutical processes. Comput Chem Eng 2018; 115: 309–322.
35. Xie X and Schenkendorf R: Robust Process Design in Pharmaceutical Manufacturing under Batch-to-Batch Variation. Processes 2019; 7: 509.

How to cite this article:
Paratkar GM, Shafi S, Bhosale SG, Suryawanshi GM and Mortate PR: Upcoming trend of pharmaceutical manufacturing sciences. Int J Pharm Sci & Res 2023; 14(6): 2695-04. doi: 10.13040/IJPSR.0975-8232.14(6).2695-04.