Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 11 [7] June 2022 : 248-255

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

A Review on Organogel Formulation by Quality by Design Concept

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ABSTRACT

The proposed study aims to review on organogel formulation considering the concept of Quality by Design, focusing on a planned development that consider the vulnerabilities of the entire process through risk analysis tools and design of experiments (DoE). Quality by design (QbD) can also contribute to design, manufacturing, and producing highly finished goods. To better explain the manufacturing processes, the FDA focused QbD in the healthcare industry, based on a comprehensive understanding of how technology and design parameters affect the quality of the manufactured product. Various elements of QbD are critical quality attributes (CQA); critical material attributes (CMAs), and critical process parameters (CPPs). The tools generally applied in QbD are risk assessment, design of experiments, and process analytical technology. The various benefits of the QbD model are preventing sampling errors and variability in research studies, less experimentation, and enhanced productivity. Since the organogel formulations need complex experimentation and an extremely time-consuming process, the application of QbD tools in such investigations can intelligently conclude the research processes. This review article provides a brief outline of the fundamentals, elements, and tools of QbD. Furthermore, it will save time and costs, and aid in scalability. This study demonstrated the efficiency of the Quality by Design methodology to understand the product variability, supporting that this approach favors a better understanding of the whole process and enables to design a robust development stage, reducing costs and generating high-quality products.

Keywords: *Quality by Design; design of experiments; response surface methodology; risk assessment*

Received 15.03.2022 Revised 21.05.2022 Accepted 24.05.2022

INTRODUCTION

The basic role of medication fabricating is to give a better based item and guarantee that satisfactory quality is dependably created. Innovative aptitude is expected to get to information gathered from exploratory investigations and assembling to recognize plan, particulars, and framework control genuineness. Modifications in the assembling system and planning and improvement are viewed as any open doors to acquire new information or animate framework plan advancement [1-5]. Quality by plan (QbD) is the study of creating and assembling details and product offerings that meet foreordained measures [6-8]. Like other administrative rules, for instance, International Council for Harmonization (ICH) Q8, Q9, and Q10, and current direction archives, current great assembling techniques (cGMP), food and medication organization (FDA), right now, the standards of QbD have acquired notoriety for quite a long time in drug revelation in the twenty-first century [9-16]. Various advantages of the QbD model are trying not to test blunders and changeability in examinations, getting away from drawn out detailed trials, forestalling confusions with administering consistence, and upgrading creation options [17-19]. Figure 1 portrays the different cycles expected in the QbD model [20,21].

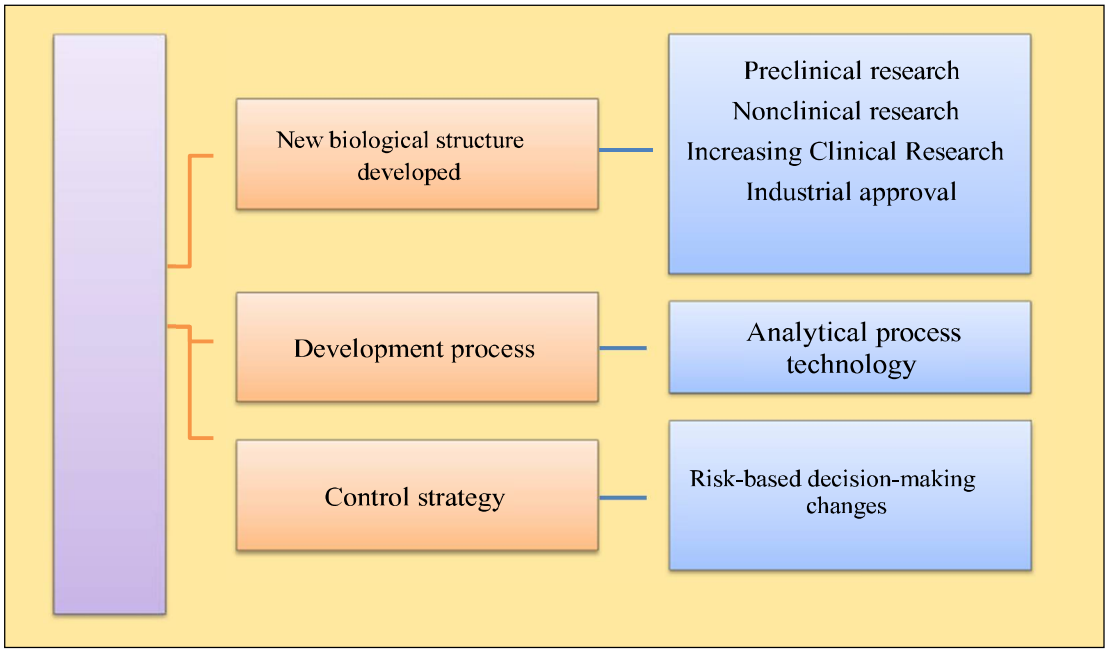

Figure 1. Pictorial representation of the progression of quality by design model.

The quality by test (QbT) approach keeps up with item quality through embracing various conventions, i.e., unrefined substance testing, the assembling pattern of characterized drug sedates, and completed item testing in expectation to satisfy FDA prerequisites and certain extra circumstances to carry the items into the business for mass assembling thus. Because of the absence of information on the strategy and vulnerability over it, the essential drivers of disappointment presently can't seem not entirely settled. In this way, providers could thusly recover the cycle before the hidden reasons for incorrectness are distinguished and treated, and besides, rethink that the consideration interaction has been followed to outperform through fruitless circumstances [21]. Table 1 shows a correlation of QbT and QbD [22].

Table 1. Comparison analysis between QbT and QbD

Constraints	QbD	QbT	Interpretation
Product development process	The criteria concentrated on interpreting qualityparameters	A norm depending on a batch's history	The QbT strategy is based on accuracy and also excludes or denied uncertainty. Flexible technique within the layout which enables long-term development in QbD system.
Validation	The model must be authenticated regularly	The focus is on reproducibility. Adaptable in the design field	In the QbT method, preliminary samples must be validated. The QbD technique emphasizes control policy.
Risk-based management	Power shifted dramatically; real-time issue	Changes in regulatory priority requirements Prior authorization	Value estimation is separated from research, and risk assessment has been carried out using the QbT method. In the QbD method, the decision was based on process identification and risk management.
Lifecycle based management	Constant adjustment within the process	Reacting to issues; space layout	Approval modifications are required in the QbT design, while change is made completely throughout the QbD model.

Elements of QbD

To address GMP's restrictions, the FDA presented cGMP in the year 2002. As indicated by cGMP, the emphasis on "programming" all through the creation stage, particularly at the administrative level, unequivocally characterizes the straightforwardness of laborers [23-26]. The ICH Q8 structure characterizes QbD as a methodical methodology for improvement, which starts from predefined targets and underscores interaction and item assessment with following, in view of approved quality and cycle risk appraisal [9]. The different exploration investigations of medication advancement and modern experience offer information and encounters that assist with making quality guidelines and controls [27].

Laying out an objective.

The quality objective profile (QTP) has been the focal point of QbD, which fills in as the establishment for item plan and improvement in regard to the underlying objective models expressed inside QbD definition. The quality objective item profile (QTPP) lays out the nature of the completed item. On account of scientific interaction advancement, this is often known as target item profile (TPP), as it incorporates an insightful objective profile (ATP). TPP might have a critical influence in all drug revelation methodology, including planning, decision, preparing, and execution of clinical examination strategies [28].

Basic quality ascribes (CQA) appraisal.

The CQAs are usually connected with the medication material, inactive parts, halfway data sources (added substances or excipients), and the dose structure itself. CQAs ordinarily impact the qualities of medication items, similar to molecule sizes, drug discharge, solvency, zeta potential, entanglement effectiveness, item yield, and medication stacking [29]. The mechanical, physical, microbial, or organic attributes or characteristics of unrefined components are portrayed as basic material ascribes (CMAs). CMAs are used during the setting of an appropriate reach assortment or creation to guarantee that item happy and excipients are reliable. This data fills in as an establishment for applying the CQA to the item's viability. The QbD worldview is one of a kind in that it utilizes thorough gamble evaluation techniques to recognize CQAs. CQAs in enormous oral conveyance frames normally influence drug discharge, quality, security, and strength [9].

Arranging and executing a control-based technique.

The objective of control-based arranging is generally to guard the item, and the framework stays inside the normal most minimal and the most noteworthy cutoff points. The elements and items are assessed routinely during the creation interaction, which guarantees heartiness. Ordinarily, hit and preliminary systems are increased. Basic interaction boundaries (CPPs) are boundaries that impact CQAs and ought to hence be observed or controlled to guarantee that the cycle creates the right exhibition. Process heartiness is characterized as a framework's capacity to keep up with normal adequacy and effectiveness while tolerating input difference [30]. CQAs are worried aboutcreation parts, while CMAs are worried about crude assets, similar to tranquilize items and inactive materials utilized in the assembling system. As a rule, QbD is utilized by and by to deliver new drug items at different levels, as shown in Figure 2 [9,31,32].

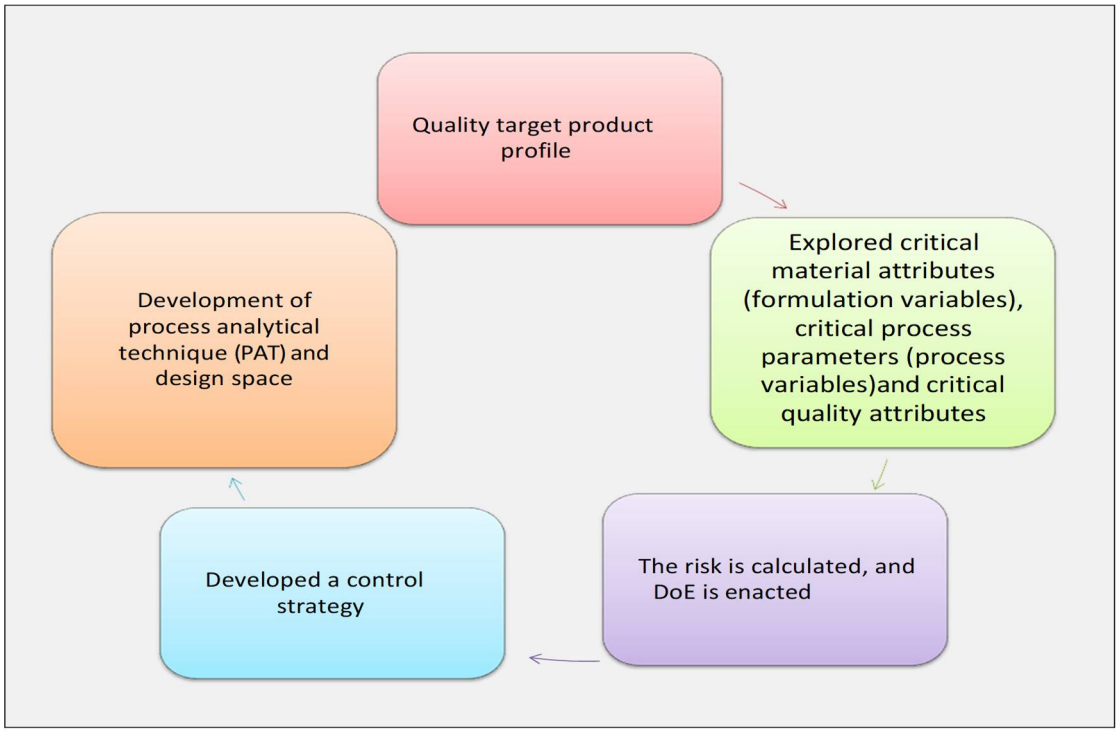

Figure 2. Steps indicating the approach of QbD

Plan format.

According to ICH Q8 (R2), the plan space has turned into a multidisciplinary structure and arrangement of cycle boundaries and assembling techniques that have been displayed to create great items. The engineer suggests a plan based format that is exposed to lawful examination and that is commonly framework and gear based; nonetheless, the plan space picked for the lab scale wouldn't be material to economically reasonable methodology. On a huge level, plan space checking is in this manner required before it is laid

out that the plan space is independent [9]. The methodology for fostering a plan space for QbD components incorporates giving information materials and handling of factors prompting the advancement of the item, trailed by appraisal and certificate by administrative bodies.

Explanation of control methodology and consistent turn of events.

Changes in the plan space's format, as in the QbD model, wouldn't require audit or freedom. Therefore, process enhancements as far as quality and execution can happen prior in the item cycle, with less requests for post-endorsement. Comparable to administrative coherence, a superior comprehension of the assembling climate would support more effective gamble the board as per ICH Q9 models for the effect of seen changes and creation deviations on quality items [9].

Tools of QbD

For grasping the parts of QbD in the modern worldview, the execution of effective QbD strategies is fundamental, which incorporate interaction insightful innovation (PAT), risk assessment, and plan of trial and error (DoE) [9].

Risk appraisal.

Risk assessment is a strategy for getting sorted out information to help with risk decision-production in a gamble alleviation climate. It involves recognizing dangers as well as surveying and concluding openness chances. This will be the initial segment of the quality-based risk the board stage, trailed by risk decrease and evaluation stages. Risk the executives involves executing results to diminish or dispense with the gamble and incorporates three parts: risk distinguishing proof, translation, and appraisal. The gamble the executives results ought to be evaluated in the last interaction to guarantee that the fundamental devices and mindfulness are considered [33]. Verifiable realities, hypothetical models, sane cases, and vital decisions are totally utilized in the ID cycle to distinguish potential reasons for dangers which prompted the gamble issue or challenge grouping. Risk investigation requirements to ascertain takes a chance with in view of the distinguished peril; risk assessment involves contrasting the reasonable courses of action with risk factors accessible through a subjective or quantitative way to deal with decide the gamble's importance.

ICH Q9 records the accompanying nine normal gamble the board devices: (1) An assessment of the essential dangers (2) assessment of the tree graph (Ishikawa fishbone layout, disperse outlines, survey sheets); (3) help techniques (4) starting gamble investigation; (5) weakness examines with control regulations; (6) an assessment of breakdown and results; (7) audit of disappointment, impacts, and dissemination; (8) evaluation of workableness risks; (9) measurable strategies to help. As a component of the QbD execution, risk appraisal is focused on through DoE. The procedures like Ishikawa fishbone and examination of results/misfortunes are generally utilized risk control draws near, either used independently or in blend [34-36].

Design of experimentation **(DoE).**

At first, a gamble-based appraisal will be acted as well as fostering an examination system. Testing configuration is a scientific, organized cycle to decide the connection between process-related factors and DoE. DOE is a computational technique being utilized to plan and carry out research and decipher the data created from the exploratory work. It is a sort of computational demonstrating used to perform measurable examination of a model, technique, and material that controlled information boundaries to investigate its impact on the determined reaction variable. This is a magnificent device that permits analysts to assess factors as indicated by a foreordained plan. DoE is a reasonable strategy for laying out connections among process data sources and results to procure a more profound information on items and cycles. It could help with deciding the best setting, CPPs, CMAs, and configuration space. This is prescribed to assemble a plan space by DoE for nonparametric investigation [31]. DoE was demonstrated to be powerful in creating different pharmacological treatments and functional circumstances, and it very well may be utilized all the more widely later on years to guarantee solid examination execution with further developed outcomes. Different benefits of DOE are addressed in Figure 3, and the arrangement of DOE strategies is illustrated in Figure 4.

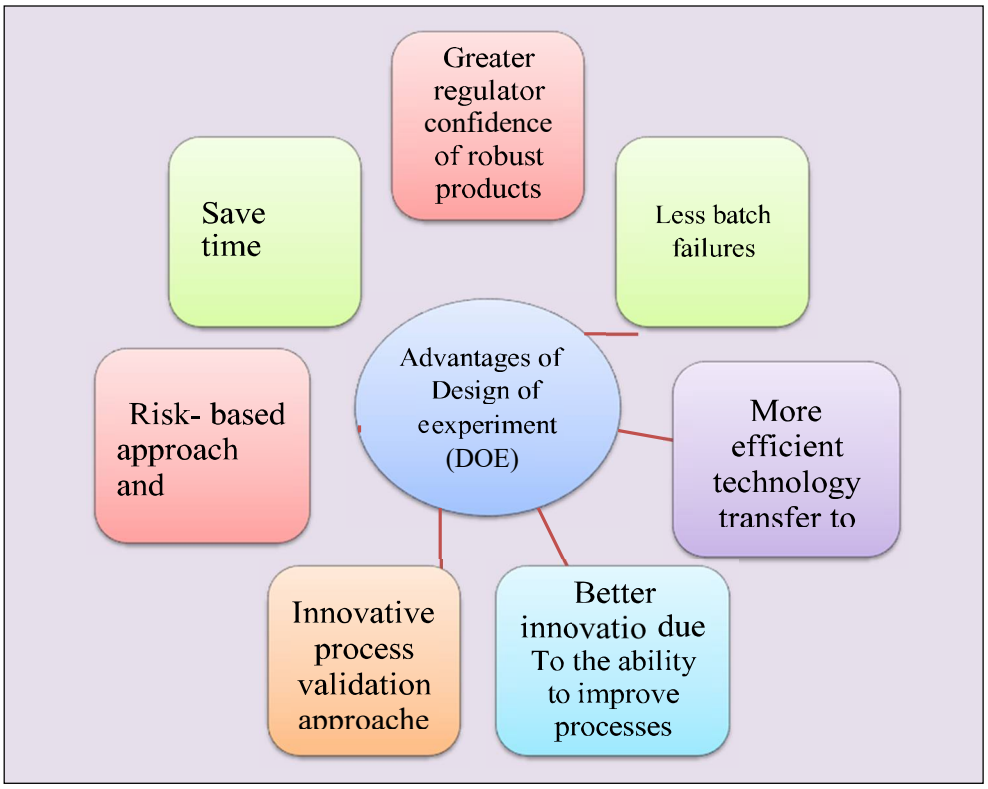

Figure 3. Advantages of design of experimentation techniques in pharmaceutical product optimization.

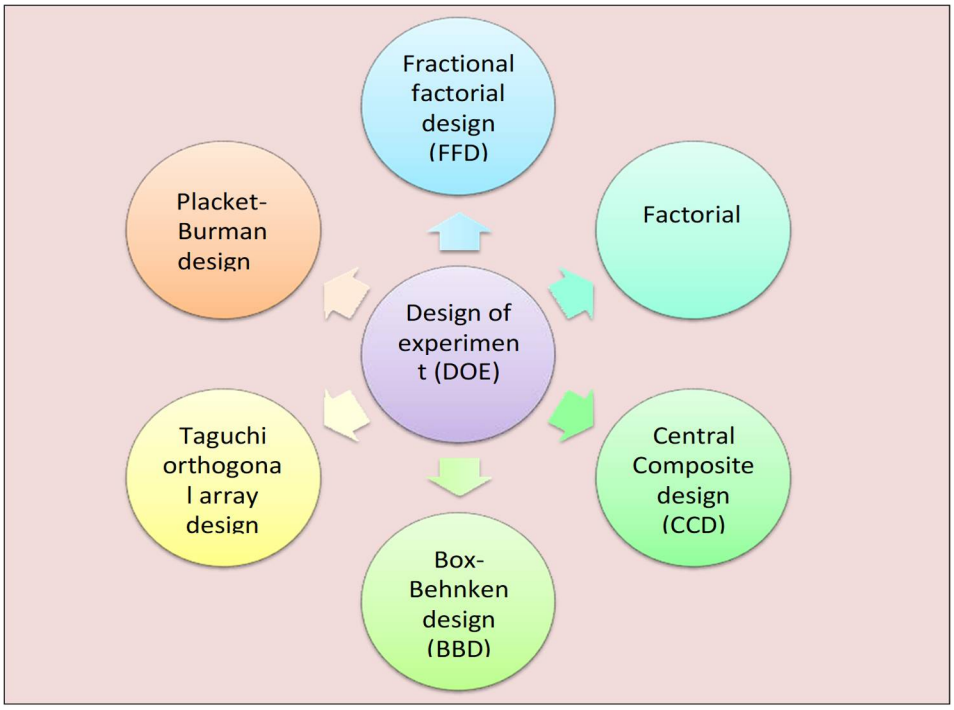

Figure 4. Classification of design of experiments techniques.

Process *analytical technology* (PAT).

PAT is portrayed as a method that utilizes real factors all through creation to give data to help improved registering to deliver an eventual outcome ceaselessly in accordance with laid out quality and execution rules [23]. ICHQ8 recognizes the utilization of PAT to guarantee cycle consistency in a plan space that has as of now been created [31]. A framework is viewed as evolved according to a PAT viewpoint when immeasurably significant reasons for fluctuation are characterized and portrayed; the framework handles difference; item value's presentation can be determined actually and precisely [34,37].

There is a three-venture technique for streamlining of drug arrangements and creation processes, which incorporates checking, study, and plan, which is regularly used to aggregate artistic works. In the checking stage, a presentation estimation program permits continuous observing of all CPPs and CQAs by straightforwardly or in a roundabout way methodical procedures and appropriate examination cycles to explore the recognized quality characteristic, required item ascribes, and handling techniques. During the plan stage, tests are completed to figure out which key factors are associated with a material's job, and the cycle conditions and information material properties might significantly affect completed item quality [38, 39]. This information is being utilized to recognize the CQA, CPP, and QTPP necessities for laying out a PAT-based process control framework [40].

According to FDA's PAT arrangement articulation, process examination could be portrayed into three sorts: at-line, in-line, and online [13]. During at-line assessment, the example is taken, separated, and examined close to the handling stream. Through web-based expectation, the examples were taken out from the contraption and could be once again introduced into the streaming liquid. Throughout in-line assessment, the example stays inside the handling stream and could be problematic or meddling. It is obvious that PAT guides in the effective authorization of QbD. It could perform continuous framework observing without interruptions by bringing mechanical and foundational factors across on the web. PAT raises innovation mindfulness which brings about better quality control and register effortlessness.

Applications of QbD in Optimization of organogel formulations

Organogels are semi-solid systems with an organic liquid phase immobilized by a three-dimensional network composed of self-assembled, crosslinked or entangled gelator fibers. More recently, the synthesis of more biocompatible organogels has strengthened the development of several biomedical and pharmaceutical applications.

The numerous advantages of QbD are deterrence of sampling errors and variability in research studies, the requirement of less experimentation, and improved productivity. The QbD is a cost-effective time-saving strategy that uses PAT, risk assessment, and DoE as tools to understand raw materials and process parameters better, making QbD a straightforward model for the development of pharmaceutical products for the healthcare sector. Quality by design (QbD) has the potential to contribute to design, manufacturing, and the ability to produce highly finished goods.

Although organogel has crises assisted with proper storing conditions, greasy property and lacking stability ; it has significant property as template vehicle: Organogels provide opportunities for incorporation of wide range of substances with diverse physicochemical characters viz: chemical nature, solubility, molecular weight, and size etc.

1. PROCESS BENEFITS: Spontaneity of organogel formation by virtue of self-assembled super molecular arrangement of surfactant molecule makes the process very simple and easy to handle.
2. STRUCTURAL/PHYSICAL STABILITY: Being thermodynamically stable, the structural integrity of organogels is maintained for longer time periods.
3. CHEMICAL STABILITY: Organogels are moisture insenstive and being organic also resists microbial contamination.
4. TOPICAL DELIVERY POTENTIAL: Being well balanced in hydrophilic and lipophilic character, they can efficiently partition with the skin and therefore enhance the skin penetration and transport of the molecules.
5. SAFETY: Use of biocompatible, biodegradable and non-immunogenic materials makes them safe for long- term applications.

REFERENCES

1. Singh, J. (2015). International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. *Journal of Pharmacology and Pharmacotherapeutics*, *6*(3), 185-187.
2. Cunha, S., Costa, C. P., Moreira, J. N., Lobo, J. M. S., & Silva, A. C. (2020). Using the quality by design (QbD) approach to optimize formulations of lipid nanoparticles and nanoemulsions: A review. *Nanomedicine: Nanotechnology, Biology and Medicine*, *28*, 102206.
3. Swain, S., Parhi, R., Jena, B. R., & Babu, S. M. (2019). Quality by design: concept to applications. *Current drug discovery technologies*, *16*(3), 240-250.
4. Munson, J., Freeman Stanfield, C., & Gujral, B. (2006). A review of process analytical technology (PAT) in the US pharmaceutical industry. *Current Pharmaceutical Analysis*, *2*(4), 405-414.
5. Sangshetti, J. N., Deshpande, M., Zaheer, Z., Shinde, D. B., & Arote, R. (2017). Quality by design approach: Regulatory need. *Arabian Journal of chemistry*, *10*, S3412-S3425.
6. Gochhayat, G., Alam, M. S., Kumar, M., Pal, P., Singh, R., & Saini, V. (2019). Quality by Design: A new practice for production of pharmaceutical products. *Journal of Drug Delivery and Therapeutics*, *9*(1-s), 416-424.

7. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. (2005). ICH harmonised tripartite guideline: Quality risk management (Q9). *ICH Database*.
8. Mishra, V., Thakur, S., Patil, A., & Shukla, A. (2018). Quality by design (QbD) approaches in current pharmaceutical set-up. *Expert opinion on drug delivery*, *15*(8), 737-758.
9. https://www.fda.gov/regulatory-information
10. Elder, D., & Teasdale, A. (2017). ICH Q9 quality risk management. *ICH quality guidelines: an implementation guide*, 579-610.
11. Woodcock, J. (2004). The concept of pharmaceutical quality. *American Pharmaceutical Review*, *7*(6), 10-15.
12. US Food and Drug Administration. (2007). Pharmaceutical quality for the 21st century: a risk-based approach progress report. *Published May*.
13. Food and Drug Administration. (2004). Guidance for industry, PAT-A framework for innovative pharmaceutical development, manufacturing and quality assurance. *http://www. fda. gov/cder/guidance/published. html*.
14. Yu, L. X., Raw, A., Lionberger, R., Rajagopalan, R., Lee, L. M., Holcombe, F., ... & Buehler, G. (2007). US FDA question-based review for generic drugs: A new pharmaceutical quality assessment system. *Journal of Generic Medicines*, *4*(4), 239-246.
15. Rozet, E., Lebrun, P., Michiels, J. F., Sondag, P., Scherder, T., & Boulanger, B. (2015). Analytical procedure validation and the quality by design paradigm. *Journal of biopharmaceutical statistics*, *25*(2), 260-268.
16. Arsiccio, A., & Pisano, R. (2018). Application of the quality by design approach to the freezing step of freeze-drying: building the design space. *Journal of pharmaceutical sciences*, *107*(6), 1586-1596.
17. Beg, S., Hasnain, M. S., Rahman, M., & Swain, S. (2019). Introduction to quality by design (QbD): fundamentals, principles, and applications. In *Pharmaceutical quality by design* (pp. 1-17). Academic Press.
18. Claycamp, H. G. (2007). Perspective on quality risk management of pharmaceutical quality. *Drug Information Journal*, *41*(3), 353-367.
19. Singh, J. (2015). International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. *Journal of Pharmacology and Pharmacotherapeutics*, *6*(3), 185-187.
20. Zhong, L., Gao, L., Li, L., & Zang, H. (2020). Trends-process analytical technology in solid oral dosage manufacturing. *European Journal of Pharmaceutics and Biopharmaceutics*, *153*, 187-199.
21. ICH Expert Working Group. (2005). Quality risk management Q9. *ICH harmonised tripartite guideline*, *25*, 781.
22. Lewis, G. A., Mathieu, D., & Phan-Tan-Luu, R. (1998). *Pharmaceutical experimental design*. CRC press.
23. Lionberger, R. A., Lee, S. L., Lee, L., Raw, A., & Yu, L. X. (2008). Quality by design: concepts for ANDAs. *The AAPS journal*, *10*, 268-276.
24. Kenett, R. S., & Kenett, D. A. (2008). Quality by design applications in biosimilar pharmaceutical products. *Accreditation and quality assurance*, *13*(12), 681-690.
25. Singh, J., & Roberts, M. S. (1989). Transdermal delivery of drugs by iontophoresis: a review. *Drug design and delivery*, *4*(1), 1-12.
26. N. Politis, S., Colombo, P., Colombo, G., & M. Rekkas, D. (2017). Design of experiments (DoE) in pharmaceutical development. *Drug development and industrial pharmacy*, *43*(6), 889-901.
27. Taticek, R., & Liu, J. (2015). Definitions and scope of key elements of QbD. *Quality by Design for Biopharmaceutical Drug Product Development*, 31-46.
28. Namjoshi, S., Dabbaghi, M., Roberts, M. S., Grice, J. E., & Mohammed, Y. (2020). Quality by design: Development of the quality target product profile (QTPP) for semisolid topical products. *Pharmaceutics*, *12*(3), 287.
29. Hinz, D. C. (2006). Process analytical technologies in the pharmaceutical industry: the FDA's PAT initiative. *Analytical and bioanalytical chemistry*, *384*(5), 1036-1042.
30. Csóka, I., Pallagi, E., & Paál, T. L. (2018). Extension of quality-by-design concept to the early development phase of pharmaceutical R&D processes. *Drug Discovery Today*, *23*(7), 1340-1343.
31. Yu, L. X., Amidon, G., Khan, M. A., Hoag, S. W., Polli, J., Raju, G. K., & Woodcock, J. (2014). Understanding pharmaceutical quality by design. *The AAPS journal*, *16*, 771-783.
32. Tomba, E., Facco, P., Bezzo, F., & Barolo, M. (2013). Latent variable modeling to assist the implementation of Quality-by-Design paradigms in pharmaceutical development and manufacturing: A review. *International journal of pharmaceutics*, *457*(1), 283-297.
33. Rathore, A. S. (2009). Roadmap for implementation of quality by design (QbD) for biotechnology products. *Trends in biotechnology*, *27*(9), 546-553.
34. Patwardhan, K., Asgarzadeh, F., Dassinger, T., Albers, J., & Repka, M. A. (2015). A quality by design approach to understand formulation and process variability in pharmaceutical melt extrusion processes. *Journal of Pharmacy and Pharmacology*, *67*(5), 673-684.
35. Boussès, C., Ferey, L., Vedrines, E., & Gaudin, K. (2015). Using an innovative combination of quality-by-design and green analytical chemistry approaches for the development of a stability indicating UHPLC method in pharmaceutical products. *Journal of pharmaceutical and biomedical analysis*, *115*, 114-122.
36. Corredor, C. C., Lozano, R., Bu, X., McCann, R., Dougherty, J., Stevens, T., ... & Shah, P. (2015). Analytical method quality by design for an on-line near-infrared method to monitor blend potency and uniformity. *Journal of Pharmaceutical Innovation*, *10*, 47-55.
37. Rathore, A. S., Bhambure, R., & Ghare, V. (2010). Process analytical technology (PAT) for biopharmaceutical products. *Analytical and bioanalytical chemistry*, *398*, 137-154.

38. Rapalli, V. K., Khosa, A., Singhvi, G., Girdhar, V., Jain, R., & Dubey, S. K. (2019). Application of QbD principles in nanocarrier-based drug delivery systems. In *Pharmaceutical quality by design* (pp. 255-296). Academic Press.
39. Read, E. K., Shah, R. B., Riley, B. S., Park, J. T., Brorson, K. A., & Rathore, A. S. (2010). Process analytical technology (PAT) for biopharmaceutical products: Part II. Concepts and applications. *Biotechnology and bioengineering*, *105*(2), 285-295.
40. Orlandini, S., Pinzauti, S., & Furlanetto, S. (2013). Application of quality by design to the development of analytical separation methods. *Analytical and bioanalytical chemistry*, *405*, 443-450.

CITATION OF THIS ARTICLE

Priyanka S. Sadgir, Vivek Srivastav. A Review on Organogel Formulation by Quality by Design Concept. Bull. Env. Pharmacol. Life Sci., Vol 11[7] June 2022 : 248-255.