ISSUE 7/2025

BDMAI BULLETIN

From the Desk of President

Dear Friends,

It is with a heavy heart that I begin this message by expressing our deepest condolences on the tragic fire accident that occurred recently at one of the pharma industries. The loss of precious lives in this unfortunate incident is a grave reminder of the inherent risks in our industry and the responsibility we bear toward the safety and well-being of our workforce.

On behalf of the Bulk Drug Manufacturers Association (India), I extend our heartfelt sympathies to the families of the deceased and our unwavering support to the management and employees of the affected company during this immensely difficult time. We stand in solidarity with them and are ready to extend any assistance that may be required.

This tragedy underscores the critical importance of prioritizing safety at every level of operations. I urge all member companies to rigorously review their safety protocols, invest in updated fire detection and suppression systems, and conduct regular training and emergency response drills for all personnel. Compliance with regulatory norms is essential, but we must go beyond mere compliance to create a culture where safety is embedded in every action and decision.

et this be a solemn call to action—to double our efforts toward risk mitigation, to learn from every incident, and to ensure that such tragedies do not repeat.

As regards to industry performance during April-May of this financial year, I am happy to share that APIs exports stood at US$ 769.07 million registering a positive growth rate of 2.41% over April-May of previous financial year.Similarly imports of APIs during the same period declined by 4.27% during April-May 2025 over same period of previous financial year. Please visit the inner pages for more detailed analysis of industry performance.

Please stay engaged with the Association's initiatives and use platforms like this bulletin to share experiences, voice concerns, and build collective wisdom. Let us continue to uphold the highest standards of excellence, ethics, and, above all, safety.

With warm regards,

R K Agrawal
National President

In this Bulletin you can expect

Global Pharma News

Investments:

Mosanna Therapeutics gains $80m to advance OSA nasal spray

The new funding will support MOS118 through its Phase II development while expanding Mosanna's product pipeline. Mosanna Therapeutics has secured $80m in a Series A funding round to advance a new nighttime nasal spray for obstructive sleep apnoea (OSA).

Pharmaceutical Technologies 10.6.25

Tagomics secures £860k grant for colorectal cancer test

Tagomics has been awarded £860k in funding from Innovate UK's Biomedical Catalyst programme to develop a novel diagnostic test for colorectal cancer. The grant forms part of a £1.2M project, with additional funding contributed by Tagomics, to customise its Interlace platform for early disease detection.

Pharma Times 10.6.2025

Drug Approvals:

FDA grants new approval for novel hepatitis drug

The FDA's authorisation helps to address the "significant" remaining need for acute hepatitis C treatments, according to AbbVie.

European Pharmaceutical manufacture 11.6.25

FDA Approves Mavyret for Treatment of Acute HCV Infection

The FDA approved a label expansion for glecaprevir/pibrentasvir (Mavyret) to treat acute hepatitis C virus (HCV) infection in patients 3 years of age and older with compensated cirrhosis or without cirrhosis, AbbVie announced in a release.[1] The therapy, which is now approved for both acute and chronic HCV, is the first and only oral direct acting antiviral approved by the FDA for this condition

Drug Topics 12th June 2025

FDA Approves Lenacapavir for Prevention of HIV

The FDA has approved lenacapavir (Yeztugo) as pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV in adult and adolescent patients weighing at least 35kg, Gilead Sciences announced in a release.[1] The decision makes the therapy the first and only twice-yearly option available in the United States for PrEP.

Drug Topics 18.6.25

FDA Approves Clesrovimab-cfor for Prevention of RSV in Infants

The FDA approved clesrovimab-cfor (Enflonsia) for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in newborns and infants born during or entering their first RSV season, Merck announced in a release.[1] The therapy is the first and only RSV preventative option using the same dose regardless of patient weight.

Drug Topics 10.6.25

MOUs / Joint Ventures

Eli Lilly lands "bargain" deal to acquire Verve Therapeutics for $1.3bn

Eli Lilly's buyout of the genetic medicine developer adds to lofty big pharma spending in 2025. Eli Lilly has agreed to acquire cardiovascular disease treatment specialist Verve Therapeutics in a deal potentially rising to $1.3bn, with market analysis describing the deal as a "bargain"

LOTTE BIOLOGICS, Axcelead Drug Discovery Partners, Inc., and Kanaph Therapeutics Inc. Sign 3-Way MOU to Develop ADC Toolbox

Lotte Biologics, South Korea *announced that e*xploring expansion of ADC services through synergy in ADC modality business via trilateral agreement Aims to enhance ADC capabilities through collaborative innovation with specialized partners.

Chosun Biz 17.6.2025

Torrent, India agrees to acquire JB Chem at Rs.25,000 cr. Valuation

Ahmedabad based drug maker Torrent Pharma has agreed to buy a controlling stake in JB Chemicals from global private equity firm KKR at an equity valuation of 25,689 cr. With this acquisition, Torrent will move to fifth rank by market share in the USD 26 bn Indian Pharmaceutical market.

The Economic Times 30.6.25

Japan delays medical expense reforms amidst political pushback

Overall health spending is still expected to surpass 12% of GDP by 2029.

Japan's plans to reform its high-cost medical expense benefit system have been postponed until autumn, following political opposition and concerns about patient financial protection. Despite the challenges, overall health spending is expected to surpass 12% of GDP by 2029, according to a BMI report.

Healthcare Asia 8.7.2025

Chugai and Gero link on antibody drugs for age-related conditions

Chugai will make an initial payment to Gero, with potential additional payments up to $250m based on milestone achievements. Chugai Pharmaceutical has signed a joint research and licensing agreement with Singapore-based biotechnology firm Gero to create new antibody drug candidates for age-related conditions. Their collaboration will utilise Chugai's antibody engineering technologies to develop new treatments for targets identified by Gero's AI platform, which analyses human datasets. Chugai gains exclusive global rights to research, develop, manufacture and commercialise antibodies for these targets.

Pharmaceutical Technologies 8.7.2025

Association Activities

Representations:

CDSCO issued a Circular on 25th June 2025 informing the industry that with effect from 15th July 2025, all WHO-GMP (CoPPs) need to the applied through online system developed by CDAC and application through hard copies will be accepted. Please see the circular here.

Based on the concerns raised by some of the members, BDMAI has made a representation to DCI requesting for transitional measures while implementing the new system. Please click here for representation.

E-Marketing Portal

BDMAI pleased to announce that soon it will be launching an **e-marketing Portal (Bulk Drug Market Access**). It is an online marketing App exclusively intended to promote APIs, Intermediates, Pallets and Pharma Services like CDMO, Consultancy, Reference Standards etc. It will be promoted in domestic as well as international markets. It helps the industry, particularly small and medium scale units to showcase their products. Salient Features of the e-Portal:

Salient Features of the e-Marketing Portal of BDMAI:

- All members of BDMAI can display their company details like Products, Manufacturing Facilities, Accreditations, Awards and any other achievements, **free of cost**.
- Non-Member Manufacturers & Traders also can showcase their products by **paying prescribed charges.**
- BDMAI will promote this Portal in India and in international markets on continuous basis to promote Indian Bulk Drugs Industry
- Buyers can search by Product name, Company name, HS code and CAS No.
- Buyers (both overseas and Indian) can send enquiry to all or selected manufacturers / traders for the products they are looking for
- There is a provision for Vendors (suppliers of chemicals/ equipment / instruments / maintenance items electrical, IT services providers, Consultants etc.) to register and display their products **by paying prescribed charges.** Vendors can also send mailers about their products to the relevant departments of member & non-member companies**.**

Bulk Drug Park at Una, Himachal Pradesh:

BDMAI has received a communication from the State Government of Himachal Pradesh informing about proposed Bulk Drug Park at Una district, Himachal Pradesh in about 1405 acre with certain common facilities like common effluent plant, hazards waste management, steam etc. A Government delegation led by Addl. Chief Secretary of the State will be in Hyderabad on 10th July 2025

and would like to interact with the members who are interested in taking land in the Bulk Drug Park. The meeting will be held at Hotel Taj Deccan, Hyderabad at 5.30 p.m.

Training of Manpower:

Free training of Rural Youth of Telangana State has been commenced in the last week of June 2025 at BDAMI's Training Center. Training is imparted under Dena Dayal Upadhyaya Grameena Khaushal Yojana (DDU GKY) Scheme of Government of India and State Government of Telangana. Training is given in Production / Quality Control / Manufacturing and duration of the training is for 3 months. Trained manpower will be made available to members for recruitment at free of cost.

Important Notifications:

Ministry of Finance, Govt. of India imposed Anti-Dumping Duty on Vitamin-A Palmitate Imports from China, EU & Switzerland

For detailed circular issued by CBIC on 6th June 2025 please click here

Members Achievements

MAITHRI DRUGS PRIVATE LIMITED

SUCCESSFULLY COMPLETED GMP INSPECTION BY USFDA

Maithri Drugs Private Limited has successfully completed an unannounced surveillance GMP Inspection conducted by the U.S. Food and Drug Administration (USFDA) from 16th June'25 to 20th June'25. This was an unannounced routine cGMP inspection for our Manufacturing Facility. The comprehensive cGMP inspection concluded with a positive outcome for the company. The USFDA issued a mere two minor Form 483 observations. The inspection was categorized as "Voluntary Action Indicated" (VAI), signifying that the observations were not related to data integrity or other critical issues. Maithri Drugs has affirmed its commitment to addressing these minor observations within the timelines stipulated by the USFDA. This successful audit underscores Maithri Drugs' robust quality management systems and its ongoing commitment to adhering to the stringent global regulatory requirements.

Aragen's Vizag Facility Leads Sustainable Shift with Cleaner Boiler Fuel

As part of its broader decarbonisation strategy and commitment to near-term Science Based Targets initiative (SBTi) goals, Aragen Life Sciences has transitioned the boiler fuel source at its Vizag manufacturing facility from furnace oil to Piped Natural Gas (PNG).

This cleaner and more efficient fuel is expected to reduce Scope 1 greenhouse gas (GHG) emissions at the Vizag site by up to 30%. The switch not only minimizes the facility's environmental footprint but also enhances energy efficiency and air quality—reinforcing our alignment with both national priorities and global climate action goals.

Aragen remains focused on advancing sustainability across its operations by integrating low-carbon technologies and cleaner fuels—creating long-term value for stakeholders and contributing meaningfully to a net-zero future.

AI IN DRUG DISCOVERY AND DRUG MANUFACTURING

By Mr. Shamal Jeewantha Fernando
Managing Director,
Slim Pharmaceuticals (Pvt) Ltd.

In drug discovery, AI is being used to predict the efficacy and safety of potential drug candidates, identify new therapeutic targets, and optimize clinical trial designs. By harnessing the power of machine learning algorithms, researchers can analyze vast amounts of biological data and identify patterns that are difficult to discern using traditional methods.

In drug manufacturing, AI is being used to optimize manufacturing processes, reduce costs, and ensure quality control. AI-powered predictive models can analyze data from multiple sources to identify potential issues and optimize production parameters, leading to faster and more efficient drug production.

In general, AI has the potential to revolutionize the pharmaceutical industry, leading to the development of safer and more effective drugs, personalized treatments, and improved patient outcomes. As the technology continues to advance, we can expect to see even greater breakthroughs in drug discovery and manufacturing in the years to come. Here's a comprehensive analysis of the use of AI in drug manufacturing:

How useful is AI in drug manufacturing?

AI in drug manufacturing can improve the efficiency of the manufacturing process by predicting the best conditions for drug synthesis and optimizing manufacturing parameters. It can also help identify impurities in drugs, increasing the quality and safety of the final product. AI can also analyze large amounts of data to discover patterns and insights, enabling pharmaceutical companies to make better decisions regarding drug manufacturing. AI has proven to be highly useful in drug manufacturing, enabling pharmaceutical companies to optimize their manufacturing processes, improve quality control, and reduce costs. Some of the key benefits of using AI in drug manufacturing include:

Cost effectiveness

AI has the potential to reduce the costs of drug manufacturing by reducing the time and resources needed to develop new drugs. This is particularly important in the early stages of drug development, where AI can predict drug toxicity and efficacy, reducing the number of expensive clinical trials required. By optimizing production processes and reducing waste, AI can help pharmaceutical companies to lower their manufacturing costs. This can lead to more affordable drugs for patients and increased profitability for the company.

Optimizing production processes:

AI algorithms can analyze data from multiple sources, such as production sensors and batch records, to identify patterns and optimize production parameters. This leads to faster and more efficient drug production, with fewer errors and less waste.

Best medicines

AI can help identify the best medicines for specific patient populations by analyzing large amounts of patient data, such as genetic information and medical histories. This personalized approach to medicine can improve patient outcomes and reduce the likelihood of adverse reactions.

Accuracy

AI can significantly improve the accuracy of drug manufacturing by identifying potential manufacturing defects and providing real-time

quality control. This reduces the likelihood of manufacturing errors, which can cause delays and increase costs.

Challenges

Despite its numerous benefits, the use of AI in drug manufacturing is not without its challenges. One of the biggest challenges is the lack of standardization in data collection and analysis, which can affect the accuracy and reliability of AI algorithms. Another challenge is the need for high-quality data, which can be time-consuming and expensive to acquire.

In general, AI has the potential to revolutionize drug manufacturing by increasing efficiency, reducing costs, improving accuracy, and enabling personalized medicine. However, to fully realize these benefits, pharmaceutical companies need to invest in high-quality data and standardize data collection and analysis. With these investments, AI can help pharmaceutical companies develop safer and more effective drugs, leading to better outcomes.

AI has become increasingly useful in drug discovery and manufacturing, offering several benefits such as increased speed, efficiency, accuracy, and cost-effectiveness.

Drug discovery AI can significantly speed up the drug discovery process by analyzing large amounts of data and identifying potential drug candidates. This is particularly useful in the early stages of drug development, where AI can predict drug toxicity and efficacy, reducing the number of expensive clinical trials required. AI algorithms can also identify new drug targets and pathways, leading to the development of innovative drugs.

AI is rapidly transforming the pharmaceutical industry, enabling companies to develop new drugs faster, more efficiently, and at a lower cost. AI is being used in drug manufacturing to optimize production processes, improve product quality, and reduce costs. AI is also being used in drug discovery to identify new therapeutic targets, design new drugs, screen potential drug candidates, and optimize drug properties.

In drug manufacturing, AI is being used to analyze vast amounts of data from sensors, cameras, and other sources to optimize production processes and improve product quality. AI-powered predictive models can identify potential issues and optimize production parameters, leading to more efficient production and higher yields. AI can also help identify potential quality issues before they become a problem, enabling operators to take corrective action before they result in quality problems. Additionally, AI can predict when equipment maintenance is needed, helping to prevent production downtime and reduce maintenance costs.

In drug discovery, AI is being used to analyze large datasets, including genomic and proteomic data, electronic health records, and scientific literature, to identify new therapeutic targets and design new drugs. AI can help researchers identify patterns and relationships in the data that may be missed by traditional methods, leading to the identification of new targets for drug development. AI can also help design new drugs by predicting how different molecules will interact with specific targets and screening large libraries of molecules to identify potential drug candidates. By using AI to optimize drug properties, researchers can predict how drugs will be absorbed, distributed, metabolized, and eliminated by the body, guiding the design of clinical trials.
Generally, AI is transforming drug manufacturing and drug discovery, enabling companies to develop safer and more effective drugs, personalized treatments, and improved patient outcomes. As AI technology continues to advance, we can expect to see even greater benefits in the years to come.

Drug design AI can optimize

Drug design by predicting the best conditions for drug synthesis and optimizing manufacturing parameters. It can also help identify impurities in drugs, increasing the

quality and safety of the final product. AI can also predict drug interactions with other drugs or with the human body, reducing the likelihood of adverse reactions. Drug design is one of the key areas where AI is making a significant impact. AI can help researchers design new drugs by predicting how different molecules will interact with specific targets and identifying potential drug candidates with the greatest likelihood of success. Here are some ways in which AI is being used in drug design:

Virtual screening: AI is being used to screen large libraries of molecules to identify potential drug candidates. By using machine learning algorithms to analyze high-throughput screening data, researchers can identify molecules with the greatest potential for efficacy and safety. AI can also help researchers design more efficient screening experiments by predicting which molecules are most likely to be active against a specific target.

Predictive modeling: AI is being used to predict how different molecules will interact with specific targets, predicting the binding affinity and identifying potential drug candidates with the greatest likelihood of success. By using machine learning algorithms, researchers can simulate the binding of molecules to target proteins, predicting the strength of the interaction and the likelihood of success.

Generative models: AI is being used to generate new drug candidates using generative models. These models use algorithms to generate new molecules that are optimized for specific properties, such as efficacy, safety, and pharmacokinetics.

Optimization: AI is being used to optimize drug candidates by predicting their pharmacokinetic and pharmacodynamic properties. By using machine learning algorithms, researchers can predict how drugs will be absorbed, distributed, metabolized, and eliminated by the body. This can help identify potential safety and efficacy issues and guide the design of clinical trials. Overall, AI is transforming drug design by enabling researchers to analyze vast amounts of data and extract meaningful insights that aid in drug development. By using AI to accelerate drug design, we can expect to see the development of safer and more effective drugs, personalized treatments, and improved patient outcomes.

Cost effectiveness

AI has the potential to reduce the costs of drug discovery and manufacturing by reducing the time and resources needed to develop new drugs. This is particularly important in the early stages of drug development, where AI can predict drug toxicity and efficacy, reducing the number of expensive clinical trials required. Best medicines AI can help identify the best medicines for specific patient populations by analyzing large amounts of patient data, such as genetic information and medical histories. This personalized approach to medicine can improve patient outcomes and reduce the likelihood of adverse reactions. Accuracy AI can significantly improve the accuracy of drug discovery and manufacturing by identifying potential errors and providing real-time quality control. This reduces the likelihood of errors, which can cause delays and increase costs. Challenges Despite its numerous benefits, the use of AI in drug discovery and manufacturing is not without its challenges. One of the biggest challenges is the lack of standardization in data collection and analysis, which can affect the accuracy and reliability of AI algorithms. Another challenge is the need for high-quality data, which can be time-consuming and expensive to acquire. AI has the potential to revolutionize drug discovery and manufacturing by increasing efficiency, reducing costs, improving accuracy, and enabling

Personalized medicine

However, to fully realize these benefits, pharmaceutical companies need to invest in high-quality data and standardize data collection and analysis. With these investments, AI can help pharmaceutical companies develop safer and more effective drugs, leading to better patient outcomes.

Collaborative AI:

Collaborative AI involves combining the expertise of humans and machines to solve complex problems. In drug manufacturing, collaborative AI could be used to identify potential drug candidates and optimize manufacturing processes. By working together, human experts and AI algorithms can come up with better solutions than either could on their own.

Continuous learning:

One of the strengths of AI is its ability to learn and improve over time. Continuous learning algorithms can adapt to changing conditions and improve their accuracy with each new data point. In drug manufacturing, continuous learning could be used to optimize manufacturing processes and improve drug quality over time.

Biomarker discovery:

AI is being used to discover new biomarkers, which are measurable indicators of a biological state or condition. By analyzing large datasets, such as genomic or proteomic data, AI can identify biomarkers that are associated with specific diseases or treatment responses. This can help clinicians identify patients who may benefit from a specific treatment or monitor treatment response.

Predictive maintenance:

Predictive maintenance uses machine learning algorithms to predict when equipment is likely to fail, allowing maintenance teams to address issues before they become serious. In drug manufacturing, predictive maintenance could help reduce downtime and ensure that equipment is running at optimal levels.

Personalized medicine:

Personalized medicine involves tailoring treatments to individual patients based on their genetic makeup and medical history. AI algorithms can analyze large amounts of patient data to identify potential drug interactions and predict which treatments are likely to be most effective. In drug manufacturing, personalized medicine could lead to the development of drugs that are more effective and have fewer side effects. AI is transforming drug discovery and personalized medicine by enabling researchers to analyze vast amounts of patient data and extract meaningful insights that aid in the development of personalized treatments. By using AI to develop personalized medicines, we can expect to see improved patient outcomes and more effective treatments for a wide range of diseases and conditions. In conclusion, the integration of artificial intelligence (AI) in drug manufacturing and drug discovery has the potential to revolutionize the pharmaceutical industry. AI has already demonstrated its ability to significantly accelerate the drug discovery process by reducing the time and cost required to bring new drugs to market, while also improving the accuracy and efficiency of drug design.

AI has also shown promise in developing personalized medicine, allowing clinicians to tailor treatment plans to the specific characteristics of each patient. By analyzing vast amounts of patient data and extracting meaningful insights, AI can help identify patient subgroups that may benefit from specific therapies and predict how patients will respond to different treatments. In drug manufacturing, AI has the potential to improve the efficiency and quality of the manufacturing process, reducing costs and increasing production capacity. By analyzing data from manufacturing processes, AI can identify opportunities for optimization and predict potential issues before they occur, improving product quality and reducing the risk of recalls.

While there are still challenges to overcome, such as the need for more comprehensive data sets and the integration of AI into existing drug discovery and manufacturing workflows, the potential benefits of AI in pharmaceuticals are undeniable. As the field continues to develop

and evolve, we can expect to see continued advancements in drug discovery and personalized medicine, bringing new treatments to patients faster and more efficiently than ever before. However, there are still challenges to be addressed, such as the need for comprehensive and diverse data sets, robust algorithms, and ethical considerations surrounding the use of AI in healthcare. Additionally, the integration of AI in drug discovery and manufacturing workflows may require significant investment and changes to existing practices.

The integration of AI in drug manufacturing and drug discovery has significant potential to transform the pharmaceutical industry. As AI continues to evolve and become more sophisticated, we can expect to see several advancements in this field in the coming years. One prediction is that AI will become more integrated into drug discovery workflows, enabling faster and more efficient drug development. AI can also help researchers identify new drug targets and design drugs with greater accuracy and precision, leading to the development of more effective treatments.

Another prediction is that AI will enable the development of personalized medicine, tailored to the unique characteristics of each patient. By analyzing patient data and genetic information, AI can help predict how individuals will respond to different treatments, enabling clinicians to select the most effective treatment for each patient.

Additionally, AI can optimize drug manufacturing processes, improving efficiency and reducing costs. AI can help identify opportunities for process optimization and predict potential issues before they occur, improving product quality and reducing the risk of recalls.

In summary, the continued development and adoption of AI in drug manufacturing and drug discovery are essential for the future of healthcare. We can expect to see several advancements in this field in the coming years, leading to the development of more effective treatments, improved patient outcomes, and a more efficient healthcare system.

Conclusion:

Nevertheless, the benefits of AI in drug discovery and manufacturing are clear. It can enable the development of innovative treatments, improve patient outcomes, and address some of the major challenges facing the pharmaceutical industry. As such, the continued development and adoption of AI in drug discovery and manufacturing are crucial for the future of healthcare, and we can expect to see ongoing advancements and breakthroughs in this area in the coming years.

Source: Pharma Focus (issue 4)

Strategic Integration of QRM in Drug Substance Manufacturing: A Roadmap

Dr. Ajay Babu Pazhayattil

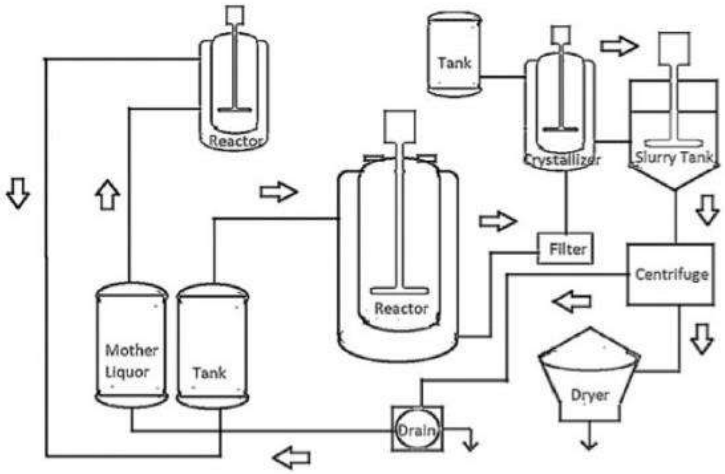
ICH Q7 Good Manufacturing Practice (GMP) guideline for active pharmaceutical ingredients (APIs) outlines the fundamental GMP requirements for drug substance manufacturing, from introduction of starting materials through processing and packaging. The guideline addresses controls related to personnel, facilities, equipment, materials, manufacturing processes, laboratories, storage, validation, change management, and quality oversight. API manufacturing involves the use of building block raw materials, designated regulatory starting materials (RSMs), and intermediates at various stages. Many of the initial building block raw materials are commercially available. The API manufacturing segment differs from drug product GMP operations. API manufacturing has early stages of manufacturing building blocks for key steps, and developing case by case rationale to determine the correct starting point of API manufacturing. ICH Q7 has attempted to clearly break down the requirements, for example, for a chemical synthesis. [Table 1]

Table 1: ICH Q7

ICH Q7 GMP Requirements					
Starting Material (SM)	API for clinical	Process steps starting with the use of SM	Intermediate manufacturing	Extraction and purification	Final processing and packaging
Do not apply	Not all apply	All controls apply			

The controls for API and intermediate manufacturing should be phase appropriate and in line with the stage of drug substance development. The guidance on development and manufacture of drug substance (ICH Q11) was published in 2012. The well-established Quality by Design (QbD) principles for drug products under ICH Q8 extend to the drug substance manufacturing with ICH Q11. Q11 guidance and associated Q&A provide details on a QbD approach to drug substance process development, justification of starting materials, lifecycle process validation and Quality Risk Management (QRM). This article discusses how QRM principles, as described in ICH Q9 (R1), can be integrated across the stages of drug substance manufacturing.

Figure 1: Drug Substance Manufacturing



The number of intermediate manufacturing steps can vary depending on the synthetic route selected, particularly in the case of small molecules [Figure 1]. Intermediate and final API manufacturing step typically involves isolation and purification processes. Common reprocessing techniques include recrystallization, distillation, filtration, column chromatography, and milling, all of which are integral to the overall manufacturing process. Mother liquor recovery of reactants, intermediates and API is performed as per the approved process, and quality is confirmed prior to use. The reaction, crystallization, and drying stages require careful management of bulk material volumes. Evaluation of safety and scale effects on the selected equipment train is important for successful commercialization. Special considerations need to be in place for the use and traceability of the recovered material. Cross-contamination controls are of particular importance when non-dedicated equipment, such as reactors, is utilized in the various steps. A robust cleaning validation and verification program, along with validated test methods, is critical to ensure minimal carryover. Addressing these requirements is challenging for newly developed API synthetic routes, as the chemistry and process understanding are not well established. Qualified/validated laboratory test methods are required for characterization at all development stages, raw material testing, registered starting material testing, intermediate material testing, final API testing, stability testing and in-process testing. In-process control (IPC)/testing of intermediate and API manufacturing encompasses assay, purity, water content, etc., to determine adequacy of material quality at various stages. In some cases, the reaction continues while the IPC results are generated for further charging calculations.

The challenges in drug substance manufacturing and qualification/validation are unique as the process incorporates multiple process loops, and the reaction process itself might be a multi-day process. The API industry utilizes optical process analytical technologies (PAT), such as FTIR, NMR, and Raman, at various stages of operations. Additionally, safety considerations are crucial, as the reactions can be exothermic in nature. Process characterization studies, including spike, fate, and

purge studies, as well as design of experiments (DoE) studies, are performed during the process design stage. Design of Stage 2 Process Performance Qualification (PPQ) studies, therefore, warrants careful planning and risk assessment. The subsequent Stage 3 Continued Process Verification plan for the drug substance needs to consider monitoring of processing loops and variables, such as drying and reaction time. Drug substance intermediate and final API manufacturing steps need to consider the input variables. Some intermediate steps may be independent of the previous steps. In most cases, the quality attributes establish the reaction endpoint, and therefore, minimal data may be available to determine within-batch variability. Continued evaluation of evolving risks is hence important in drug substance manufacturing to enhance the control strategy. A preliminary risk categorization is the first step towards implementing QRM principles in drug substance manufacturing.

The drug substance manufacturing process for chemical entities involves synthetic route development and process development to enable successful chemical reaction conversion mechanisms. In some cases, it may involve numerous chemical conversions in multiple process steps to produce a few grams of a highly potent active pharmaceutical ingredient. The manufacturing process can extend to months. Process design becomes an important aspect of drug substance development and scale-up for commercialization. Each drug substance manufacturing process is unique, depending upon complexities such as the number of chiral centers and reaction mechanisms. Multistep synthesis strategies, such as convergent or telescoping synthesis, are commonly applied in isolating the API. Product yield, material cost, safety, environmental, quality and process efficiency are important in drug substance manufacturing and need to be considered as part of process development. Flow chemistry is an emerging segment of API process manufacturing with proven advantages for safety and efficiency. However, the possibility of different reaction pathways presents challenges in implementing standard processes. The industry thus has some unique needs and has advanced in certain areas of PAT in comparison to the drug product manufacturing process, for example, NIR. This scenario presents an opportunity to strengthen drug substance operations by identifying and using quality risk management tools at each stage.

Table 2: Risk Scale

Category	**1**	**2**	**3**	**4**	**5**
Manufacturing Process	Early phase development (Stage 1)	Clinical, registration, stability, demonstration batches (Stage 1)	Clinical, registration, stability, demonstration batches (Stage 1)	Process performance qualification batches (Stage 2)	Commercial batches (Stage 3)

Analytical Method	Non validated test methods	Non validated test methods	Validated test methods	Validated test methods	Validated test methods

API development, manufacturing and testing can be divided into five categories and related to the lifecycle stages (Process Validation Stage 1, 2 and 3) as indicated [Table 2]. The product and patient risk level increases as development moves from its early stages to commercial manufacturing (1-5). Category 1 primarily includes early development study batches, including DoE's to define critical process parameters and for process optimization. The analytical test methods at this stage are non-validated methods. Categories 2 and 3 are primarily clinical, registration, stability, and demonstration batches, some of which will be utilized for human clinical trials. The only difference between categories 2 and 3 is the use of non-validated analytical test methods versus the use of validated test methods. Analytical test methods, including in-process methods, are typically in validation at this stage. Category 4 PPQ batches may be utilized for drug product-formulation development batches, PPQ batches, and commercial batches. The analytical test methods need to be fully validated at this stage. The drug substance PPQ studies involve an increased level of sampling and testing plans. Category 5 includes commercial batches undergoing continued process verification. Throughout stages 1-5, the maturity of the risk management tools increases to accommodate the data and product/process knowledge captured throughout the lifecycle of the process.

The criticality of Stage 1, which includes QbD based development principles (ICH Q11) and the unique processing steps, makes drug substance development and commercialization a distinctive segment. The reaction mechanism and processes, for example, the ongoing charging, make the in-process analysis critical in ensuring attainment of established quality attributes. The drug substance manufacturing operations involve multiple intermediate steps and variables, of which some are dependent and some are independent. Therefore, a tailored roadmap for QRM is recommended in drug substance development. Each of the categories defined requires varying levels of risk assessment and associated tools based on the development phase of the product [Table 3].

Table 3: Roadmap- QRM for Drug Substance Manufacturing

Category	**Risk gauging steps**	**Facilitator/ Collaborators**	**Recommended QRM Tools**
1	Synthetic route selection assessment	R&D	Scientific rationale

	Impurity, stress studies risk assessment	R&D/Analytical	Scientific rationale, Checklist, Decision Tree, Criticality Analysis
	Initial QbD process development risk assessment	R&D	Fault Tree Analysis (FTA), Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).
	Occupational health toxicity/potency categorization	Toxicologist/R&D, Technology Transfer	Preliminary Hazard Analysis (PHA), Hazards Analysis and Critical Control Points (HACCP)
	RSM and key material supplier qualification	Quality/R&D	Checklist, Decision Tree, Custom Risk-based Approach
2	Post QbD process development risk assessment	R&D	Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA), Semi-Quantitative Risk Determination (SQRD)
	Pre QbD method development risk assessment	Analytical	Fault Tree Analysis (FTA), Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).
	Pre scale up risk assessment	R&D/Technology Transfer	Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA), Semi-Quantitative Risk Determination (SQRD)
	Facility/Equipment assessment	Engineering/Technology Transfer	Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).
	Method transfer risk assessment	Analytical/Quality	Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).
	Pre-clinical risk assessment	Clinical/R&D	Checklist, Fault Tree Analysis (FTA), Hazards and Operability Studies (HAZOP)
	Stability study risk assessment	Analytical/R&D	Fault Tree Analysis (FTA).

3	DMF submission risk assessment	RA/Quality	Checklist.
	Post scale up/pre-PPQ risk assessment	Technology Transfer/Operations, Quality	Semi-Quantitative Risk Determination (SQRD).
	PAI audit risk assessment	Quality/Technology Transfer, R&D	Checklist.
4	Risk based determination of Stage 2 PPQ batches	Technology Transfer/Quality	Statistical data driven # of batch estimation tools.
	PPQ risk assessment	Technology Transfer/Quality	Reconfirmation of post scale up Semi-Quantitative Risk Determination (SQRD).
	Risk based determination of Stage 3a batches	Technology Transfer/Quality	Statistical # of batch estimation tools.
5	Post Stage 3a risk assessment	Technology Transfer/Quality	Semi-Quantitative Risk Determination (SQRD).
	Ongoing annual product review/CPV risk assessment	Quality	Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).
	Investigation risk assessment	Quality	Risk-based Impact Assessment
	Change implementation risk assessment	Quality	Risk Estimation Matrix and/or Failure Mode and Effects (and Criticality) Analysis (FMEA/FMECA).

Throughout the product lifecycle, the data collected is captured, and risk assessment is performed to enable knowledge of the process under assessment. Each stage of the process utilizes a combination of scientific data and risk management principles to ensure process robustness and ultimately ensure product quality. The list is not comprehensive and may act as a roadmap for selecting the most appropriate tool at each stage. A critical assumption in the execution of these risk assessments is cross-functional involvement, Research and Development is responsible for the synthetic route development and QbD process development; Analytical Support is responsible for AQbD based method development, validation and transfer; the Quality Unit is responsible for quality control laboratory operations, quality assurance, investigation, annual quality review and compliance; and Technology Operation is responsible for scale up, process

transfer and PPQ. It is the cumulative involvement of all these players that enables a robust risk assessment.

Drug substance development and manufacturing are evolving with the adoption of ICH Q7, ICH Q11, and process validation lifecycle guidance. These frameworks introduce expectations that call for specialized quality risk management (QRM) approaches, reflecting the complex and varied attributes encountered across different stages of the product lifecycle. This article outlines a practical roadmap for implementing end-to-end QRM within drug substance development and manufacturing operations. The goal is to embed QRM principles into the organization's quality management system, supporting routine risk assessments and proactive mitigation efforts. The effective use of statistical and data visualization tools is emphasized, as these are critical in identifying, evaluating, and communicating potential risks. Regular risk reviews and clear communication of risk status are essential to ensure timely control of residual risks, ultimately safeguarding patient health, enhancing operator safety, and maintaining product quality. Given the differences between drug substance and drug product processes and control strategies, a customized QRM approach is necessary. The proposed roadmap highlights specific areas where QRM tools can be applied to drug substance manufacturing, facilitating consistency and standardization across the sector.

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4. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Q9 (R1)- Quality Risk Management, Jan 2023. https://database.ich.org/sites/default/files/ICH_Q9%28R1%29_Guideline_Step4_20250115.pdf

Analysis of Exports and Imports of APIs & Intermediates

Pharma Exports during April-May (All Categories) Values in $ Mn							
Month(s)	**2023-24**	**2024-25**	**% Change between 23-24 & 24-25**	**Apr-May 2024-25**	**Apr-May 2025-26**	**% Change between Apr-May 24-25 & 25-26**	**% Change between months Apr-May FY26 (B)**
Apr	2262.01	2428.36	7.35%	2428.36	2486.02	2.37%	
May	2084.03	2305.56	10.63%	2305.56	2475.70	7.38%	-0.42%
Apr-May	**4346.04**	**4733.91**	**8.92%**	**4733.91**	**4961.71**	**4.81%**	

Exports of Bulk drugs & drug Intermediates($ Million)							
Product Category	**2023-24**	**2024-25**	**% Change**	**Apr-May FY25**	**Apr-May FY26**	**% Change**	**% Share**
Bulk Drugs & Drug Intermediates	4755.25	4869.98	2.41%	736.65	769.07	4.40%	15.50%

- The second major category by value is **Bulk drugs and drug intermediates.** During **Apr-May 2025-26** this segment expanded by 4.40%. The value of exports in this category was **USD 769.07 million.**

Imports of Pharma all Categories In April - May (Values in $ Mn)							
Month(s)	**2023-24**	**2024-25**	**% Change**	**2024-25**	**2025-26**	**% Change**	**% Change between months Apr-May FY26**
Apr	577.05	683.59	18.46%	683.59	748.45	9.49%	
May	702.29	762.34	8.55%	762.34	785.99	3.10%	5.01%
Apr-May	**1279.34**	**1445.93**	**13.02%**	**1445.93**	**1534.44**	**6.12%**	

Imports of Bulk drugs & Drug Intermediates ($ Million)							
Product Category	**2023-24**	**2024-25**	**% Change**	**Apr-May 24-25**	**Apr-May 25-26**	**% Change**	**% Share**
Bulk Drugs & Drug Intermediates	4548.75	4627.70	1.74%	789.05	755.36	-4.27%	49.23%

- India’s major categories of pharma products imported during May 2025-26 were **Bulk Drugs and Drug Intermediates** which **comprised 49.23%** of India’s total pharma imports. The value of imports in this category was **USD 755.36 million**. Imports in this category decreased by 4.27%.

India's Exports of Bulk Drugs during April-May (Values in $ Mn)				
Month	2024-25	2025-26	Change%	Change in Revenue
April	235.88	268.07	13.65	32.19
May	274.04	275.97	0.70	1.93

- Exports have Grown at a lower pace in the month of May 2025.

India's Bulk Drugs Exports by Region $ Mn(Regions as defined By DOC)				
Region	2023-24	2024-25	Change%	Contbn%
Africa	29.54	28.16	-4.67	5.34
Asean	53.89	42.74	-20.68	8.10
CIS	14.29	13.97	-2.20	2.65
EUROPE	172.44	159.73	-7.37	30.28
LAC	35.93	32.67	-9.08	6.19
NAFTA	61.44	89.47	45.62	16.96
NEA	48.37	53.27	10.13	10.10
Oceania	2.14	1.78	-16.68	0.34
Others	1.74	24.07	1282.97	4.56
South Asia	33.59	28.80	-14.27	5.46
WANA	56.54	52.83	-6.57	10.02
Grand Total	509.92	527.50	3.45	100.00

Manufacture of Bulk drugs & Drug intermediates have increased in the region of Europe. This is in accordance of EU parliament resolution that Dependency of Pharmaceuticals on India & China must be reduced. Europe had some issues during 2023 & part of 2024 due to import of oil from Russia which is sorted out to an extent thereafter.

In the region of Asean, some of the Basic manufacture of Bulk drugs & Intermediates has been shifted to Vietnam by China. This has given a boost to Vietnam’s Manufacture. Thailand is also building its API structure with the help of Japan.

Bulk drug Exports to top 10 countries $ Mn(April-May)					
Rank	**Country**	**2024-25**	**2025-26**	Change%	**Contribution**
1	U S A	46.10	63.19	37.07	11.98
2	CHINA	17.77	23.34	31.33	4.42
3	Brazil	22.44	18.50	-17.56	3.51
4	Bangladesh	20.17	18.45	-8.53	3.50
5	Netherlands	13.01	17.73	36.24	3.36
6	Germany	16.53	17.49	5.82	3.32
7	France	16.34	16.31	-0.21	3.09
8	Canada	5.08	16.19	218.62	3.07
9	Turkey	15.80	14.95	-5.35	2.83
10	Egypt	14.02	14.78	5.39	2.80
	Total Of the above	187.26	220.92	17.97	41.88
	Rest	322.66	306.58	-4.98	58.12
	Grand total	509.92	527.50	3.45	100.00

India's Bulk Drugs Imports by Region $ Mn				
Region	**2023-24**	**2024-25**	**Change%**	**% contribution**
Africa	0.04	0.00	-100.00	0.00
Asean	10.11	13.26	31.16	2.19
CIS	0.01	1.22	16473.98	0.20
EUROPE	90.80	88.03	-3.05	14.56
LAC	1.38	0.52	-62.24	0.09
NAFTA	14.65	16.00	9.22	2.65
NEA	516.15	484.83	-6.07	80.18
Oceania	3.38	0.01	-99.81	0.00
Others	0.00	0.00	-100.00	0.00
SouthAsia	0.00	0.35	9796.51	0.06
WANA	6.70	0.42	-93.76	0.07
Grand Total	643.22	604.64	-6.00	100.00

Important Note:

The organizers of Global ChemiShow offered 30 stalls (fully furnished 9 sq. meter stalls) on Complimentary basis. 12 of our members have already taken the Stalls. Members who are interested to avail these FREE stalls, please write to ed@bdmai.org ; info@bdmai.org; Stalls will be allotted on first-come-first-serve basis.