



Addressing Local Manufacturing of API: A Challenge in Pakistan

Dr. Shaherbano, Pharmacist

HIGHLIGHTS

In Pakistan, many challenges are being faced by the local manufacturing of Active Pharmaceutical Ingredients (API). Maintaining international quality standards during production is a major problem. Compliance with the strict regularity is also a major problem. While the lack of adequate infrastructure for efficient manufacturing remains a significant problem. Production costs have increased, and competitiveness is reduced due to the existing gap in infrastructure. In addition, lack of investment for R&D, and insufficient support from regular bodies are also concerning points during the manufacturing process.



Understanding the hurdles faced during the manufacturing of API

Manufacturing of API active pharmaceutical ingredient in Pakistan means production of high-purity active pharmaceutical compound with basic and daily used raw chemicals by using different techniques like distillation, fermentation, extraction, in batch or continuous manner at industrial scale, ensuring their quality, purity, concentration, and their mechanism of action involving different equipment (mills, dryers, filters). As manufacturing is not a simple process, it also faces some hurdles. Here we will discuss a few of them.

Quality Standards:

For Pakistan, API manufacturers ensuring internationally recognized quality is a major barrier that limits their ability to export and compete.

A. Difficulty Meeting International Certification:

Obtaining certification from national regulatory bodies recognized for high-standard, rigorous, and evidence-based evaluation of products, like the World Health Organization (WHO-PQ), the U.S. Food and Drug Administration (USFDA), or the European Medicines Agency (EMA), is a long, difficult, and extremely expensive process. Just a few (around 3) Pakistani pharmaceutical companies have achieved WHO Prequalification currently, and no Pakistani API product has ever received approval from the USFDA or EMA.

B. Low GMP Compliance:

Good Manufacturing Practices (GMP) are the set of rules that ensure medicines are produced consistently and are safe for consumption. In Pakistan, only about 31% of pharmaceutical firms pass periodic GMP inspections conducted by regulators. Moreover, only 23% of firms are supplied with modern real-time data recording systems, which are essential for proving to international regulators that the product was made correctly at every step of the production.

C. High Cost of Upgrades:

Bringing old factories up to modern international standards requires heavy investment. Upgrading a single facility to meet standards like WHO-GMP can cost extremely high amounts for most local manufacturers who operate on thin profit margins.

Infrastructure Gaps:

The physical and industrial infrastructure required for chemical synthesis is either missing or inadequate in Pakistan.

a) Missing Petrochemical Feedstock (Naphtha Cracker):

Chemical building blocks derived from petroleum, such as benzene, toluene, and methanol, are required for the manufacturing of API which are produced in advanced technology sectors or industrial plants called a Naphtha Cracker Complex. Pakistan does not have such infrastructure, so most basic precursor chemicals are also imported, which is a more expensive procedure and keeps the industry dependent on foreign sources from the initial step.

b) Energy Insecurity:

Local manufacturing of API is an energy-consuming process. Chemical reactions often require machines to run 24 hours for weeks to months. Pakistan's sky-high electricity bills with high tariffs and unreliable power supply, with frequent load shedding, make production costs uncompetitive and operations risky.

c) Lack of Specialized Industrial Zones:

Fully operational and high-technology-equipped API Parks or cluster-based industrial zones would ideally provide "plug-and-play" infrastructure that contains a reliable gas supply, specialized waste treatment plants to handle chemical wastes, and an uninterrupted power supply. As Pakistan is an underdeveloped country and struggling with the manufacturing of API, it lacks companies that just enter and start working.

d) Inadequate Testing Infrastructure:

Pakistan has a severe shortage of advanced laboratories needed for drug development and testing. As an underdeveloped country that has only 6 bioequivalence (BE) study centers, and not a single one is internationally accredited. That's why manufacturers send samples and patients abroad to get the data needed to register their products.

Regulatory Hurdles:

Maintenance of the regulatory environment itself presents a significant hindrance.

a. Outdated and Punitive Legal Framework:

In Pakistan, for the last half-century, industries have been regulated by the Drug Act of 1976. This old law uses terminology that compares simple quality deviations in formulations to intentional wrongdoing (crime). This creates an environment where the focus is on punishment rather than encouraging pharmaceutical industries to report issues and fix them.

b. Complexity and Inconsistency:

There is a complication of regulations of the Drug Act 1976 and the DRAP Act 2012, side by side, as many rules in them overlap. This complexity, combined with a difficult and prolonged approval process for new drug manufacturing and random pricing controls, creates uncertainty for investors.

c. "Policing" vs "Facilitation" Mindset:

Stakeholders have identified that the regulatory culture focuses on policing means catching mistakes and punishing them instead of facilitating industries to grow and meet standards assigned by national or international regulatory bodies.

d. Policy Instability and Slow Implementation:

The API promotion policy was introduced in 2022; before that, there was no predictable long-term policy framework. Even when policies exist, their implementation is a very difficult task due to bureaucracy.

Lack of R&D Investment

A weak ecosystem for research and development of API suppress progress and keeps the industry focused on simple and low-value molecules.

A. Industry-Academia Gap:

There is no collaboration of university research with industrial needs. The education system and industrial system work independently. As a result, valuable research remaining trapped in academic journals and industries till now depends on imported technology instead of making their own.

B. Critically Low R&D Spending:

Pakistan spends a very low margin of its GDP on research and development. This is far less than competitors like India and China. The private sector's contribution is negligible. The Central Research Fund (CRF) is also established to support the sector, which is not effectively used, as a major portion of funds is spent on administration rather than actual research.

C. Lack of a Centralized Research Body:

Unlike other countries, Pakistan lacks a centralized public research center for research and development of pharmaceutical sciences. Such an institution could develop cost-effective synthesis processes for off-patent drugs and provide them to the local industry.

Solutions

Quality Standards:

The Step-by-Step Certification Model

Instead of aiming for certification from national regulatory bodies immediately, which is too expensive and time taking process, DRAP should implement a Graduated Compliance Path. Start with a National Export-Ready certificate that offers a handful of tax benefits that help industries save budget for the next certifications from WHO-GMP.

Centralized Digital Compliance Hub

The government can allow software engineers to build a country-wide software for local API manufacturing industries rather than buying expensive real-time data software. This will reduce the cost and give a boost to the budget for other expenses.

Quality Mentorship Program

Companies provided by the WHO-prequalified allow for sponsoring 5 small firms on regulatory documentation after paying taxes.

Infrastructure:

The Virtual API Zones

Building a new industry with advanced infrastructure and technology is a very slow and costly process. Instead of building the whole, we can build Virtual API zones, which are provided by advanced infrastructure and technology using the existing electricity grid, but provide these blocks with Priority Power (Zero Load-shedding) by diverting power from less critical sectors.

The Buy Technology, Not Feedstock Approach

Instead of importing the raw material along with heavy advanced machinery with trained personnel, which is a multi-billion-dollar project, import Advanced Intermediate processing and perform the final 2-3 synthesis steps in Pakistan. This requires much less energy and simpler waste management.

Common Effluent Treatment Plant (CETP)

The government should build **one centralized chemical waste plant** in Industrial areas so that industries can pay a small pay-per-use fee, which is cheaper for them than building individual treatment plants.

Regulatory Hurdles:

Softening of the law

Do some amendments in the 1976 Drug Act for terms used for technical faults as criminal offenses. This costs 0 rupees but improves investor confidence.

Sunset Clauses for Approvals

Implement a **"Deemed Approved"** rule. If DRAP does not respond within 60 days for an API manufacturing application, it is automatically considered for approval. This forces efficient production without wasting time and without requiring any extra budget.

DRAP Help Desk

Shift DRAP's role from just inspecting and punishing to a Pre-Audit Consultation service. Companies can pay a small fee to have DRAP officials review their plans before or during construction to ensure they meet standards.

R&D:

Central Research Fund (CRF)

The CRF is already funded by pharma companies; stop using it for administration. Must give money to the industry that successfully manufactures an off-patent API locally.

Research center in the University

Instead of theoretical research at the university level, do some authentic research for developing the recipe for top imported APIs and give it to the local industry for free.

Tax Credits for PhD Employment: Offer a specific tax deduction on the salary of any research scientist hired by an API firm. This moves a talented student from academia to the factory floor at zero cost.

To be a facilitator

The government should try to be a facilitator instead of being a manufacturer. The priority should be finding an import substitution for the API

Conclusion

Addressing the local manufacturing of API in Pakistan requires a comprehensive, multi-pronged approach that resolves the issue from multiple angles to achieve sustainable solutions.

Firstly, certification and software must be provided by the government instead of importing every single thing. This step reduces the cost of establishing a company.

Secondly, work on the infrastructure of industries by making virtual API zones or waste plants.

Thirdly, DRAP should make new rules or laws according to need, which will give new directions to work in the future.

Lastly, research opportunities should be provided to students and a connection between industries and educational institutions.

Authors profile

Shaher Bano is a final-year Doctor of Pharmacy student from Gulab Devi Educational Complex. Having a strong academic interest in pharmaceutical policy and the health care system. Demonstrate a keen interest in improving the pharmaceutical sector in Pakistan. She has a passion to contribute to better healthcare solutions and aspires to continue her career in research and advancing policy reform in the pharmaceutical sector.