© AUG 2026 | IRE Journals | Volume 10 Issue 2 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV10I2-1722610

API and Drug Master File Quality as Key Enablers of Pharmaceutical Manufacturing Localization in Saudi Arabia

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Abstract- ***The extent to which Saudi Arabia's programme for localising its pharmaceutical industry relies on whether local manufacturers are able to obtain, comprehend, transfer, and consistently sustain control over high-quality active pharmaceutical ingredients (APIs) and the chemistry, manufacturing, and controls knowledge contained in Drug Master Files (DMFs) is examined in this review. Rather than viewing API quality and DMF quality as separate regulatory documents, the review treats them as linked industrial capabilities. It brings together recent work on pharmaceutical localisation, supply-chain resilience, Quality by Design, Process Analytical Technology, continuous manufacturing, and impurity control with the requirements of the Saudi Food and Drug Authority and the international ICH, FDA, EMA, and EDQM guidelines. The analysis states that localisation is successful when an API is not only in compliance with pharmacopeial standards at the time of release but is also backed by a reproducible process, scientifically justified specifications, qualified analytical methods, traceable impurity control, stability data, lifecycle change governance, and a current DMF that can be used to support regulatory assessments and technology transfer. In the context of Saudi Arabia, such attributes can help reduce uncertainty associated with technical transfers, shorten investigation periods, improve supplier qualification, strengthen local release testing, and enable effective post-approval change management. Two conceptual models are presented: an API-to-localisation value chain and a dual-engine readiness matrix that connects material quality with DMF maturity. The review concludes that policy on localisation should assess manufacturing readiness in terms of the depth of the quality system and the ability to transfer knowledge, rather than simply on the physical location of the final dosage-form production. The key priority actions should be benchmarking of DMF quality, the development of API suppliers on a risk-based basis, building up local analytical expertise, establishing structured lifecycle governance, using digital CMC data, and introducing incentives to encourage greater upstream manufacturing competence.***

I. INTRODUCTION

The localisation of pharmaceutical manufacturing has now become a strategic element of Saudi Arabia's efforts to diversify its economy and improve its health security. As part of Vision 2030 and the National Industrial Development and Logistics Program, pharmaceuticals have been identified as a key industrial area, and Saudi academic work has on several occasions pointed out the high degree of imports, the concentration of active ingredients and sophisticated inputs abroad, as well as the necessity of moving beyond just packaging or secondary manufacturing to achieve higher-value capabilities. Localisation is therefore not simply a matter of setting up production lines; it is about determining whether a local facility is able to produce a drug product with consistent safety, efficacy, and quality while at the same time controlling the scientific and regulatory knowledge that affects the performance of the material throughout the product's lifecycle.

For the vast majority of small-molecule medicines, the active pharmaceutical ingredient is the most important of the materials introduced. Variability in the API can affect the assay, the level of impurities, particle size, the polymorphic form, moisture content, flow properties, compressibility, dissolution behaviour, and in the end the performance of the final product. A material can still satisfy a compendial certificate of analysis and yet cause transfer problems if the manufacturer does not have adequate knowledge of the process controls, the fate of impurities, the physical form, the residual solvents, the elemental impurities, the retest period, the packaging, the storage conditions, or any changes to the synthesis route. The difference between complying with release requirements and having a proper understanding of the process is at the heart of today's pharmaceutical

quality systems. ICH Q7 calls for APIs to be produced under an appropriate quality system, while Q9, Q10, Q11, and Q12 together stress science- and risk-based development, process understanding, lifecycle management, and controlled change.

The Drug Master File is an approach for arranging and securing this knowledge. According to the SFDA, a DMF is a confidential file which includes detailed information regarding the facilities, processes, or items used in manufacturing, processing, packaging and storage, generally comprising the CMC information for components such as drug substances. The SFDA guidance covers drug substances, drug-substance intermediates and the materials employed in their preparation. It mandates administrative information, current version control, details about the manufacturing site, and a letter of access before the authority can refer to the file. On an international level, the FDA DMFs, the European Active Substance Master File procedure and EDQM Certificates of Suitability all aim to achieve similar objectives although they do so using different judicial and procedural structures.

The reference review that is attached shows a sound approach to quality management even though it deals with the subject of pharmaceutical three-dimensional printing. It connects Quality by Design and Process Analytical Technology with the systematic relationship between the critical material attributes, the critical process parameters, and the critical quality attributes, and it states that real-time or analytically controlled measures at appropriate points are necessary when it is essential to understand variability rather than just detecting it at the end of the production process. This kind of logic can be directly applied to localization: the local manufacturer must have a justifiable understanding of which API attributes are important, how they occur, how they are tested, and how changes are communicated. Quality in the context of a DMF is therefore not simply a matter of administrative completeness; it also involves the accessibility, coherence, currentness, and regulatory usability of manufacturing knowledge.

II. AIM AND OBJECTIVES

The purpose of this review is to assess the way in which the quality of both the API and the DMF enables reliable localisation of pharmaceutical manufacturing in Saudi Arabia and to convert that assessment into a practical readiness framework for use in regulatory and industrial decision-making. Unlike other reviews which focus on market size or the incentives for localisation, this analysis centres on the quality of the knowledge of upstream materials and on the transfer of that knowledge into a local pharmaceutical quality system.

The aims are five in number: first, to establish the API quality characteristics that have the greatest impact on technology transfer and on the performance of the final product manufactured locally; second, to pinpoint the content, lifecycle, and governance features that set a high-quality DMF apart from a merely complete one; third, to link API and DMF quality to the SFDA's expectations and to the relevant ICH lifecycle guidelines; fourth, to explain how these factors affect supplier qualification, the development of local analytical competencies, process validation, handling of changes after approval, and supply resilience; and fifth, to suggest a model for achieving readiness for localization in Saudi Arabia that can assist in deciding which products and suppliers should be prioritised for further domestic manufacturing.

III. REVIEW METHODOLOGY

The integrative review approach was chosen since the research question involves regulatory guidance, pharmaceutical quality science, industrial policy, and supply-chain literature. A traditional systematic review focused only on randomized or homogeneous empirical studies would not be suitable because governance of DMFs, control of the API lifecycle, and localization policy are generally found in regulatory documents, technical guidance, review articles, and policy reports rather than in similar clinical or manufacturing trials. By using an integrative method, it is possible to combine these different kinds of evidence while still preserving clear selection criteria and thematic transparency.

The literature was found by carrying out focused searches on biomedical and multidisciplinary scholarly sources available via PubMed, publisher databases, Google Scholar, and records linked through Crossref, together with official regulatory and government websites. The search terms included phrases such as "active pharmaceutical ingredient", "API quality", "drug master file", "active substance master file", "chemistry manufacturing controls", "Quality by Design", "Process Analytical Technology", "continuous manufacturing", "impurities", "pharmaceutical localization", "drug security", "Saudi Arabia", and "supply chain resilience". A preference was placed on peer-reviewed publications from 2020 up to August 2026; earlier sources were included if they contained foundational analysis of Saudi policy or referred to regulatory structures that were still in force. The MDPI review was used as a methodological and conceptual framework for linking material attributes, process understanding, analytical control, and regulatory implementation.

The regulatory sources were deliberately chosen from the SFDA, ICH, the US Food and Drug Administration, the European Medicines Agency, and the European Directorate for the Quality of Medicines and Health Care. They were included since they set out the expectations regarding API GMP, the development of drug substances, quality risk management, lifecycle control, the organisation of the CTD, DMF or ASMF procedures, and changes to CMC information. Saudi policy documents and peer-reviewed studies from Saudi Arabia were used in order to establish the local context. Articles were excluded if they dealt with pharmaceutical marketing or clinical outcomes in the absence of any connection with manufacturing quality, if they discussed finished products without implying any transferable aspects relating to the API or CMC, or if they lacked adequate methodological or bibliographic traceability.

The evidence was thematically synthesized in four stages. In the first stage, the evidence related to API were coded under the following categories: identity and structure, synthesis and control strategy, impurity profile, physical properties, analytical methods, stability, packaging, GMP, and change management. In the second stage, the DMF evidence was coded in terms of scientific completeness, consistency, traceability, interfaces for applicant-restricted information, version control, letter-of-access governance, and lifecycle maintenance. In the third stage, each code was linked to various localization activities, including supplier qualification, formulation bridging, process validation, local release testing, deviation investigation, regulatory submission, and post-approval change control. Finally, the themes that had been mapped were incorporated into two conceptual frameworks and a readiness scorecard. Since the literature is diverse and does not offer comparable quantitative effect sizes that directly link DMF quality to the outcomes of localization in Saudi Arabia, a meta-analysis was not carried out. The conclusions are thus interpretive and based on mechanisms, and the areas that need empirical confirmation are clearly identified.

IV. API QUALITY AS A LOCALIZATION ENABLER

API quality should be viewed as a feature that extends throughout the entire lifecycle and not simply as a final outcome stated on a certificate of analysis. At the first level there is chemical identity, strength, and purity: the API has to be properly characterized, manufactured in a reproducible manner, and kept within specifications that have been justified. The second level involves process-derived knowledge, comprising the starting materials, the key transformations, the reagents, solvents, catalysts, hold times, the work-up conditions, the purification steps, and the controls that explain how quality is achieved. The third level is concerned with the physical quality that is relevant to performance, this including particle-size distribution, morphology, polymorphism, crystallinity, hygroscopicity, bulk density, and surface properties, since these characteristics affect manufacturability or bioavailability. ICH Q11 establishes the relationship between drug-substance development, the control strategy, and an understanding of the manufacturing process, while Q7 brings routine API manufacturing in line with GMP.

It is important to take these layers into account when carrying out localization since the processes used to produce the final product are often affected by

variations in the API in a manner that cannot be detected by assay alone. A tablet formulation moved from an overseas site could suffer blending segregation, compression variability, dissolution shifts, sticking, or stability failures if the API obtained locally or which has just been qualified has a different particle size distribution or solid state even though the compendial chemical tests are passed. In a similar way, sterile or low-dose products may be particularly affected by trace impurities, bioburden, or differences in material handling. Research into medicine quality shows that the amount of API is still a basic factor in determining the quality of medicine. On the other hand, more comprehensive reviews of impurities highlight the increasing complexity involved in controlling process-related, degradation, elemental, mutagenic, and possibly nitrosamine-related impurities.

In the case of localization programmes, an understanding of impurities is particularly important since transferring the manufacturing process can change exposure to the raw materials, the equipment, the utilities, the solvents, the packaging and the storage conditions. A solid API package should be able to identify both known and possible impurities, explain where they come from and what happens to them, define the analytical sensitivity, give a qualification or toxicological justification when necessary, and set trendable limits. The analytical methods used should be validated or otherwise shown to be suitable for their intended purpose, and when transferred to a laboratory in Saudi Arabia, should contain details on system suitability, traceability to a reference standard, the sample preparation and the acceptance criteria for method transfer. New analytical technologies and PAT can improve this control system by enabling faster or non-destructive characterisation. However, the value of these technologies depends on model validation, instrument suitability and data governance rather than simply on their novelty.

Stability and the need to retest are also dependent on the location. When APIs are imported, they may have to travel long distances, experience temperature variations, be exposed to high ambient temperatures, or be subjected to humidity before arriving at a production site in Saudi Arabia. The local manufacturer therefore has to understand the evidence that supports the retest period, the storage conditions, the container-closure system, the transport requirements, and the degradation pathways. This entails more than just warehousing information. Knowledge of stability affects the size of procurement batches, the level of safety stock, the quarantine strategy, the capacity for retesting, and the economic viability of local manufacturing. A localization project that does not have an adequate stability margin may result in a domestic plant that continues to be operationally reliant on frequent shipments of imported APIs and in emergency testing, thus undermining the reasons for pursuing localization.

The need for manufacturing consistency is closely linked to the quality systems of the supplier. An API supplier that performs well should have in place effective systems for dealing regarding deviations, carrying out investigations, handling cases of out-of-specification results, implementing corrective and preventive actions, guaranteeing data integrity, managing change control, and processing complaints. Local manufacturers must assess whether the supplier can alert them of any relevant changes before they are put into effect, supply comparability data, and help with any regulatory differences. This is especially important when other suppliers are being qualified in order to reduce geopolitical or transportation risk. As supply resilience literature indicates, diversification by itself does not ensure continuity; if there is a weakness in material equivalence or in change governance, substitutions can give rise to new quality and regulatory risks. A second source is therefore only valuable if its process knowledge and analytical comparability can be incorporated into the registered control strategy.

The practical consequences for Saudi localization are clear. When assessing APIs, product-selection committees should go beyond considering only price and nominal availability. An API that is suitable for localization must have a stable and transparent supply chain; a satisfactory record of inspection and quality; reproducible critical characteristics; adequate development knowledge; transferable methods; impurity controls that are justified; and a trustworthy system for notifying changes. In the case where local manufacture of APIs is planned, the same framework then functions as a roadmap for building capability:

synthetic or bioprocess know-how, the ability to control the critical attributes of the materials, process validation, state-of-the-art analytical testing, and disciplined documentation all need to develop together. Research into continuous and flow manufacturing indicates that modern API platforms are able to reduce the footprint and allow for intensified production, but successful implementation still demands a solid understanding of the process, effective equipment control, and a carefully planned regulatory strategy.

V. DMF QUALITY AS A KNOWLEDGE-TRANSFER ENABLER

The use of a DMF is beneficial for localization since it separates the confidential manufacturing knowledge from the dossier submitted by the applicant of the finished product and at the same time enables the regulatory authority to evaluate the information by referring to it. According to SFDA guidance, a DMF is described as a confidential source of detailed information regarding the facilities, processes, or articles used in manufacturing. In order to use the file in support of an application, the authority must first receive a letter of access. While this arrangement safeguards the proprietary knowledge of the API manufacturing process, it also poses an interface risk in that the local applicant may need a sufficient amount of publicly available information in order to develop, validate, investigate, and control the finished product, even though certain parts of the API manufacturing process remain restricted. The quality of the DMF therefore relies on both the scientific soundness of the information that is restricted and on the adequacy of the information provided to the applicant.

The first quality aspect to consider is scientific completeness. The DMF for a potent drug substance should tell a consistent and coherent story that links the choice of route, the justification for the starting material, the process controls, the formation of impurities and the purging process, the specifications, the analytical methods, the reference standards, the container closure, and the stability. It is just as important to have internal consistency. The synthesis schemes, the batch analyses, the specifications, the validation reports, and the stability sections must all refer to the same material, the same manufacturing sites, and the same current version of the process. Regulators often experience delays when the submission is technically detailed but inconsistent between its various modules, responses, or versions. This lack of consistency has an effect when it comes to localization: the manufacturer in Saudi Arabia may approve a material based on one set of specifications, while at the same time the holder of the DMF makes changes to a site, a process step, or an analytical method without first carrying out a coordinated regulatory and technical evaluation.

Traceability is a second dimension; each important claim must be backed by data that can be found, understood, and connected to the registered control strategy. The quality of the DMF decreases when impurity limits are given without a development rationale, when validation summaries fail to include performance details, or when process changes are recorded merely as individual amendments. ICH Q10 and Q12 are useful in this context since they incorporate knowledge management and change management into a lifecycle pharmaceutical quality system. The localization project should regard the DMF version as a controlled configuration of knowledge and the active version, the applicant's portion, the restricted portion, the manufacturing sites, the letters of access, the commitments, and the post-approval changes should all be reconcilable at any time.

There is also a regulatory aspect concerning usability within different jurisdictions. The FDA makes it clear that a DMF is not approved or disapproved; instead, it is examined whenever it is referred to in an application. The European ASMF process does the same by separating the applicant's section from the restricted part. By contrast, the EDQM's CEP procedure offers an alternative way of showing that a substance's quality can be adequately controlled by a pharmacopoeial monograph together with approved additional controls. These systems cannot be used interchangeably, and a supplier familiar with one market may still have to adjust the content, the lifecycle procedures, and the administrative controls to meet SFDA requirements. Saudi Arabia's localisation teams should therefore look not just at whether a

supplier "has a DMF" but at whether it keeps a up-to-date, SFDA-usable file with active regulatory supervision.

The fourth dimension is lifecycle currency. According to the SFDA's DMF guidance, information relating to versions must be provided and the holder is required to certify that the document is current; if no changes have taken place during the specified period, the holder should state that the file remains up to date. In reality, however, localization makes lifecycle management more important since local production can keep a product available for many years and will certainly involve changes in suppliers, analytical updates, new knowledge about impurities, modifications in scale, and changes to the manufacturing site. An out-of-date DMF represents a concealed liability since it can delay variations, weaken investigations, and cause differences between what is actually manufactured and what has been committed to in the registration. A well-developed DMF programme makes use of formal governance to ensure that technical reality, quality agreements, regulatory dossiers, and site procedures are kept in step.

DMF quality thus acts as a multiplier when it comes to the transfer of knowledge. Even if the material data is of a high quality it will still be hard to put into practice in the absence of a coherent and up-to-date dossier, and a perfectly formatted dossier cannot make up for a poorly understood or variable API process. The best example of localization involves both elements. The API supplier must produce consistent quality and provide a scientific explanation of its controls; the DMF then records and preserves that explanation; the SFDA is able to evaluate it efficiently; and the manufacturer in Saudi Arabia receives enough non-confidential information to develop an effective local control strategy. This two-part relationship is the main point of this review.

VI. SAUDI REGULATORY AND INDUSTRIAL CONTEXT

There are a number of factors which make it strategically important to ensure quality in API and DMF production in Saudi Arabia. The size of the domestic market, the importance of both public and private purchases, and the fact that national policy aims at increasing local involvement in the creation of pharmaceutical value are all examples of this.
However, it is possible for a lack of improvement in the upstream areas of materials, analytical science, and regulatory supervision to maintain dependence on foreign sources in a more subtle way. Tawfik and his colleagues saw drug security as the main reason for local manufacturing, while later evaluations in Saudi Arabia stressed the importance of technology transfer, research capacity, advanced manufacturing, and a greater integration of the pharmaceutical ecosystem. These outcomes lend support to a quality-depth understanding of localization in that organizational independence increases as local companies acquire the knowledge and capabilities necessary to deal with variation and change.

SFDA requirements create the regulatory bridge between this industrial objective and product quality. Its DMF guidance covers drug substances and related materials, defines the letter-of-access mechanism, and requires current administrative and manufacturing information. SFDA's GMP framework entails expectations for API manufacture, and its human-drug submission and variation guidance establish the wider dossier and lifecycle environment. These requirements mean that localization projects should engage regulatory affairs early. A plant transfer, new source, new API site, changed manufacturing process, or revised analytical method may require regulatory assessment before routine supply can proceed. Capital investment that ignores dossier readiness can therefore produce idle capacity or delayed launches.

The policy implication is that localization incentives should distinguish levels of manufacturing depth. A basic level may involve secondary packaging; a higher level may involve formulation, filling, and finished-product testing; a deeper level includes local analytical development, process validation, supplier qualification, and lifecycle CMC ownership; the highest level adds domestic API or key-intermediate manufacture and associated process development. Measuring all levels with a single local-production label obscures important differences regarding resilience. A Saudi plant that can independently test an API, comprehend its critical attributes, manage

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DOI: https://doi.org/10.64388/IREV10I2-1722610

deviations, qualify a second source, and prepare regulatory change packages contributes more to drug security than a plant that relies on a single foreign knowledge package for routine decisions.

Localization also creates opportunities for capability clustering. Central or shared analytical laboratories can support solid-state characterization, impurity profiling, elemental analysis, sophisticated spectroscopy, and reference-standard management. Universities and research centers can support route development, process intensification, chemometrics, and PAT. Local contract development and manufacturing organizations can connect smaller marketing-authorization holders into GMP manufacturing. Lifera and other industrial initiatives shall anchor technology transfer as well as strategic products. At the same time, procurement policies can reward suppliers that transfer knowledge and create strong domestic quality systems rather than only performing final assembly. The important criterion is that each institutional layer should reduce an identified quality or supply vulnerability.

VII. INTEGRATED QUALITY-LOCALIZATION MODEL AND IMPLEMENTATION PRIORITIES

Figure 1 presents localization as a sequential yet feedback-controlled value chain. The quality of the API provides the scientific basis; the DMF is responsible for organizing the protected CMC knowledge; regulatory assessment turns that knowledge into an accepted control strategy; technology transfer then implements the strategy at the site level in the form of specific processes and analytical capabilities; local commercial manufacturing produces new knowledge regarding process performance; and ongoing lifecycle monitoring sends the experience back into the governance of both the supplier and the dossier. A breakdown at any stage of the process can delay localization. Even if the plant in question is technically capable, it cannot make up for a poorly controlled API, and high-quality API alone cannot compensate for a lack of information when the local site has to investigate an unexpected dissolution shift or evaluate a supplier change.

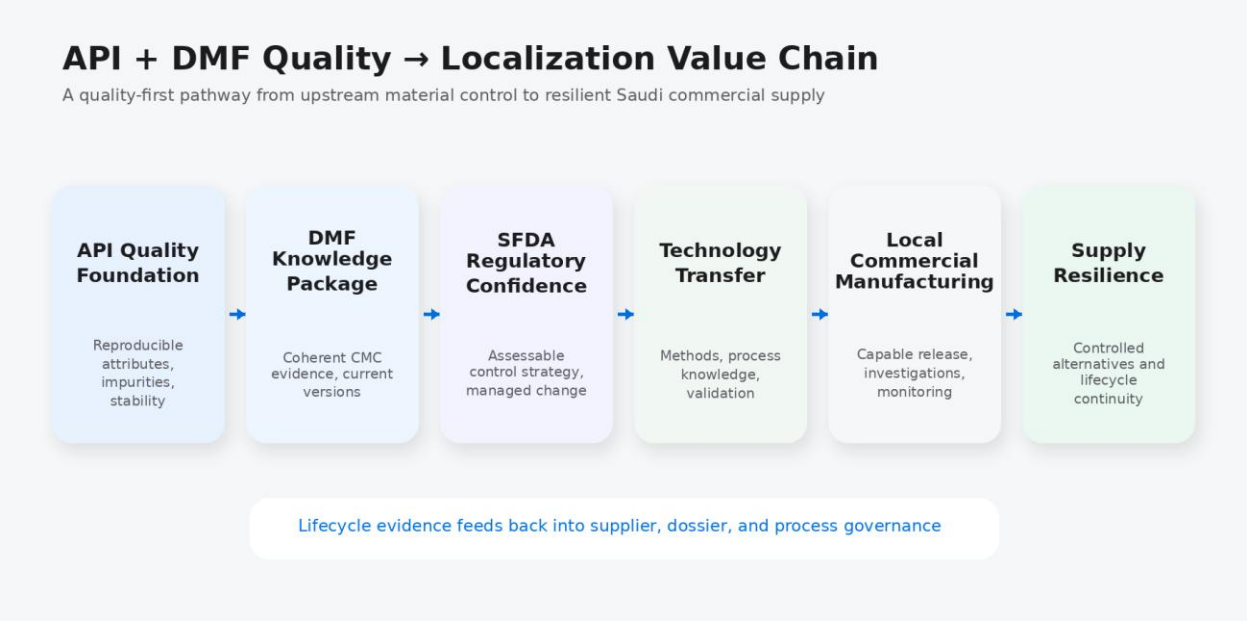

Figure 1. API and DMF quality-to-localization value chain

The first thing to focus on should be dividing products and suppliers. All medicines do not need the same degree of localization. Products should be ranked according to their clinical criticality, the level of imports, the concentration of API sources, the complexity of the technical transfer, sensitivity to the cold chain or stability, market volume, and the feasibility of having the capability at home. In the case

of products that have high priority, supplier assessment must include a structured review of the API/DMF maturity before any commercial negotiations take place. This review should look at the GMP status, the history of the manufacturing sites, the critical attributes, the impurity strategy, the analytical methods, stability, batch consistency, change governance, the status of the regulatory files, and the supplier's willingness to assist with technology transfer. Table 1 gives a summary of the most important interfaces between API/DMF quality and localization risk.

Table 1. API and DMF quality dimensions that influence localization readiness.

Quality domain	Evidence expected	Localization failure mode	Strategic effect
API identity and physical form	Characterization; polymorph/particle controls where relevant	Process or dissolution variability after transfer	Predictable formulation and process performance
Impurity control	Origin/fate rationale; validated sensitive methods; trend data	Unexpected impurities, investigations, regulatory delay	Safer supplier changes and reliable release
Process/control strategy	Defined critical steps, parameters, in-process controls	Scale/site transfer cannot reproduce material	Transferability and root-cause capability
Analytical methods	Fit-for-purpose validation, standards, transfer protocol	Local laboratory dependence or method failure	Independent local release and troubleshooting
Stability and packaging	Retest evidence, degradation pathways, container and transport conditions	Expiry loss, excursion uncertainty, high safety stock	More resilient procurement and warehousing
GMP and data integrity	Effective deviations, CAPA, change control, traceable data	Hidden quality events or unreliable batch history	Supplier confidence and auditability
DMF lifecycle quality	Current versions, coherent AP/RP, sites, LoA, change history	Dossier/manufacturing mismatch; delayed variations	Regulatory continuity and controlled change

The next thing to do is to set up a quality standard for Saudi DMFs. Although administrative acceptance is required it does not on its own show how efficiently a file will support the assessment or lifecycle management. A benchmark could be used to assess scientific coherence, completeness, consistency, traceability, currentness, response history, the quality of cross-references, the adequacy of the applicant's information, the clarity regarding the manufacturing site, and the level of maturity of the change-control process. Manufacturers and investors could make use of such a benchmark internally without altering the SFDA's formal review standards. It would enable localisation teams to pick out poor files early on and allow technology-transfer agreements to be conditioned on meeting remediation milestones.

The third priority is to achieve local analytical sovereignty. This does not mean that each method has to be developed within the country; rather, it means that a Saudi facility should be capable of carrying out, troubleshooting, interpreting, and improving the analytical controls required for its products. When transferring a method, it should involve not only the test procedure but also the analysts, the instruments, the reference standards, the data systems, the way in which atypical results are handled, and the statistical expectations. If the physical attributes of the API are

performance-critical, incoming testing may have to go beyond the pharmacopeial requirements for identity and assay. Techniques such as Raman, NIR, XRPD, particle-size analysis, thermal analysis, and chromatography can offer a greater understanding of the material. The reference MDPI review is helpful in that it illustrates how PAT and multivariate approaches can link material or process signals to product quality, while at the same time cautions that the methods must be validated and transferable before they can be used for routine control .

The fourth priority should be lifecycle-centered quality agreements. While traditional agreements tend to focus on release testing and complaint management, they are unclear regarding regulatory changes. Localization agreements must specify what is considered a notifiable API change, the minimum notice period, the data packages to be provided, the availability of samples, the expectations concerning comparability, the responsibilities relating to DMF updates, and the decision-making authority in the case of a change that affects the locally registered product; they should also include provisions for subcontractors and secondary manufacturing sites. As noted in ICH Q12, there is a useful conceptual foundation for distinguishing the established conditions and procedures for managing post-approval CMC changes within a mature pharmaceutical quality system. Even though different jurisdictions implement the specific tools of Q12 in different ways, the fundamental principle is still valuable in that predictable change is dependent on prior knowledge and clearly governed commitments.

The fifth priority should be to combine resilience metrics with quality metrics. Although supply-chain studies place importance on redundancy, visibility, diversification, and coordinated risk management, in the pharmaceutical field a seemingly redundant source may still be unusable if it fails to meet the registered impurity profile, does not have a suitable DMF, or if it requires a long variation. That is why the readiness scorecard shown in Table 2 links supply indicators with CMC evidence. A product must be regarded as being strongly localized when the local organization is able to ensure the supply by means of controlled and previously understood alternatives, not just when one domestic manufacturing route is running under normal conditions.

Figure 2 presents the same concept in the form of a dual-engine readiness matrix: when both API quality and DMF maturity are low, the result is an import-dependent or unstable situation since neither material reproducibility nor regulatory knowledge can be relied upon. If API quality is high but DMF maturity is low, there is transfer fragility, meaning that the material may perform well, but changes, investigations, and regulatory assessments remain difficult. In the case of low API quality but a well-polished DMF, documentary readiness is achieved even though manufacturing reliability is not there. The only quadrant that truly signifies localization readiness is the high-high one, since material capability and knowledge governance support each other. The matrix can be used at the product, supplier, or technology-platform level and can be reviewed again as evidence becomes available.

For investors and policymakers, this system transforms the due diligence process. The main questions then are: Which of the critical quality attributes are managed at the local level? Which API risks still remain outside the Kingdom? Can the local laboratories verify on their own the relevant material attributes? Is the DMF currently complete and responsive? Are changes in regulatory and technical terms coordinated? How quickly could a second source be qualified? And what knowledge would be lost if the foreign licensor pulled back their support? These questions reveal the hidden dependencies that factory-capacity statistics fail to show. They also provide a way forward for step-by-step improvement, since each dependency is able to be turned into a capability project with a designated owner, specific evidence requirements, and a maturity target.

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DOI: https://doi.org/10.64388/IREV10I2-1722610

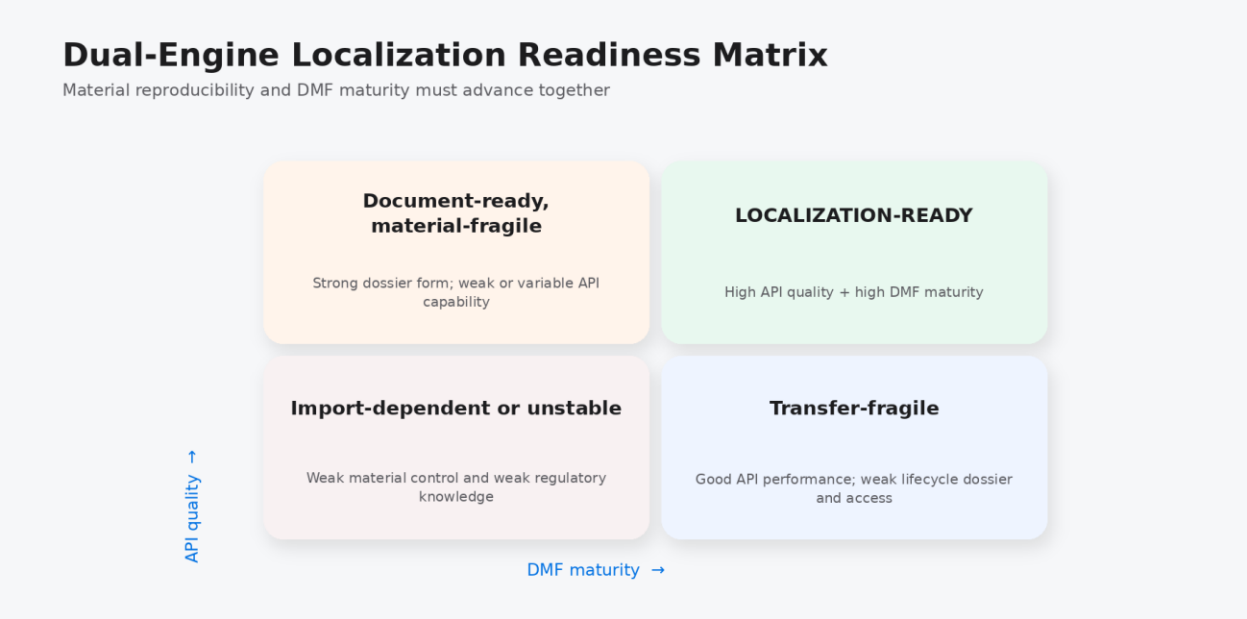

Figure 2. Dual-engine localization readiness matrix linking API quality with DMF maturity

Table 2. Proposed Saudi pharmaceutical localization readiness scorecard.

Readiness pillar	Illustrative evidence / KPI	Regulatory-quality link	Localization decision use
API source resilience	Qualified sources; lead time; change history; supply concentration	Q7/Q9 supplier and risk controls	Prioritize strategic products and backup-source work
DMF maturity	Current file; coherent sections; timely responses; clear LoA	SFDA DMF; CTD; lifecycle governance	Gate supplier selection and transfer readiness
Analytical capability	Local execution of critical methods; standards; transfer success	Q2/Q14 principles; data integrity	Assess independence of local quality control
Technology-transfer depth	Process knowledge, risk assessment, validation and troubleshooting ownership	Q8/Q10/Q11 concepts	Distinguish real capability from equipment relocation
Lifecycle change control	Advance notice; impact assessment; synchronized dossier updates	Q10/Q12; SFDA variations	Estimate ability to sustain supply after changes
Digital CMC integrity	Controlled versions, linked evidence, audit trails	PQS knowledge management	Reduce mismatch and improve impact assessment
Workforce and governance	Qualified CMC, QA, analytical, regulatory and supply-quality roles	Management responsibility and PQS	Measure sustainability of domestic capability

Readiness pillar	Illustrative evidence / KPI	Regulatory-quality link	Localization decision use
Continuity performance	Deviation closure, batch success, stock-out exposure, recovery time	Ongoing process verification and risk review	Track whether localization improves resilience

VIII. CONCLUSION

Only when domestic manufacturing in Saudi Arabia is backed by a thorough control of both materials and manufacturing knowledge will pharmaceutical localisation be truly sustainable. The quality of the active pharmaceutical ingredient provides the reliable chemical, physical, microbiological, and stability base upon which a finished product is constructed. The quality of the DMF gives a structured, confidential, lifecycle-managed explanation of how that quality is achieved and controlled. Neither of these aspects is adequate by itself; even with a very good dossier a poor performance of the API can still lead to failure, while an API that performs well may still be difficult to transfer or maintain if its CMC knowledge is incomplete, inconsistent, inaccessible, or out of date.
This relationship indicates that for Saudi Arabia localization criteria should go beyond simply considering the site location and the amount of finished product produced. A more effective approach would be to assess whether local organizations are able to understand the key API attributes, carry out substantial analytical controls, manage their suppliers, investigate any departures, validate transferred processes, keep up to date their regulatory files, and implement changes all without having to rely uncontrolled on outside parties. The SFDA's DMF and GMP frameworks, along with the ICH lifecycle principles, offer the regulatory basis for this kind of progress.

The proposed API-to-localization value chain, dual-engine matrix, and readiness scorecard provide a practical means of spotting weaknesses prior to making major investments or transferring a product. Policymakers may use them to direct their incentives towards knowledge-intensive localization; manufacturers can apply them when carrying out due diligence on suppliers and their portfolios; and researchers can turn them into verifiable hypotheses. The aim is not to isolate oneself from global pharmaceutical networks, but rather to participate in those networks in a resilient way, having at the same time sufficient domestic capabilities in the areas of scientific research, analysis, regulation, and manufacturing to make sure that quality and continuity are maintained when external conditions change. Accordingly, the quality of APIs and DMFs is not a secondary regulatory issue; it is fundamental infrastructure for a competitive and secure Saudi pharmaceutical industry.

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