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Original Research Article

Accelerating Access to High-Quality Generic Medicines in Saudi Arabia through Advanced SFDA Regulatory and CMC Practices

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Abstract: Saudi Arabia is aiming to increase the use of generic medicines in order to improve affordability, access to treatment, and pharmaceutical security, but in order to speed up the registration process it is essential to ensure pharmaceutical equivalence, bioequivalence, consistency in manufacturing, and quality throughout the product's lifecycle. This review looks at how the advanced regulations of the Saudi Food and Drug Authority (SFDA) together with its requirements in the areas of chemistry, manufacturing, and controls (CMC) can help to reduce unnecessary delays in both development and review while at the same time maintaining confidence in generic drugs. A structured integrative review was carried out of 30 sources published between 2020 and 2025, these comprising SFDA guidance, WHO and ICH standards, empirical studies conducted in Saudi Arabia and literature on pharmaceutical quality. The evidence was grouped according to the design of the regulatory pathway, CMC development, the equivalence strategy, analytical lifecycle management, inspection, and post-approval access. The Saudi data indicate that there is a well-developed bioequivalence system, but preventable problems are still occurring due to the quality of the study centres, the readiness of the dossier, and fluctuating public confidence. The application of a quality-by-design approach, risk-based control measures, reliable dissolution methods, active-substance master files, stability science, and proactive control of impurities can lead to greater success in the first cycle of review. The review suggests an integrated model that includes obtaining early scientific advice, carrying out product-specific equivalence planning, applying a risk-based review and reliance approach, ensuring high quality in the digital dossier, and carrying out lifecycle surveillance. Regulatory acceleration should therefore be achieved by improving the structure of the evidence rather than by reducing the amount of evidence, thus allowing for faster access to medicines, greater local manufacturing, reliable interchangeability, and increased trust in high-quality generics.

Keywords: Saudi Food and Drug Authority (SFDA), Generic Medicines, Bioequivalence, Pharmaceutical Equivalence, Chemistry, Manufacturing and Controls (CMC), Quality by Design (QbD).

1. INTRODUCTION

Generic drugs are at the heart of sustainable pharmaceutical systems since they offer therapeutically equivalent alternatives following the expiry of the originator's exclusivity, promote competition, and make it possible to allocate resources to other health priorities. In Saudi Arabia, their importance is particularly significant as the

health system works to achieve wider access, improve cost efficiency, develop domestic manufacturing, and ensure a reliable supply. The regulatory issue is not merely about approving more generic drugs; it is about making sure that high-quality products get to patients quickly enough to affect their use while at the same time maintaining confidence in their identity, strength, purity, performance, and interchangeability. The reference paper given for this review presents a similar issue as one involving a balance between speed, safety, and market accessibility, stating that acceleration can only be sustained if it is accompanied by solid evidence and post-market supervision. With regard to generic drugs, the focus of the evidence changes from new clinical efficacy to CMC comparability, bioequivalence, manufacturing control, and lifecycle assurance.

The SFDA has developed a framework which is becoming more detailed concerning the registration of medicinal products. The registration rules establish the legal and procedural basis for both manufacturers and their products, the Regulatory Framework for Drug Approval lays out the various approval routes, and the revised data requirements indicate what dossier is expected for human medicines. Specific guidance is available on matters such as bioequivalence, product-specific recommendations, biowaivers, drug master files, stability, and documentation relating to manufacturing sites. Taken together, these measures offer a means of achieving greater efficiency without compromising scientific standards.

The possibility is now real thanks to recent evidence from Saudi Arabia. Althunian and his colleagues looked at 590 bioequivalence trials that had been submitted to the SFDA: 521 of these showed bioequivalence, 87.3 per cent of the successful trials employed the conventional 2×2 crossover design, and a large number of the rejected studies had issues relating to the study centre . It therefore appears that delays are caused not just by regulatory examination but also by the study design at an earlier stage, by the qualification of the centre, by the implementation of the protocol, by data integrity, by analytical performance, and by the sponsor's understanding. Likewise, the SFDA inspection data indicate that bioequivalence centres accounted for a meaningful number of observations, which supports the idea that acceleration should be linked to better quality systems.

There is also the factor of confidence following approval. Surveys carried out in Saudi Arabia indicate that the public's knowledge of generic drugs is uneven. Almohammed *et al*., found that only 40.5% of the participants had adequate knowledge, even though the general attitudes were more positive. Subsequent studies have shown that the factors influencing the choice of a generic drug are advice from clinicians, perceived effectiveness, price, the availability of information, previous experience, and the country of origin. Evidence has to be produced and made believable by means of transparent standards, surveillance, and consistent performance.

The review states that extensive experience in CMC practice serves as the practical link between quicker reviews and long-term trust. The use of QbD, risk-based control strategies, analytical lifecycle management, justified biowaivers, product-specific bioequivalence planning, proactive impurity assessment, and improved digital submissions can help reduce cycles of preventable deficiencies. This method brings about speed in line with the SFDA's aim of making trusted pharmaceutical products more available, including by offering incentives for drugs that are either not currently available or are needed in the Saudi market.

2. AIM AND OBJECTIVES

The purpose of this review is to establish a regulatory and CMC framework based on existing evidence in order that high-quality generic medicines may be made available more quickly in Saudi Arabia without lowering the standards relating to pharmaceutical quality, bioequivalence, compliance with manufacturing procedures, or post-market assurance.

The analysis is guided by four objectives. The first is to identify the main SFDA requirements that affect the development of generic drugs and to spot delays that can occur at various stages of dossier preparation, CMC assessment, bioequivalence evaluation, inspection, and lifecycle management. The second involves assessing advanced CMC tools which can enhance regulatory predictability and lead to first-cycle approval, such as quality by design, quality risk management, the concept of an analytical lifecycle, robust dissolution testing, impurity control, stability programmes, and documentation of the active substance. The third looks at how product-specific bioequivalence, BCS-based biowaivers, reliance, and a risk-based review can be used to assign regulatory effort in accordance with the level of uncertainty rather than treating all products the same. The fourth consists of suggesting priorities for implementation and providing measurable indicators for SFDA, manufacturers, bioequivalence centres, and other stakeholders who wish to achieve faster access while maintaining public confidence.

3. METHODOLOGY

A structured integrative review was chosen since the question involves various areas such as regulatory policy, pharmaceutical science, clinical bioequivalence, inspection practice, market access, and public perception. A meta-analysis was not suitable as the evidence consists of heterogeneous guidance, descriptive regulatory datasets, cross-sectional surveys, quality studies, and policy analyses. The method adopted the reference paper's approach of using predefined sources, eligibility criteria, staged screening, data extraction, and narrative synthesis, but adapted it to the context of generic medicine regulation and CMC.

The time frame for the evidence was 2020 to 2025, and the searches used the following terms: "Saudi Arabia", "SFDA", "generic medicines", "bioequivalence", "biowaiver", "CMC", "quality by design", "drug master file", "stability", "dissolution", "analytical procedure", "quality risk management", "regulatory reliance", "inspection" and "generic access". Peer-reviewed evidence was found using biomedical and multidisciplinary scholarly search and indexing services, and regulatory evidence was selected from the official SFDA, WHO and ICH repositories.

To be eligible, one had to make a direct contribution to at least one of the following five areas: the impact of SFDA requirements on generic registration; the way CMC quality affects reviewability and performance; the role of bioequivalence or biowaiver strategy in supporting interchangeability; the extent to which risk-based regulation, reliance, or inspection can enhance efficiency; or the effect of generic acceptance and utilization on access in Saudi Arabia. Any material that dealt solely with discovery-stage innovation, non-transferable biologic issues, veterinary products, or clinical effectiveness unrelated to equivalence was excluded. Furthermore, opinions alone were not counted as primary evidence.

In order to reduce selection bias, a hierarchy of sources was established in advance. The current requirements of the SFDA were regarded as authoritative with regard to Saudi regulatory expectations; the documents of the WHO and ICH were referred to in order to understand the internationally harmonised regulatory science; empirical studies carried out in Saudi Arabia were used to identify the gaps that had been observed in implementation; and where the local studies did not directly address a CMC mechanism, the wider peer-reviewed literature was consulted. Before being included, each source was verified for its publication details, the organisation that issued it, the year of publication and its DOI or official document provenance. The evidence was not assessed solely on the basis of the prestige of the journal; instead, more weight was given to a source if it had directly measured the submissions reviewed by the SFDA, the inspections carried out by the SFDA, the use of generic drugs in Saudi Arabia, or the laboratory performance of products sampled from the Saudi market.

The synthesis ended up with 30 records: ten SFDA documents, eight WHO/ICH standards, and twelve peer-reviewed or scholarly sources, one of which was the article provided. The data were put into a thematic matrix which included the regulatory function, the CMC element, the evidence requirement, the bottleneck, advanced practice, and the expected access effect. Emphasis was placed most strongly on Saudi empirical evidence and on the official standards. The findings were combined in a narrative format throughout the product lifecycle, since no pooled effect estimate was calculated as the review is concerned with regulatory-science mechanisms and not with a common clinical intervention.

4. SAUDI GENERIC-MEDICINE ACCESS: THE QUALITY–SPEED PROBLEM

Saudi Arabia currently shows a high level of generic drug usage, but this does not mean that optimal competition or confidence will necessarily result. A claims analysis published online in 2025 found that the use of generic drugs had risen from 70% to 76% and that considerable current and potential cost savings had been achieved; local generics made up a large portion of drug use. Similarly, research into regional policy indicates that price regulation and tendering are not enough when the confidence of prescribers, pharmacists, or patients limits the adoption of generics. Greater registration therefore brings the most value when quality assurance, the substitution policy, procurement, and communication all proceed in a coordinated manner.

The regulatory burden also varies according to the type of product; immediate-release oral formulations containing active ingredients that have been well characterised generally involve less uncertainty than modified-release products, drugs with a narrow therapeutic index, highly variable drugs, or dosage forms in which local delivery is essential. If all applications are treated in the same way, this can waste the time of the reviewers, while arbitrarily shortening the review process may leave unresolved risks which later result in variations, recalls, shortages, or a loss of confidence. The suitable aim should be 'right-sized rigor'—that is, a level of evidence sufficient to address the uncertainty associated with a specific product.

This difference is also important in the case of shortages: if a high-priority generic drug is delayed then single-source dependence will be maintained, while a badly prepared rapid entrant may fail to provide a consistent supply following approval. Availability should therefore be judged in terms of reliable commercial availability and not merely on the date of marketing authorisation. Matching the review priority to actual market need and to the state of manufacturing readiness can help to reduce both types of failure.

The SFDA already has the necessary components in place for this approach. Guidance specifically directed at products helps to ensure that the expectations regarding studies are more consistent, and the incentive scheme connects availability requirements with the possibility of priority registration, pricing flexibility, technical support, and reductions in fees. The CMC-readiness criteria can reinforce these mechanisms. A product that is needed should be able to progress more quickly since the evidence is ready for review: the rationale for the formulation is clear, the key material and process variables are understood, the analytical methods are appropriate for their intended use, stability supports the shelf life, and the equivalence strategy corresponds to the product's risk.

Public confidence is still important. According to studies carried out in Saudi Arabia, consumers take into account the advice of the clinician, the effectiveness of the product, its price, previous experience, the availability of information, and the place of manufacture. The publication of clear requirements, effective market surveillance, and firm quality measures can serve as evidence of regulatory competence rather than cause suspicion.

5. SFDA REGULATORY ARCHITECTURE FOR GENERIC ACCELERATION

The key factor in achieving quicker access to generic drugs is regulatory predictability. Sponsors waste time because they have to make development decisions before they have a clear understanding of the relevant evidence standard, and regulators also waste time since their applications need to be clarified repeatedly. The SFDA's registration rules and the drug-approval framework form the foundation, while the data requirements specify how quality and regional information should be organised. In the case of generic drugs, the requirements should be converted early on into a pathway that includes the Saudi label, the dosage form, the strength, the comparator, the manufacturing network, and the equivalence strategy.

Scientific advice is most useful when applied to products that have high variability, involve complex formulation characteristics, have unusual strengths, are manufactured at more than one site, are compared with nonstandard reference products, or have uncertain eligibility for a biowaiver. The aim of this advice is not to secure pre-approval but to eliminate uncertainties before it becomes necessary to produce costly batches or carry out studies. Since there is evidence from Saudi Arabia of bioequivalence applications having been rejected due to problems relating to the centre and the study, it is important to reach agreement early on matters such as the suitability of the centre, the study design, sampling, bioanalysis, feeding conditions, and the statistical approach in order to avoid failures which cannot be corrected by an accelerated review timetable.

Another important feature is the modularity of dossiers. It should be possible for reviewers to trace the connections between the target product profile, the formulation development, the material attributes, the process parameters, the specifications, the analytical methods, stability, and equivalence without having to reconstruct them. The SFDA's drug master file system enables the structured management of confidential information relating to the active substance. DMFs lead to a reduction in duplication only if the open and restricted sections are consistent, changes can be tracked, and the finished-product sponsor takes account of the relevant API variability. A current site master file also helps with inspection planning by outlining the pharmaceutical quality system, the operations, the quality control, and the responsibilities.

Proportional review is the third element. The principles of WHO reliance promote the use of reliable regulatory work while retaining national responsibility and directing local resources towards activities which add value; good regulatory practice stresses transparent, consistent and evidence-based decisions. In the case of the SFDA, reliance means making targeted use of previous assessments, inspections, pharmacopoeial standards or knowledge of comparable products when the product and the regulatory issue in question are aligned it does not involve automatic acceptance.

Acceleration should also be linked to lifecycle discipline. Initial authorization becomes counterproductive if post-approval changes are poorly controlled. Development should therefore define change-management responsibilities and evidence expectations from the outset, connecting CMC understanding with future variations. Table 1 summarizes the principal bottlenecks and advanced responses.

Table 1: Evidence-based bottlenecks and advanced responses for accelerated high-quality generic

Domain	Typical bottleneck	Advanced regulatory/CMC response	Quality safeguard	Expected access effect
Regulatory planning	Late comparator/pathway clarification	Early triage + targeted scientific advice	Risk-based questions documented before pivotal work	Fewer redesigns and deficiency cycles
Formulation/process CMC	Empirical formulation with weak linkage to performance	QTPP, CQAs, material/process risk mapping, design space where justified	Controls tied to clinically relevant product performance	Higher first-cycle CMC acceptance
API / DMF	Unclear API variability or supplier-change impact	Current DMF, supplier qualification, impurity and solid-state understanding	Traceable API controls and change communication	Less duplicated review and fewer late queries
Analytical lifecycle	Methods validate once but transfer or stability poorly	ICH Q2(R2)/Q14 lifecycle development and robustness	Fit-for-purpose, stability-indicating, transferable methods	More reliable submission and lifecycle data
Equivalence	Default in vivo studies or poorly matched designs	Product-specific BE + BCS biowaiver assessment + ICH M10 bioanalysis	Comparator, study design, and data integrity matched to risk	Avoids unnecessary studies and repeats
Inspection / reliance	Uniform scrutiny and duplicated regulatory work	Risk-based inspection + justified reliance on trusted outputs	SFDA retains final decision and targets local risks	Reviewer/inspector capacity focused on uncertainty
Stability / lifecycle	Late packaging selection and reactive change control	Early representative stability, packaging integration, continued verification	Shelf-life and post-approval changes remain evidence-based	Faster launch with lower shortage/recall risk

6. ADVANCED CMC PRACTICES AS THE ENGINE OF FIRST-CYCLE APPROVAL

CMC is occasionally regarded as registration documentation, but it is in fact an evidence framework that explains how a manufacturer will consistently produce a medicine with the intended performance. In the case of generic drugs, this framework must link the reference product to formulation, manufacturing process, release controls, stability behaviour, and equivalence. The greatest potential for speeding up the process therefore lies in resolving the CMC issues before the pivotal batches and before the submission.

The Quality by Design (QbD) approach provides the framework. It is described as a method that is based on science and risk assessment, involving the definition of the target product, the identification of the critical quality attributes (CQAs), linking these to the material attributes and process parameters, and then establishing an appropriate control strategy. In the case of a generic tablet, the quality target product profile should take into account the dosage form, the strength, the release characteristics, the route of administration, stability, and other attributes related to use. The critical quality attributes can include assay, content uniformity, degradation products, dissolution, water content, performance-linked physical attributes, and microbiological quality where applicable.

The main benefit from the regulatory point of view is that there are fewer surprises. When the particle size of a poorly soluble active pharmaceutical ingredient affects dissolution, the supplier's procedures regarding milling, blending, and dissolution discrimination should take into account that relationship. In the case where the grade of an excipient affects release or manufacturability, the functional properties should be supported by justification rather than being controlled merely by compendial identity. On the other hand, evidence

showing that a particular parameter has little effect within a given range can be used to allow functional flexibility. As a result, the evaluation changes from being a list of tests to becoming a coherent explanation of an understanding of the product.

The ICH Q9(R1) document supports this by calling for systematic quality risk management. A generic development risk register should be used to prioritise issues such as API polymorphism, particle size, excipient functionality, scale-up, granulation endpoint, coating variability, dissolution, cross-contamination, temperature exposure, or changes in supplier. A dossier in which the reasons for tightly controlling high-risk variables and for scientifically justifying low-risk variables are given is easier to assess than one that contains disconnected data.

Analytical science acts as a second accelerator; according to ICH Q2(R2), validation is placed within the analytical lifecycle and stresses the need for the method to be suitable for its intended purpose . ICH Q14 promotes the establishment of an analytical target profile, a understanding of the parameters, robustness, and lifecycle control. These principles apply to assays, related substances, dissolution, residual solvents, elemental impurities, and product-specific tests. A method which has been validated once can still fail when it is transferred or during stability testing; a method that is well understood is more likely to yield consistent results at different sites, thus reducing the number of deficiencies and investigations.

Dissolution serves as a strong link between CMC and equivalence; a study by Saudi researchers into generic vildagliptin demonstrated that comparative dissolution profiles can be used to assess pharmaceutical equivalence and to aid in post-production quality control. The method has to be sensitive enough to identify significant differences in formulation or manufacturing process, not merely cause each batch to show rapid and complete release. The development process should connect dissolution to the key material and process variables and, where appropriate, to the API's biopharmaceutic risk.

It is just as important to have control over the API. Although the SFDA's DMF framework organises information on the active substance, the applicants must still ensure that the drug product is robust with regard to realistic variability in the API. Attributes that are relevant here can be polymorphic form, particle size, water content, residual solvents, elemental or genotoxic impurities, and risks associated with the synthetic route. Even when the assay does not change, a change in supplier can lead to different impurity profiles, which is why proactive qualification and technical agreements should form part of regulatory readiness.

The importance of impurity control lies in the fact that it can speed up access. Cases involving nitrosamines show that impurities can be caused by the synthesis of the active pharmaceutical ingredient, the use of reagents, recycled solvents, the excipients, the manufacturing conditions, cross-contamination, packaging, or degradation during storage. Relying on an assessor to identify these risks results in delayed testing and a delay in launching the product. Before the validation batches are carried out, the possible pathways for impurity formation should be mapped in advance, sensitive analytical testing should be carried out where necessary, and preventative controls should be put into place.

The stability study concludes the process. According to guidance from the SFDA, there must be evidence that both the active pharmaceutical ingredients and the finished products stay within specification when exposed to defined conditions. Because of the climatic conditions in Saudi Arabia, packaging, protection from moisture, sensitivity to temperature, and control of distribution become particularly important. Acceleration should result from initiating representative stability programmes early, using stability-indicating methods, investigating trends, and setting the shelf life in line with the available evidence not by providing insufficient support for the shelf life.

Process validation should be seen as a way of confirming a process that is already well understood, rather than representing the first instance when robustness is tested. It is necessary for commercial-scale or representative batches to show that the selected operating ranges, material controls, in-process tests, and the release strategy function together. Continued process verification can then make use of trend data to pick up any drift before the specifications are breached. This is especially beneficial in the case of local technology transfer, since there may be differences between the equipment geometry, environmental conditions, raw-material sources, and operator practice at the local site and those at the development site.

Packaging should be given similar attention since container-closure systems can affect moisture ingress, light exposure, extractables or leachables, tablet hardness, and dissolution over the shelf life. If packaging is selected late it may be necessary to carry out further stability studies or result in differences that are specific to various markets. By incorporating packaging selection into the QTPP and stability planning it is possible to avoid a common cause of delays after development and to ensure that supplies

can be obtained under the distribution conditions in Saudi Arabia.

These practices have the effect of increasing first-cycle approval by reducing uncertainty prior to submission; they also enhance local manufacturing since technology transfer is more reliable when the site receiving it inherits a well-defined package of product and process knowledge rather than just a recipe. Advanced CMC is thus a strategy which serves both regulatory and capability-building purposes as well as improving supply resilience.

7. BIOEQUIVALENCE, PRODUCT-SPECIFIC GUIDANCE, AND BIOWAIVERS

To establish generic interchangeability it is necessary to provide evidence that the product in question performs in an equivalent manner to an appropriate comparator. The SFDA's bioequivalence guideline sets out the essential requirements for studies, and product-specific guidance can make clear the expectations regarding strength, study conditions, analyte, and other factors. This level of specificity helps to speed up development by reducing the need for different protocols and repeat studies.

The data on regulation shown by Saudi Arabia indicate both a high level of development and the presence of potential opportunities. In the 590 studies examined by Althunian *et al*., 521 showed bioequivalence and 455 of the successful ones used a 2×2 crossover design. Drugs with a high degree of variability were found mainly in BCS Classes II and IV, and a great number of the trials that were rejected had to do with issues at the study centres. Although standard designs are efficient provided that the assumptions are satisfied, drugs that are highly variable, have a long half-life, are fixed combinations, or have a narrow therapeutic index may require alternative designs or more stringent controls. The structure of the studies should be based on the properties of the drug rather than on convention.

Bioanalytical quality is just as important. The ICH M10 document lays down the requirements concerning method validation and the analysis of study samples in bioavailability and bioequivalence studies. A statistically sound study design cannot compensate for unreliable concentration data; pre-study validation, analyte stability, reanalysis of the samples that have already been processed, the chain of custody, and data quality must therefore be considered essential components of the equivalence package.

Biowaivers offer the greatest decrease in both time and participant exposure when they are justified. According to the SFDA guidance and the WHO guideline based on BCS published in 2024, some immediate-release oral products can be shown to be equivalent by means of their biopharmaceutic properties and by comparing their dissolution rather than carrying out an in vivo study. The WHO guideline for multisource products also specifies when it is appropriate to use in vivo or in vitro evidence. The fact that a clinical study is avoided does not mean that the standard of rigor is lowered; rather, it represents evidence substitution in cases where the in vitro performance can confidently address the regulatory question.

The assessment of biowaiverness should start as part of the formulation development process. Before the pivotal batches are produced, the solubility, permeability, differences in excipients, dissolution in the appropriate media, strength proportionality, and therapeutic-index aspects should all have been settled. If there is any doubt about eligibility, it is advisable to seek early advice from the SFDA in order to avoid committing to an inappropriate course of action. Guidance that is specific to the product should also be developed step by step so that the questions which recur during assessment become publicly known rather than remaining as repeated private shortcomings.

8. RISK-BASED REVIEW, RELIANCE, INSPECTION, AND DIGITAL DOSSIER QUALITY

Regulatory acceleration demands just as much capacity as it does policy. Since reviewers' time is limited, long-term benefits can only be achieved by directing expertise towards areas of uncertainty. The WHO reliance principles enable authorities to make use of reliable existing outputs while at the same time focusing their national resources on tasks that call for local judgment. In the case of generic drugs, reliance might involve the results of previous GMP inspections, methods recognised by pharmacopoeias, trusted assessments of the active pharmaceutical ingredient, or an evaluation by another authority provided that the product and site can be shown to be comparable. The SFDA would keep its own decision but would reduce duplication.

Risk-based inspection should be based on the same principle. Data from 131 inspections and 722 observations obtained from Saudi GCP inspections indicate that the patterns of deficiencies vary according to the type of organization, such as bioequivalence centres [21]. Inspection intensity can therefore take into account a company's compliance history, the risk of the product, the importance of the data, any changes made, and previous deficiencies. A centre which has ongoing problems with data integrity should be subject to more thorough examination than a well-established centre with a

good record. This reasoning also applies to manufacturing sites.

The quality of digital dossiers is an additional means of ensuring standards are met. Even if a product is technically sound it can be delayed because of inconsistent cross-references, mismatched batch numbers, outdated certificates, unexplained changes to specifications, the absence of method versions, or conflicting site responsibilities. Before submission, automated validation should verify document currency, the integrity of hyperlinks, metadata, numerical consistency, site naming, and the agreement between the summaries and the source documents in Module 3. Reviewers should focus on the science rather than on clerical contradictions.

Another increase in efficiency can be achieved by addressing independent matters in parallel rather than one after the other. Where it is both legally and scientifically appropriate, the CMC assessment, the bioequivalence evaluation and the inspection planning can all be carried out at the same time, using a single integrated risk log to identify any issues that might affect the final decision. Carrying out the work in parallel reduces the calendar time without reducing the amount of scientific work involved.

A learning regulatory system should also turn recurring deficiencies into public guidance, templates, sponsor education, and assessor checklists. When the same questions keep coming up regarding dissolution, comparator selection, API controls, or stability commitments, each review should serve to lessen the burden of future reviews.

9. FROM APPROVAL TO ACCESS: UTILIZATION, LOCALIZATION, AND TRUST

Approval is merely an intermediate achievement; the true aim of public health is to ensure that patients can access medicines that are affordable and which they use with confidence. Studies conducted in Saudi Arabia indicate that knowledge gaps still exist and that people's choice of a product is influenced by professional advice and by their previous experience. Similarly, regional analysis finds that generic policy works best when supply-side pricing measures are combined with demand-side prescribing and substitution mechanisms. Regulatory authorities cannot decide on prescribing by themselves, but they can help to strengthen the trust system on which substitution relies.

A key element is transparent communication. Both patients and clinicians should realise that a generic drug which has been approved by the SFDA must satisfy pharmaceutical standards of quality and equivalence, not just the fact that it is cheaper. A second element is obvious market surveillance. Comparative dissolution studies, specific laboratory testing, pharmacovigilance, tracking of complaints, and the quick investigation of any quality signals can show that these standards are maintained after approval has been granted. The third aspect is supply resilience. Local manufacturing can enhance availability provided that it is based on solid technology transfer, the use of qualified suppliers, validated processes, and lifecycle controls; however, localisation that does not involve equivalent quality maturity shifts the risk.

A strong economic argument is therefore based on giving quick approval together with ensuring competition and continuity. The analysis of Saudi claims for 2025 shows that there is already substantial use of generic drugs and furthermore potential for cost savings. In order to secure that value over the long term, regulatory acceleration should focus on products which have a clinical need, are subject to scarce competition, are vulnerable to shortage, or have a high budget impact, while maintaining the same quality standard. The incentive scheme currently in place with the SFDA offers a foundation for such a prioritisation.

10. AN INTEGRATED SFDA–CMC ACCELERATION MODEL

The evidence points to a six-stage model for accelerated generic access. In the first stage there is regulatory triage: the sponsors determine the Saudi target product, the comparator, the strengths, the manufacturing network, and the likely route of equivalence, while the products are classified according to their biopharmaceutic complexity, therapeutic risk, manufacturing novelty, and supply importance. Scientific advice is focused on unresolved uncertainty.

In the second stage we have CMC-by-design; the manufacturer defines the quality target product profile, identifies the critical quality attributes, carries out a risk assessment, and acquires sufficient knowledge regarding the formulation and the manufacturing process in order to be able to implement controls. Before the pivotal batches are produced, the issues of API variability, the functionality of the excipients, scale-up, dissolution, impurity risks and packaging are all taken into account, in accordance with the QbD and ICH risk-management principles.

In stage three the approach is one of equivalence by design; the sponsor uses the product-specific SFDA guidelines where these are available, chooses either an in vivo or a biowaiver strategy on the basis of the drug and formulation properties,

qualifies the study centre, and checks that the bioanalysis is valid before the study starts. The objective is to establish an auditable chain of evidence from the formulation attributes through to the in vitro results and, if necessary, the in vivo results.

Stage four is review-ready submission. Before filing, summaries, source documents, certificates, batches, methods, stability datasets, DMF references, and site responsibilities are reconciled. Major risks are discussed explicitly, and digital validation identifies technical inconsistencies.

Stage five is proportionate review. SFDA retains independent judgment but uses risk stratification and justified reliance to avoid unnecessary duplication. Low-uncertainty elements move efficiently; higher-risk elements receive deeper assessment, and inspection resources reflect compliance history. Deficiency requests should be consolidated and tied to decision-critical uncertainties.

Stage six is lifecycle assurance. Authorization is followed by targeted surveillance, change management, quality trending, and rapid signal response. Real-world quality information feeds back into reviewer knowledge and product-specific guidance. Figure 1shows this pathway; Figure 2 depicts the quality-to-access flywheel created when robust CMC evidence reduces uncertainty, supports predictable approval, and sustains reliable market supply.

11. IMPLEMENTATION METRICS, LIMITATIONS, AND FUTURE DIRECTIONS

Assessment of acceleration should be based on a range of metrics rather than just on approval time. Useful indicators are: the time taken to obtain scientific advice, the proportion of applications that pass technical validation on their first submission, the first-cycle CMC approval rate, the number of major deficiencies per application, the use of eligible biowaivers, the reasons for bioequivalence rejections, the rate of inspections being repeated, the number of major post-approval quality defects, the number of shortage days, and the time from approval to commercial availability. Table 2 suggests a practical collection of such indicators. It would not indicate success if a shorter review period is associated with a higher number of recalls or repeated deficiencies. Localization.

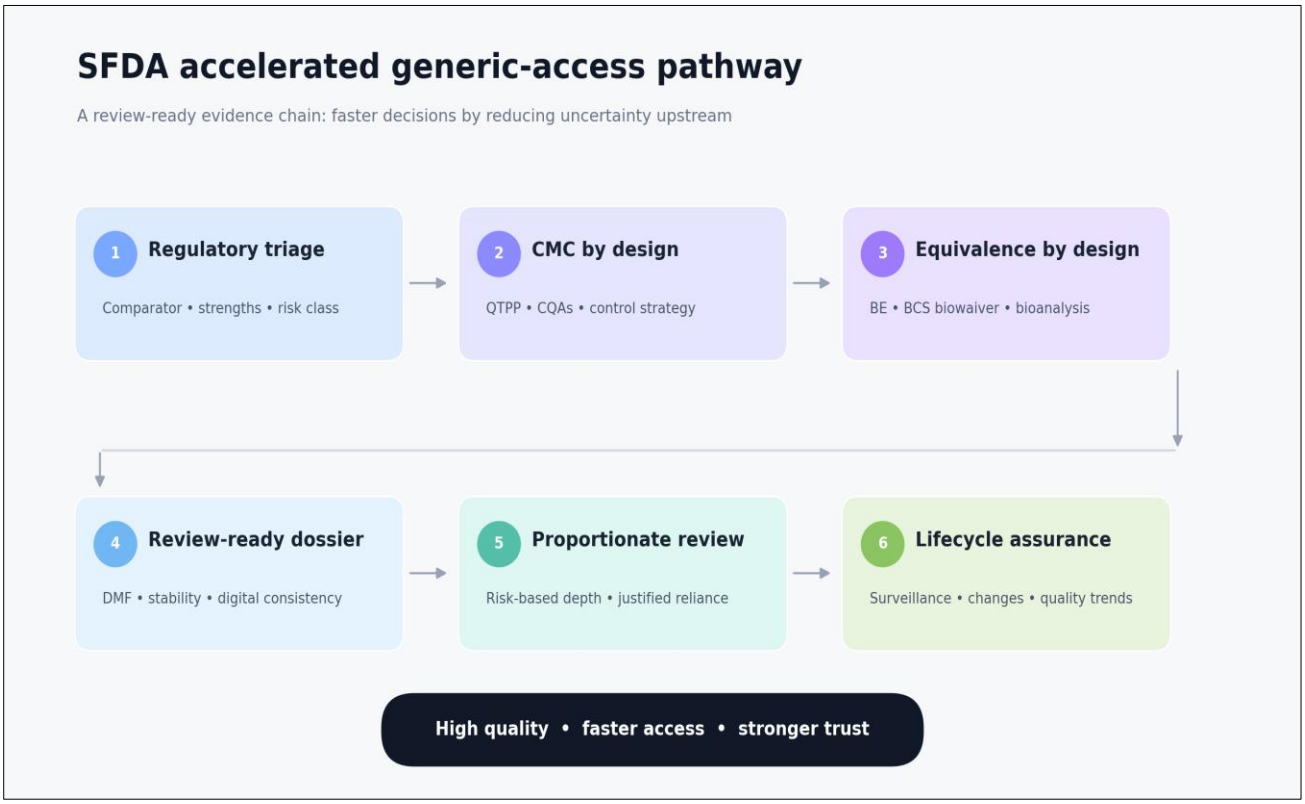

Figure 1: Integrated SFDA generic-access pathway

Figure 2: Quality-to-access flywheel

Table 2: Balanced implementation indicators for SFDA–industry generic acceleration

KPI	Operational definition	Desired direction	Why it matters
Technical validation pass rate	Applications passing eCTD/administrative checks at first filing	Increase	Separates avoidable dossier defects from scientific review
First-cycle CMC acceptance	Share of applications with no major CMC rework after first assessment	Increase	Direct measure of development and dossier readiness
Major deficiencies/application	Decision-critical CMC or BE questions issued per application	Decrease without quality-signal increase	Tracks avoidable uncertainty and review burden
Eligible biowaiver utilization	Share of scientifically eligible products using an accepted biowaiver	Increase	Measures substitution of appropriate in vitro evidence for unnecessary trials
BE study repeat/rejection rate	Share of submitted studies requiring repetition or rejected for design/center/data issues	Decrease	Targets study quality and center qualification
Risk-based reliance use	Applications where trusted external assessment/inspection evidence is formally leveraged	Increase where justified	Releases capacity for Saudi-specific risks
Approval-to-launch interval	Calendar days from marketing authorization to commercial availability	Decrease	Distinguishes regulatory approval from real patient access
Major post-market quality signals	Recalls, critical defects, confirmed major OOS or serious manufacturing signals	Stable/decrease	Ensures speed is not purchased with lower quality
Shortage days for priority generics	Days a priority generic is unavailable due to supply disruption	Decrease	Connects CMC robustness and regulatory policy to drug security

The review does not aim to estimate a single causal effect but instead combines heterogeneous regulatory and observational evidence. Since the public information provided by the SFDA does not show every internal review practice or every trend in confidential deficiencies, and although the Saudi evidence is better regarding bioequivalence and consumer perception it is not so strong when it comes to analytics of the CMC review cycle, the model should be tested prospectively using anonymized performance data.

An effective pilot should compare the conventional methods with the improved ones for a group of immediate-release generics, assessing first-cycle completeness, assessor time, the number of questions, study repetition, authorization time, launch delay, and post-market quality signals. When the data are stratified according to manufacturing origin, BCS class, and reliance eligibility, it will be possible to identify the areas in which acceleration provides the greatest benefit without increasing risk.

Further research should involve extending the guidance given specifically for products, incorporating structured quality data in electronic submissions, predicting which dossier elements are high risk, and publishing aggregated lessons from the review process. Additionally, the SFDA and the industry could carry out tests using 'review-ready' pre-submission checklists. The aim is still to get rid of any delays that do not add value by improving both the data and the processes used, while at the same time keeping intact the regulatory functions that reduce uncertainty.

12. CONCLUSION

Saudi Arabia has the possibility of achieving faster access to high-quality generic medicines without having to compromise quality. The reliable approach is to direct effort towards the earlier stages: carrying out clearer planning, engaging scientifically from the beginning with respect to complex products, developing formulations and understanding the manufacturing processes on the basis of quality by design, using analytical methods that are appropriate for their intended purpose, adopting proactive strategies regarding impurities and stability, carrying out bioequivalence studies to a qualified standard, and granting biowaivers on the basis of scientific justification. These practices reduce the uncertainty which causes the review cycles and allow faster decisions to be made on scientific grounds.

The SFDA has already got a number of the necessary building blocks via its registration framework, its guidance on equivalence, its product-specific recommendations, its requirements regarding DMF and stability, its inspection system, and its availability incentives. The WHO and ICH standards provide well-developed methods concerning reliance, good regulatory practice, risk management, analytical lifecycle control, and equivalence. Research carried out in Saudi Arabia has established the priorities for implementation: study-center quality, public confidence, comparative product performance, and efficient generic utilization.

Regulatory acceleration should therefore result in fewer questions that can be avoided, not in fewer questions concerning quality; it should lead to better designed studies, not to weaker evidence; and it should involve proportionate oversight, not a reduction in accountability. Having solid CMC knowledge can make the review process more predictable, timely entry can enhance competition and supply, and consistent performance can strengthen trust. Since advanced regulatory and CMC practices by the SFDA therefore constitute a practical way of achieving affordable access and drug security while at the same time preserving the scientific basis for interchangeability and quality.

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