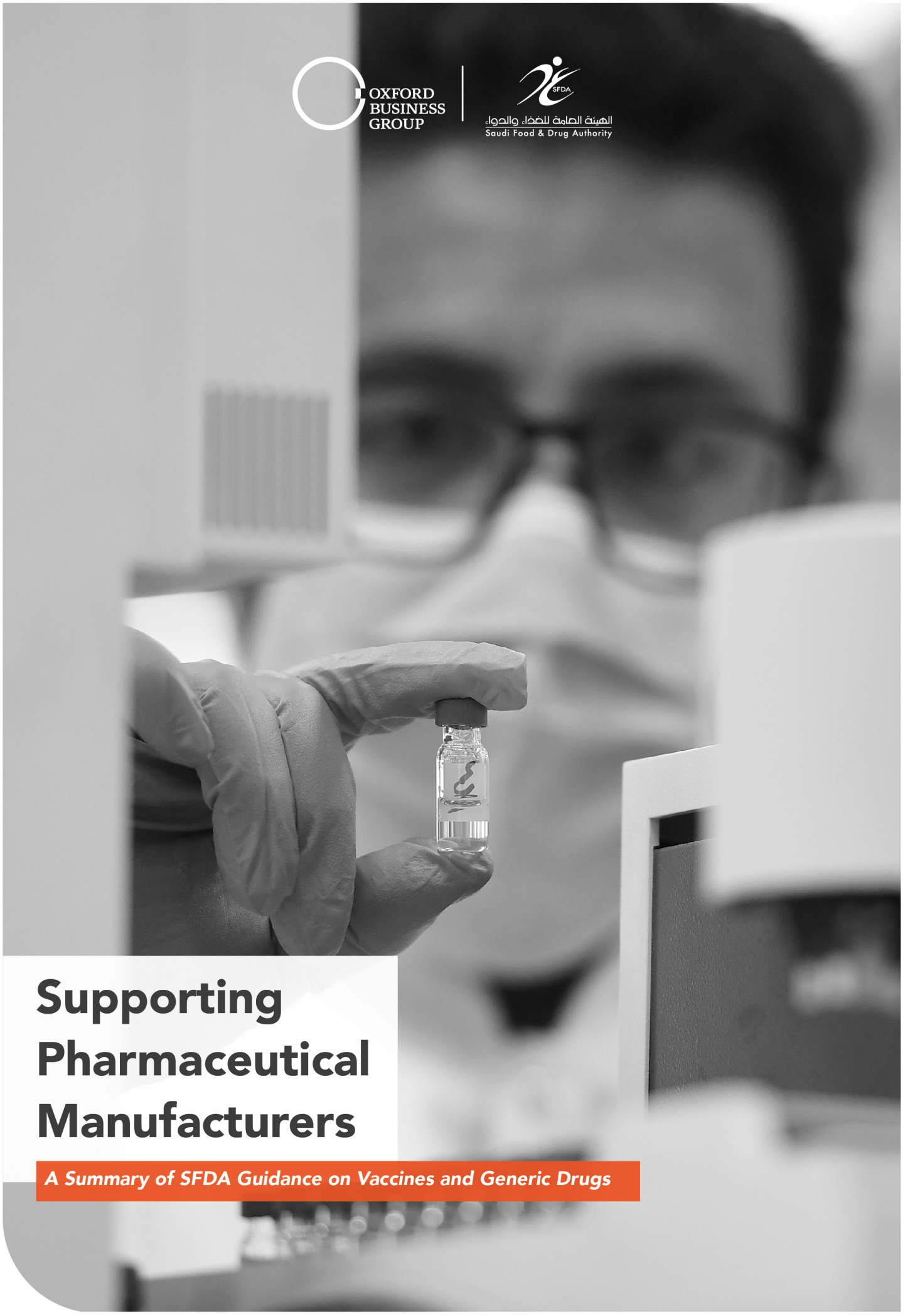

OXFORD BUSINESS GROUP

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Supporting Pharmaceutical Manufacturers

A Summary of SFDA Guidance on Vaccines and Generic Drugs

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The SFDA has recently developed two new guideline documents to assist pharmaceutical manufacturers in registering their products in Saudi Arabia. Gaining access to a market and meeting regulatory requirements can be a complex process in many countries. The SFDA is working to support manufacturers to overcome these challenges and provide them with clear and relevant information. This will help companies do business in Saudi Arabia and, by doing so, further develop and expand the health care sector in line with Vision 2030. The SFDA's latest guidelines focus on bioequivalence studies for generic drugs and clinical trials for vaccines. This article details the background of these documents and introduces their contents.

Drug Safety

In order to ensure drug safety, or pharmacovigilance, the SFDA consistently evaluates the safety, efficacy and quality of all types of pharmaceuticals in the Saudi market. This helps to prevent any adverse effects of pharmaceutical products. Before products can enter the Saudi market, they must receive SFDA approval. The SFDA supports manufacturers at all stages of this process, including providing guidance on how to register their products successfully in the Kingdom.

SFDA Guidelines

The SFDA aims to produce clear guidelines for companies to ensure they meet the minimum requirements for product registration and minimise the number of applications that are rejected. Such guidance helps applicants meet the expectations of regulators. When developing guidelines, the SFDA first publishes draft guidelines on the website of Saudi Arabia's Public Consultation Platform: https://istitlaa.ncc.gov.sa. The platform is affiliated with the National Competitiveness Centre and enables public entities and private sector players to express their views and give feedback on draft laws related to economic and development affairs before they are approved.

The SFDA collects feedback from companies on the draft guidelines, which it considers before publishing a final version of the guidelines to serve as official guidance. Many authorities in the MENA region look to the SFDA for expertise and examples of best practices, including for publishing guidelines. In addition to supporting manufacturers, the SFDA's guidance documents help other authorities understand the level of assessment Saudi Arabia requires in order to grant product approval.

Generic Drugs, Reference Drugs and Bioequivalence Explained

Ensuring the safety and quality of generic drugs is an especially important priority for regulators like the SFDA. A generic drug is a medication created to be the same as an already marketed, brand-name drug, also known as a reference drug. The reference drug would normally be the innovator product for which efficacy, safety and quality have been established. A generic drug is essentially a lower-cost version of this. It should be the same as a reference drug in a number of ways, including dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. It should stand as an equal substitute for its brand-name counterpart. When this is the case, the generic drug is considered "bioequivalent" to the reference drug. Bioequivalence is when a generic medicine contains the same active ingredient in the same quantity as an innovator medicine, and provides the same therapeutic effect.

Bioequivalence Studies

Companies wishing to manufacture a generic drug are required to undertake a bioequivalence study in which they compare the reference drug to the generic drug. This ensures the drug is safe and meets specified standards. Regulators in different countries have their own requirements on bioequivalence. This includes how many studies they require manufacturers to undertake in order to grant approval for a generic drug. These requirements are often detailed in specific guidelines. Indeed, guidelines help in a variety of ways. Some generic drug tests are complex and challenging, and sometimes companies do not know about certain testing approaches. Guidelines assist and inform companies in this regard.

SFDA Bioequivalence Guidelines

In November 2020 the SFDA published draft guidelines on bioequivalence under the title *SFDA's Product Specific Bioequivalence Guidance*. The final version is expected to be published in the coming months. The guide serves to facilitate generic pharmaceutical product availability and support the generic pharmaceutical industry in identifying the most appropriate methodology for designing bioequivalence studies. It includes specific guidance for more than 400 generic drugs, including tablets, capsules, creams and ointments. For each drug, the guide describes the active ingredient, dosage form and recommended study. It describes the SFDA's current thinking and expectations on how to develop bioequivalence studies for the generic pharmaceutical product.

Prior to publishing these guidelines, the SFDA used a combination of documents and references from other authorities – such as the European Medicines Agency, the UK's Medicines and Healthcare products Regulatory Agency, and the US Food and Drug Administration (FDA) – to determine the bioequivalence studies required. The SFDA will now use these new guidelines when assessing product registration. It is expected that other authorities will use these documents for registering products in their jurisdiction as well, especially authorities within the MENA region. Once the final version of the guidelines is published, the SFDA will be second in the world after the US FDA in terms of the amount of product-specific guidance published. In the coming years the SFDA plans to increase the number of drugs covered in its guidance.

Vaccine Assessments

All vaccines that wish to enter the Saudi market must undergo clinical assessments. For each vaccine type, there is an antigen or active ingredient that stimulates a specific immune response. As the national regulator, the SFDA requires manufacturers to submit details of clinical trials they have undertaken during the development of a vaccine. The SFDA extensively reviews the evidence the company submits, which includes but is not limited to the study protocol, statistical analysis plan and full clinical study report. The authority then deicides to approve or reject the vaccine.

SFDA Vaccine Guidelines

In 2020 the SFDA published guidelines on vaccines under the title *Clinical Considerations for Vaccines*. The final version was published in August 2021. This serves as general guidance for all vaccine submissions and is not specific to Covid-19 vaccines. It represents the current thinking of the SFDA regarding the appropriate level of evidence to support vaccine applications, helping to ensure efficiency and consistency of submissions by applicants. The guidelines detail the types of vaccine application submissions that the SFDA accepts; the type of immune response required for vaccines with known antigenic components and the specific level of response required to provide an immune protection against a specific pathogen; and pharmaceutical inactive ingredients, known as excipients, included in SFDA-reviewed vaccine submissions.

The SFDA has four types of application routes for vaccines, each with its own testing requirements:

1. **Novel Vaccines**: A novel vaccine contains new components that were not used in previously licensed vaccines. The clinical requirements for novel vaccines comprise a phase-1 study that assess the product safety, a phase-2 study to determine the appropriate dose and, most importantly, a well-designed phase-3 study to establish appropriate efficacy and the safety profile of the applicant vaccine.
2. **Vaccines with Known Components**: This application route follows similar general clinical requirements.
3. **Combination Vaccines**: Combining antigens that protect against multiple types of infections could result in a negative effect on immune response due to the possibility of interactions between the vaccine components, or a negative immune interference effect towards some antigenic component. For this registration route, the applicant should be able to provide justification that weighs the risks and benefits of the combination by citing local or international guidelines and relevant clinical trials.
4. **Major Variations**: This application route covers any changes in product composition. This may include changes such as updating seasonal influenza strains or modifying the age group for known vaccines.

In addition to its published guidelines, the SFDA offers meetings if companies require assistance when seeking to register their products in the Saudi market.