In Case You Missed It: Key Saudi Medical Device and Pharmaceutical Laws and Regulatory Developments of 2021

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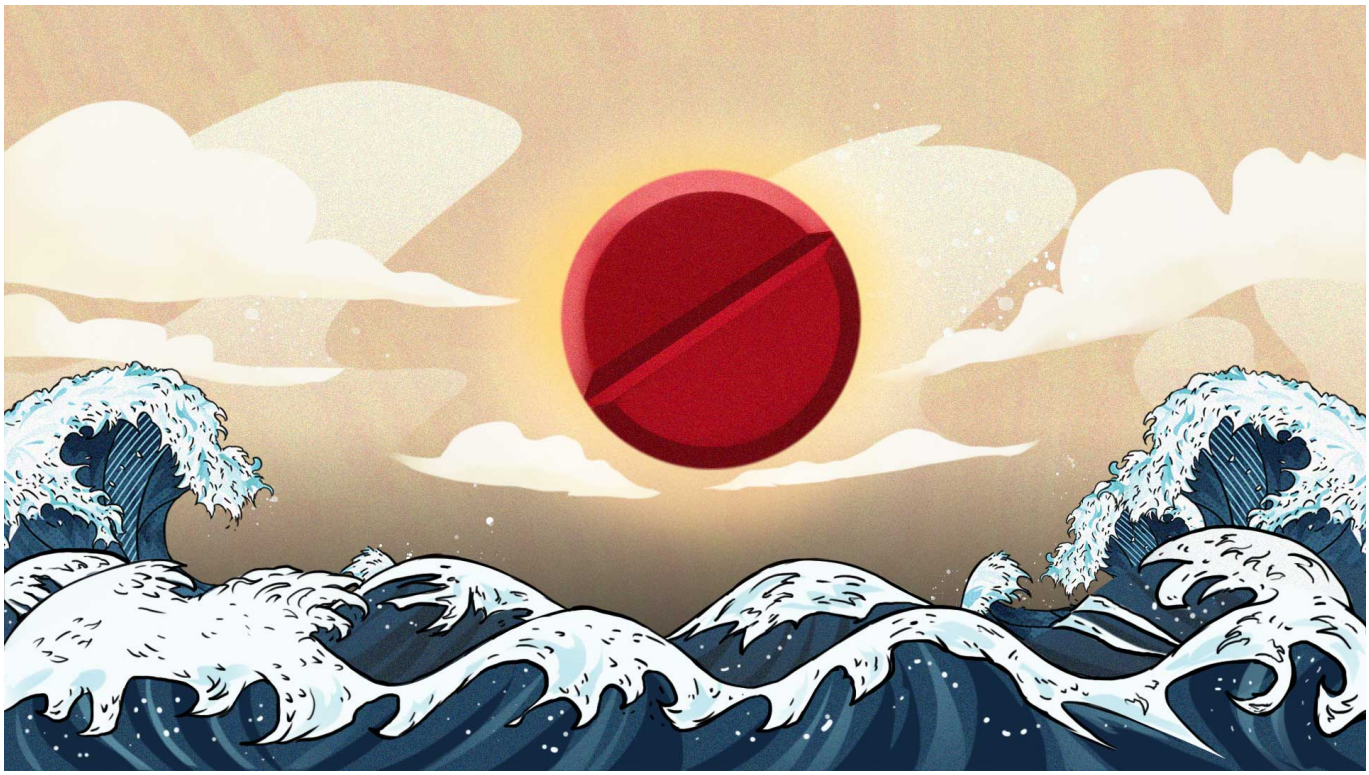

*This illustration is inspired by the original woodblock print of **The Great Wave off Kanagawa** by Hokusai.*

In the last few years, there has been a very noticeable increase in regulatory activity from the healthcare regulators across the Middle East. Staying on-top of the updates and new regulations, circulars, and guidance from the Saudi Food & Drug Authority ('**SFDA**') is no longer a passive exercise; things are changing too quickly.

Set out below, we summarise the key new or updates pieces of legislation pertinent to pharmaceuticals, biologics, medical devices and other medical products in the Kingdom of Saudi Arabia ('**Saudi**') issued in 2021, through October.

1. Pharmaceuticals, Biologics, and other medicinal products

GCC Guidelines for Bioequivalence – new version

The importance of bioequivalence requirements is increasing in the Gulf Cooperation Council ('**GCC**') region particularly due to the growth of the generic drug market. In May, version 3 of the GCC Guidelines for Bioequivalence, issued by the Gulf Health Council, was issued to include updates to the design, conduct, and evaluation of bioequivalence studies, including:

1. Reference products must be the original brand-name product (i.e. manufactured in the country of origin of the original brand name). If this product is not available in the local market, then the brand-name product from the same company but different country of origin will be used if marketed in the GCC region, International Conference on Harmonisation countries, or in any recognized regulatory authority. If the original brand-name is not available in the market or no longer produced, then the product that is the local market leader may be used as a reference product;
2. For a sound bioequivalence study, in general, at least 24 normal healthy subjects, preferably non-smoking, 18 years of age or older, and within 15 per cent of ideal body weight, height, and body build (as per the Metropolitan Life Insurance Company Statistical Bulletin, 1983) should be enrolled in a crossover bioequivalence study. A number of subjects of less than 24 may be accepted (with a minimum of 18 subjects) when statistically justifiable; and
3. In relation to in vitro dissolution tests for bioequivalence studies, for an application that has more than one active pharmaceutical ingredient ('**API**') source intended for registration, the applicant should ensure that the specifications are essentially the same as those of the API originally used in the biobatch. The application will need to provide comparative in-vitro dissolution data at three different buffers and the media intended for drug product release, between the biobatch and batch with the additional or alternate API source(s) in order to demonstrate the similarity.

Regulatory Framework for Drugs Approval – new version

In October, version 6.2 of the Regulatory Framework for Drugs Approval was issued to add that: 1) a drug application will be considered to be a generic if the innovative product is registered in one of the recognised regulatory authorities (such as the US FDA, EMA, MHRA(UK), Swissmedic, Health Canada, and TGA (Australia), for human products) irrespective of whether the innovative product is registered or not at the SFDA.

SFDA Guidance for Periodic Safety Update Reports of COVID-19 Vaccines – new document

This new document provides section-by-section guidance and requirements for periodic safety update reports ('**PSURs**') of COVID-19 vaccines approved in the Saudi market and was mainly adopted from the European Medicines Agency ('**EMA**') document 'Consideration on core requirements for PSURs of COVID19 vaccines'. It is supplemental to the SFDA guideline on good pharmacovigilance practices.

SFDA Guidance for Drafting Risk Management Plans of COVID-19 Vaccines – new document

This new document provides section-by-section guidance and requirements for drafting the risk management plans ('**RMPs**') of COVID-19 vaccines approved in the Saudi market and was mainly adopted from the EMA document 'Consideration on core requirements for RMPs of COVID19 vaccines'. It is supplemental to the SFDA guideline on good pharmacovigilance practices.

Regulation and Requirements for Conducting Clinical Trials on Drug – new version

Version 2 was published in June and expanded the scope of the clinical trial regulation, including adding requirements for bioequivalence studies, phase I trials, and biological products studies (vaccines, gene therapy, stem cells and biosimilar). In November 2021, version 2.1 was published to, amongst other updates, require that early phase trials must submit a progress report annually, and to allow the SFDA to take decisions and provide exemptions regarding regulatory requirements and application review priority in specific cases, such as emergencies and pandemics.

Clinical Considerations for Vaccines – new document

This new guideline represents the current thinking of the SFDA regarding the appropriate level of evidence to support vaccine applications. This guidance should be read in conjunction with SFDA Regulatory Framework for Drugs Approvals, the GCC Data Requirements for Human Drugs Submission, Guidelines for Production and Quality Control of Vaccines, and international vaccines relevant guidelines produced by the World Health Organisation ('**WHO**').

Guidance for Presenting PIL and Labelling Information of Herbal and Health Products – new version

As a result of the Gulf Health Council's guide, the SFDA updated its guidance twice this year, thus far, with version 2.2 being the latest. Updates to this guideline include changes to the particulars that must appear on the outer packaging and the immediate packaging. Removed from the labelling requirements are the SFDA registration number and the price. When submitting a new application for registration, renewal, or variation, the information presented by the applicant regarding the patient information leaflet ('**PIL**') and labelling must follow this guidance. Additionally, it should be noted that products with different strengths must have different packaging colour codes that differentiate between different strengths. Following the SFDA's approval of the PIL and labelling contents, such contents cannot be changed except with the approval of the SFDA following a variation application.

Similarly, the SFDA Clearance Conditions and Requirements was updated to version 1.6, which removed the price printing condition for products that are priced by the SFDA.

Guideline for Naming and Graphic Design of Packaging for Herbal and Health Products – new document

This new guideline will be implemented in May 2022 and is directed to applicants who are submitting a proposed name for herbal and health products. It provides guidance on the process of herbal and health products naming and recommendation on packaging design. The packaging graphic design in this guideline detail the ideal designs for primary packaging, intended for solid oral dosage forms. The design considerations and principles outlined also can be applied to other products dosage forms.

GCC Guidance for Presenting the Labelling Information, SPC and PIL – new version

This is the GCC guidance, issued by the Gulf Health Council, which was updated twice this year thus far, with version 3.2 being the latest. Updates to this guideline include changes to the particulars that must appear on the outer packaging and the immediate packaging. Removed from the labelling requirements are the registration number and the price.

Guidance for Naming of Medicinal Products – new version

This new version, 2.0, updates guidance regarding medicinal product names with:

- obvious similarities in spelling and pronunciation of proprietary names: Generally, proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other registered products at SFDA;
- inert or inactive ingredients: Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that creates an impression that the ingredient's value is greater than its true functional role in the formulation;
- United States Adopted Name (USAN) stems: Proprietary names should not incorporate USAN stems in the position that USAN designates for the stem as this can result in the creation of multiple similar proprietary names and/or proprietary names that are similar to established names. According to the WHO and USAN, the well-established stem should not be used in or as trademarks;
- Incorporation of company's name: Proprietary names should not incorporate the company's name, or some part of the company's name across multiple products. If the company submits a generic name plus either an abbreviation of a company or full name after the name (not attached to the name), this will be accepted. For example: Cepecitabine SFDA. If the company submits a brand name attached to the company's abbreviation, either on the beginning or at the end of the name, this will be rejected. For example: CefaSFDA; and
- Biological products: The same criteria apply as for any other medicinal products in respect to the (invented) name.

Guide to Good Manufacturing Practice for Medicinal Products – new version

The SFDA issued version 4, consisting of 375 pages, in line with the European Commission Volume 4 of 'The rules governing medicinal products in the European Union' laid down in Commission Directives 91/356/EEC, as amended by Directive 2003/94/EC, and 91/412/EEC respectively.

Pharmaceutical products allowed to be sold in food retail stores – new version

The SFDA issued version 2.0, listing pharmaceutical products allowed to be sold in food retail stores, including: tablets and capsules containing paracetamol or ibuprofen; lozenges if they do not contain vitamins or minerals; creams, gels, ointments, lotions (for muscle pain or cold symptom relief) containing menthol, camphor, eucalyptus, and/or methyl salicylate; and hand sanitizers only containing isopropyl alcohol or ethanol. It remains that pharmaceutical products can only be sold at prices approved by the SFDA.

Food retail stores inside cities (include medium grocery stores, large grocery stores, and supermarkets) and on the highways that have the proper storage conditions and requirements for pharmaceutical

products are allowed to sell any of the above pharmaceutical products individually.

Food retails stores, food wholesale stores, and food distributors are not allowed to sell any of the above pharmaceuticals as wholesale items; only licensed pharmaceutical warehouses are allowed to do so.

Guideline on strategies to identify and mitigate risks for first-inhuman and early clinical trials with investigational medicinal products – new document

This guideline has been adopted from the EMA to address first-in-human ('**FIH**') and early phase clinical trials ('**CTs**') with integrated protocols. The document includes considerations on quality aspects, non-clinical and clinical testing strategies, study design, and on conduct of FIH/early CTs.

Guidance for Priority Review of Product Registration – new version

This version 5 provides udpates to the criteria for qualifying for priority review designation, including the criteria for first generic and biosimilars as well asupdating the process for designating a generi and biosimilar drug for priorirty review. The priority review process for the generic or biosimilar drug is intended for those products that are considered the first generic or biosimilar to the innovative product. It adds criteria for veterinary drugs priority review.

2. Medical Devices:

New Medical Device and Products Law

On 26 August 2021 the new Medical Device and Products Law came into effect, replacing the Medical Devices Interim Regulation, although it retains most of the provisions of the interim regulation.

Guidance on Approval Requirements for Medical Devices Advertising (MDS-G11) – new version

Version 2.1 provided several updates, including adding medical device importers to the scope and specifically addressing requirements for advertising on internet and social media platforms. Where advertising material is published by individuals on social media platforms, SFDA must be notified at least 12 hours prior to publication through email, providing the advertiser's name and social media account.

It also clearly distinguishes the approval requirements and process for advertising materials directed to healthcare practitioners and those directed to consumers. Any medical device intended to be advertised in Saudi must follow the requirements and procedure for obtaining an approval for medical device advertising from the SFDA, whether the advertising is directed to consumers or healthcare practitioners. Medical devices intended to be advertised must be registered in the SFDA.

Guidance on Requirements for Storage, Handling and Transportation of Medical

Devices (MDS-G25) – new version

Establishments involved in the importation and/or distribution of medical devices must ensure that medical devices are stored and/or transported under conditions specified by the manufacturer and ensure traceability of devices supplied in the market. Importers, distributors, local manufacturers involved in distribution activities, or authorized representatives involved in importation and/or distribution activities of medical devices within the KSA must have a Medical Devices Establishment License. This new version 2 provides various updates, including: a) a new requirement regarding the temperature mapping; and b) the addition of adverse reporting requirements, obligating reporting through the National Centre for Medical Device Reporting ('**NCMDR**') in case of any adverse events related to stored or transported medical devices according to 'Guidance on Requirements for Reporting and investigation of Incident and Adverse Event of Medical Devices MDS-G39'.

Guidance on Review and Approval of Artificial Intelligence (AI) and Big Data based Medical Devices (MDS-G53) – new document

This guideline applies to standalone software type medical devices, to which machine-learning-based artificial intelligence ('**AI**') technology is applied in order to diagnose, manage, or predict disease by analysing medical data. It also applies to AI software that is configured with hardware, such as clinical decision support ('**CDS**') software or computer-aided detection/diagnosis ('**CAD**') software. The guideline details whether 'big data' and AI based medical software is a medical device and SFDA considerations for review and approval of applications for medical device marketing authorisation.

Guidance for Medical Devices Maintenance Facilities (MDS-G49) – new document

This new guidance applies to all medical devices maintenance facilities in KSA. It clarifies the SFDA's requirements for medical device and supplies maintenance services in healthcare facilities in order to ensure the performance of the medical device according to its intended purposes by applying calibration, planned preventative maintenance, and corrective maintenance during the usage of the medical device.

Guidance on Requirements of Importation and Re-Exportation for Radioactive Materials Used in Medical Applications (MDS-G24) – new version

SFDA issued this version 2 guidance document to reflect changes in processes, including that the Radioactive Materials Registration System ('**MRMR**') is now the electronic system to be used by healthcare providers, importers, exporters, and carriers to register and apply for importation or re-exportation of radioactive materials used in medical applications. Updates were made to the required documentation, including requirements for clearance in port, transportation, and importers and exporters.

Guidance on Requirements for Import / Re-export Medical Imaging Materials (MDS-G52) – new version

Permission from the SFDA is required to import or re-export imaging materials used in medical applications. The request for permission should be submitted in the unified system of the SFDA, 'GHAD'. Guidelines of ports clearance requirements are contained in MDS-G21.

Guidance on Requirements for Licensing Service Providers for Quality Assurance and Ionizing Radiation Measurements in Healthcare Facilities (MDS-G51) – new document

This guidance clarifies SFDA requirements for licensing providers of quality assurance and radiation measurements to healthcare facilities This guideline applies to ionizing radiation protection and safety service providers for healthcare facilities and healthcare providers. Amongst other requirements, facility employees must have a bachelor's degree, as a minimum, in biomedical engineering or medical physics or any related specialty. There must be a Saudi national licensed radiation protection officer.

Essential Requirements for Medical Radiation Protection Programs – new document

This new guidance clarifies the general requirements for the implementation of radiation protection programs ('**RPP**') by healthcare providers ('**HCP**'). Any HCP that uses medical radiation sources for medical procedure, either radiation X-ray generator or radioactive material, is required to develop, document, and implement an RPP. The HCP must audit the program every two years to ensure that the RPP remains within the scope and the level of protection required in accordance to the HCP's radiology department scope and the level of radiation activities.

Updates on the compliance timeframe for the requirements of medical devices unique device identification (Saudi -DI).

The SFDA announced requirements for medical devices unique device identification ('**Saudi-DI**' or '**UDI**') and launched the UDI database. For class B and C (medium risk) and class D (high risk) devices, compliance is required by 1 September 2022. For class A (low risk) devices, compliance is required by 1 September 2023. MDS-G34, Guidance on Requirements for Unique Device Identification (UDI) for Medical Devices. A finished device packaged and labelled prior to the applicable compliance date may be distributed without being UDI compliance for an additional one year after the applicable compliance date.

Requirements for Clinical Trials of Medical Devices (MDS-REQ 2) – new version

This document applies to clinical research organization ('**CRO**') or other parties wishing to conduct clinical investigations of medical devices or clinical performance studies of in vitro diagnostics medical devices within KSA. Version 4 implements a number of updates basedon the new medical devices law including requiring that CROs operating in Saudi obtain an SFDA establishment licence. The new version now incorporates two previous, separate guidance docuemnts: 1) Guidance on Requirements for Clinical Investigations (Trials) of Medical Devices (MDS-G20); and 2) Guidance on Requirements for Performance Evaluation Studies of In Vitro Diagnostics Medical Devices (PESIVD) (MDS-G32).

Requirements for Medical Devices Marketing Authorisation (MDS – REQ 1) – new version

This document applies to manufacturers of medical devices for the purpose of making available with the

KSA, and their authorized representatives. In general, it has been changed to comply with the new medical devices law and its regulations. This document replaces Guidance on Requirements for Medical Device Listing and Marketing Authorization (MDS-G5).

We do not expect legislation developments to slow down anytime soon. Stay tuned for more updates.

Our Healthcare & Life Sciences sector group regularly advise on these types of matters. For further information, please contact healthcare@tamimi.com.