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Israel: Law & Practice

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ISRAEL

Law and Practice

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1. LIFE SCIENCES REGULATORY FRAMEWORK

1.1 Legislation and Regulation for Pharmaceuticals and Medical Devices

Medicinal Preparations

The principles governing medicinal preparations are entrenched in the Pharmacists Ordinance (New Version), 1981 (the "Ordinance") and various regulations enacted under it. Said principles are broadly implemented by the Ministry of Health (MOH) in various guidelines and circulars (internal procedures) published by it from time to time.

Medical Devices

Medical devices will be governed by the Medical Device Law, 2012 (the "Medical Device Law"), which is expected to enter into force only after completion of the enactment of specific relevant regulations. Currently, only some of those regulations have been enacted (eg, the Medical Device Regulations (Registration of a Medical Device and the Renewal Thereof), 2013 ("the Medical Device Regulations")). Nonetheless, in February 2014, the MOH published a circular advising on the implementation of the principles of the Medical Device Law as of April 2014. Therefore, the regulatory law governing medical devices is still under development.

The Israeli regulatory system is centralised. The MOH (through its Pharmacy Division and Medical Devices Division) is the authority responsible for applying and enforcing the regulatory regime covering pharmaceuticals and medical devices, as applicable.

1.2 Challenging Decisions of Regulatory Bodies that Enforce Pharmaceuticals and Medical Devices Regulation

MOH decisions can be challenged, subject to internal appeal proceedings, and in any event are subject to judicial review, exercised within the ambit of an administrative petition filed with the Supreme Court (sitting as the High Court of Justice).

The criteria for challenging MOH decisions are prescribed in the general administrative law and include, lack of authority (ie, the decision is ultra vires), the decision is unreasonable, it violates basic rights, etc.

The same procedures can generally be applied for challenging decisions covering other regulated products (eg, foodstuffs).

1.3 Different Categories of Pharmaceuticals and Medical Devices

The regulatory law distinguishes between three different categories:

- prescription preparations (Rx) that can be obtained only by prescription from a physician;
- over-the-counter (OTC) preparations (both such preparations can only be dispensed to consumers by a qualified pharmacist; and
- general sales list (GSL) preparations, which can be sold by anyone (not being a pharmacist) in a specific authorised location which need not be a pharmacy.

Disparate regulatory requirements may apply in respect of these categories, particularly regarding the permissible marketing, promotion and general advertisement of the different preparations.

Classification of the relevant preparations falls under the auspices of the MOH, at the time of their registration. The registration holder may apply to reclassify an Rx preparation as OTC.

No similar classification applies for medical devices, but the MOH has the authority to prescribe conditions regarding the manner in which

the specific device is distributed, dispensed and used.

2. CLINICAL TRIALS

2.1 Regulation of Clinical Trials

Clinical trials are largely regulated by regulations and guidelines, which generally provide guidance with regard to the filing and approval process for conducting clinical trials. Such regulations include the Public Health Regulations (Medical Trials in Human Beings) 1980, and MOH Guideline 14 for Medical Trials in Humans, as updated in 2020.

Additional guidelines include MOH Guideline 144/01, whose provisions lay down the framework for the supervision of clinical trials in human beings (either by the MOH or the relevant institutional bodies), MOH Guideline 164 (relating to reporting and monitoring safety information during the conduct of a clinical trial), MOH Guideline 169/01 (relating to digitisation of the informed consent process) and Guideline 168 (concerning a pilot project for the approval of clinical trials classified as "non-special").

2.2 Procedure for Securing Authorisation to Undertake a Clinical Trial

Generally, an application to conduct a clinical trial should be filed by the investigator, on behalf of the sponsor of the trial and must be approved by the manager of the institute at which the clinical trial is to be conducted, the Helsinki Committee of the institute (the Israeli equivalent of the Institutional Review Board (IRB) and the MOH, prior to the anticipated start date of the clinical trial. "Special clinical trials", in which the level of risk to the subjects is limited and raise no exceptional ethical issues concerning the risk-benefit ratio, generally do not require MOH approval. Classifying a clinical trial as "special" or "non-special" is determined by the IRB after the full application is received. Applications covering "non-special" trials are forwarded to the MOH and reviewed by the IRB. The decision of the IRB in this regard, should be sent to the MOH immediately after the application has been reviewed.

Securing authorisation entails the submission of the sponsor's undertaking, the sponsor's response to a questionnaire (which serves as a recommendation for classifying the trial), and other ancillary documents (eg, the informed consent form or the study protocol).

Furthermore, the engagement between the sponsor and the lead investigator requires the approval of a committee established and operated under the supervision of the MOH.

Following a clear, verbal and non-coerced explanation given to each participant about the trial, the investigator is required to request and obtain the informed consent form duly signed by each participant.

In 2020, a new pilot was launched for the approval of multi-centre trials. According to the pilot, such studies will be approved by a national committee as opposed to being approved on a site-by-site basis.

2.3 Public Availability of the Conduct of a Clinical Trial

In 2017, the MOH launched a new website containing a registry of clinical trials conducted in Israel with human participants. Registration is required for clinical trials involving one or more clinical interventions and assessing their medical effects (excluding trials in which the participants are healthy volunteers).

Additional registration on the NIH website, which was previously a prerequisite, is no longer mandatory.

2.4 Restriction for Using Online Tools to Support Clinical Trials

MOH Guideline 169/01 (the "Guideline"), issued in October 2020, sets out the framework for using digital means as part of the process for obtaining a participant's informed consent for participation in a clinical trial.

According to the Guideline, the use of digital means may improve the process of obtaining the required consent, including by enabling it to be more efficient and more accurate. It may even improve the accessibility of certain population groups to participate in clinical trials. At the same time, it may exclude other population groups. Hence, it is important to ensure and maintain the accessibility of all relevant population groups when using such digital means. At the very least, it should still be possible for the participant to give the required consent using traditional means.

The decision on whether to use digital means as part of the process for obtaining the required informed consent should be made when considering the study, as well as by balancing the benefits that may be gained from using such means against the associated risks involved. The greater the risks (given the specific circumstances of the trial), use should be made of such digital means that will fulfil the purpose of the process of obtaining the required consent with a higher degree of certainty. In particular, the following considerations should be taken into account:

- the nature of the study;
- the extent of the medical intervention in the trial;
- the risk to the participants;
- the characteristics of the target population;
- their existing medical condition and accessibility to the proposed digital means; and
- the number of participants and the extent of their accessibility to the location where the trial is to be conducted.

In general, a face to face meeting should be held between the investigator and the participant; however, in appropriate cases, the process of obtaining the informed consent for participation in a clinical trial may be conducted, either wholly or partially, using digital means. It is crucial to confirm that the participant fully understands the details of the trial and is capable and willing to consent to participate in the trial (digital means may be used only in trials intended for adults who are legally competent to consent). The Guideline further specifies possible means for confirming the identity of participants, if their signature on the consent form is indeed obtained using digital means. The use of digital means must comply with all privacy and data protection requirements as required by law. In addition, use of such means must be approved by the IRB as part of its overall approval of the clinical trial.

2.5 Use of Resulting Data from the Clinical Trials

Any identifiable information relating to one's health is considered sensitive information.

According to the informed consent form template (the use of which is mandatory; the IRB may nonetheless approve certain deviations and exclusions), consent to participate in a clinical trial also constitutes consent to the transfer of personal and medical information to a third party for the purpose of processing the data. The information will be transferred in coded form.

Participants may also consent to additional uses of their data or samples, eg, for future trials, but such consent is not mandatory.

The IRB may approve additional uses of de-identified data (eg, for additional analyses or

future studies) without the need for separate consent from participants.

2.6 Databases Containing Personal or Sensitive Data

The Israeli Privacy Protection Law, 1981 and regulations enacted under it set out the general requirements relating to the creation and maintenance of databases.

Among others, a database containing sensitive data (eg, health-related data):

- must be registered with the Databases Registrar;
- the information in the database may only be used for the registration purposes and in accordance with the consent of the data subject; and
- data subjects may inspect their information and request its deletion or amendment if it is inaccurate (subject to certain exceptions).

The Protection of Privacy Regulations (Data Protection), 2017 specify additional requirements relating to data protection responsibilities and means. Restrictions on the transfer of data abroad are detailed in the Protection of Privacy Regulations (Transfer of Data to Databases Abroad), 2001.

3. MARKETING AUTHORISATIONS FOR PHARMACEUTICAL OR MEDICAL DEVICES

3.1 Product Classification: Pharmaceutical or Medical Devices

Generally, the distinction between preparations, medical devices and other products (eg, biological preparations and food supplements) is made based on their respective definitions, as outlined in the applicable legislation. It should nonetheless be noted that the term "medical device" excludes any product defined as a "pharmaceutical" in the Ordinance.

In the case of combination products, MOH Guideline 47 provides that the classification between pharmaceuticals and medical devices would be based, first and foremost, on the relevant product's primary mode of action.

The classification should also correlate with the product's classification in the "recognised country" from which the product was imported.

Medical products that are manufactured in Israel, will be classified based on similar registered products, or in in the same fashion as similar products are registered in a "recognised country".

If a product is registered in more than one "recognised country", including the United States, the preference will generally be to adopt the classification of the FDA (the US Food and Drug Administration).

3.2 Granting a Marketing Authorisation for Biologic Medicinal Products

No specific obligations need to be fulfilled in order to procure the registration (which is equivalent to obtaining marketing authorisation) of biological medicinal products. However, the registration of biosimilars requires the presentment of additional experimental data when compared to "regular" generic products (including in vitro, clinical and non-clinical data). Proving their similarity to the reference preparations. Furthermore, biosimilars and their reference preparations are not interchangeable, unless decided otherwise at the time of registration. Following registration, the interchangeability will be reviewed periodically and at the registration holder's request, ad hoc, by an advisory committee to the MOH.

3.3 Period of Validity for Marketing Authorisation for Pharmaceutical or Medical Devices

Pharmaceuticals

The initial registration certificate (equivalent to marketing authorisation) for pharmaceuticals is valid for five years. Following renewal, the registration will generally be valid for ten years. Registration certificates are renewed by submitting appropriate requests for their renewal.

Medical Devices

The registration certificate (and subsequent renewals, if any) for medical devices, is valid for a period of up to five years, save for implants, whose registration is valid for up to two years only. A medical device that is registered based on a prior registration in a "recognised country" is granted authorisation until the expiration of the corresponding authorisation in the recognised country, but no more than five years. The registration certificate is automatically extended for an additional two years, provided a request for renewal is submitted to the MOH while the registration certificate for the applicable medical device is still valid.

The MOH is authorised to revoke suspend, or withdraw the registration certificate (for both pharmaceuticals and medical devices), where the conditions or facts upon which the granted authorisation was based, have changed (mainly in the context of the relevant product's safety, efficacy and quality).

According to the Medical Device Law, if a device is found to no longer be in compliant with its registration conditions or any of the restrictions prescribed by the MOH, or its registration in a recognised country has been revoked, or the MOH suspects that it may harm public health, the MOH has the authority to impose administrative sanctions, including order for the discontinuation of, or restriction on, the manufacture or marketing of a device, or deletion of its registration, or restriction on its advertisement and initiate a product recall.

In general, a registration certificate will not be revoked for failure to place the pharmaceutical on the market within a prescribed period. However, the MOH may require that the registration holder undertake to ensure and provide a sufficient and continuous supply of the product as a condition for granting the relevant registration certificate.

The Minister of Health has the authority to appoint inspectors to supervise the proper implementation by registration holders of the provisions of the Medical Device Law.

3.4 Procedure for Obtaining a Marketing Authorisation for Pharmaceutical and Medical Devices

Medicinal Preparations

The application for registration must be submitted to the MOH, according to the guideline related to the registration of medicinal preparations (the "Registration Guideline"), which broadly specifies the data required to be submitted in order to procure registration. Varying an existing registration is governed by Guideline EX-009/04, which lays down specific procedures and conditions for approving quality variations (ie, formulation and process variations), similar to the applicable EU regulations. The registration guideline (REG 08_2012) prescribes the procedure for other variations (such as indication and dosage regime).

Transferring the registration certificate from one registration holder to another is permissible, subject to specific conditions as specified in Guideline 36 (largely a declaration by the manufacturer requesting to so transfer the registration and approving the new registration holder's access to the information included in the

registration file). The former registration holder has the right to oppose such transfer request (although the MOH would not necessarily intervene in the event of a commercial dispute arising between the parties in this context).

Medical Devices

According to a guideline published in 2013, the MOH confirms that, subject to filing an appropriate request, it will be possible to transfer the registration certificate to a new registration holder, subject to obtaining the consent of the current registration holder. Should evidence of such consent not be submitted, a new application for registration would then need to be submitted.

3.5 Access to Pharmaceutical and Medical Devices without Marketing Authorisations

Medicinal Preparations

Generally, pharmaceuticals may be marketed in Israel only if they are duly listed in the [Israeli Drug Registry (the "Drug Registry"), maintained by the MOH. Nonetheless, the MOH has the authority, under corresponding regulations and guidelines, to approve the marketing of a preparation even if it is not registered, or not in accordance with its registration conditions, provided that the preparation falls within the ambit of the specific exemptions as detailed in a notice published by the MOH Director, in accordance with the Pharmacists Regulations (Preparations), 1986. These exemptions include, among others, preparations imported by a pharmacy or sick fund for essential lifesaving treatment where no alternative treatment is available in Israel, for off-label use (by physicians only), and "compassionate use".

The exemption may also include the importation of a preparation for the personal use of a specific (ie, named) patient.

Medical Devices

Medical devices may similarly be marketed in Israel only if they are duly listed in the Medical Devices Registry, maintained by the MOH. The MOH has the authority to approve the manufacturing and marketing of medical devices that are unregistered or not in accordance with their registration conditions, among others, for "essential medical treatment", R&D activities, or exportation purposes. To date, no specific guidelines implementing exemptions of this nature have been published.

3.6 Marketing Authorisations for Pharmaceutical and Medical Devices: Ongoing Obligations

Medicinal Preparations

The MOH imposes pharmacovigilance (PV) and technovigilance (TV) duties as specified in the Pharmacists' Regulations (Preparations), 1986 (the "Pharmacists' Regulations") and, particularly, in Guideline 6 titled "Reporting Adverse Events and New Safety Information", that was issued by virtue of those regulations. Within the ambit of those duties, the registration holder is also required to establish and maintain a PV system and to appoint a qualified person for the purpose of fulfilment of the PV duties. In general, the level of the PV requirements imposed in Israel is similar to that currently prevailing in the EU.

Furthermore, the manufacturer or importer must maintain an independent quality assurance (QA) department. QA is required, among others, to deal with batch release stability tests and complaints concerning the quality of the preparation as well as to investigate recalls from the market.

The MOH has a general authority to request additional information from the registration holder, especially post-marketing. However, as Israel has adopted a 'second-line' country policy (ie, registration as granted by a recognised country, would be a condition for registration

and marketing in Israel). Therefore, given that no formal procedure exists regarding the MOH's authority to impose conducting Phase IV clinical trials, Israel relies on the positions adopted in recognised countries when decisions are taken to avoid conducting them.

In addition, the registration holder is required to inform the MOH of any relevant change to the registration conditions. The manufacturer may not make material changes unless approved in advance by the MOH.

Medical Devices

Currently, no formal PV/TV obligations are imposed on the registration holder of a medical device. In any event it is expected that upon enactment of the required regulations under the Medical Device Law, all necessary obligations will be duly addressed and incorporated.

3.7 Third-Party Access to Pending Applications for Marketing Authorisations for Pharmaceutical and Medical Devices

The entire registration process covering pharmaceuticals and medical devices is confidential. However, with regard to pharmaceuticals, in 2016 the MOH began to publish a list of all APIs for which registration had been sought together with their Anatomical Therapeutic Chemical classification. Nonetheless, it seems that such list was last updated in May 2018.

3.8 Rules against Illegal Medicines and/or Medical Devices

Medicinal Preparations

The Ordinance imposes punitive measures, in the form of imprisonment or a fine, based on the type and nature of the offence.

The most severe form of punitive measures amount to three years' imprisonment or a fine of NIS 226,000 for manufacturing, marketing and possessing a preparation (or a raw material) that is contrary to the registration requirements, and which may consequently mislead customers with regard to an "essential detail" of the preparation. In this context, an "essential detail" is restricted to the preparation's name, dosage form, labelling, indication, its classification as a preparation, composition, strength, batch number, expiry date, origin and marketing or release documentation.

The Ordinance also allows for the imposition of monetary administrative sanctions, which are likewise subject to the severity of the relevant breach.

Further, the Ordinance empowers the MOH to appoint inspectors, who will have the authority, among others, to demand information or documents, enter a place where there exists a reasonable basis to assume that supervised preparations are being manufactured, stored or marketed and take measurements or obtain samples of preparations. These authorities are enforced by the Department for Fighting Pharmaceutical Crime, which forms part of the Division of Enforcement and Inspection within the MOH.

Medical Devices

Breach of the following provisions of the Medical Device Law would be considered a criminal offence:

- manufacturing or marketing unregistered devices, not for personal use or not in accordance with their registration conditions;
- instructing the use of, or using, unregistered devices; and
- instructing the use of, or using, devices not in accordance with the MOH's explicit instructions or restrictions.

Upon the commission of any such offence (and subject to the proper entry into effect of the Medical Device Law), the court will have the authority to impose criminal sanctions, including imprisonment and fines. In the case the offence is committed by a company, the amount of the stated fine to be imposed will be double.

3.9 Border Measures to Tackle Counterfeit Pharmaceutical and Medical Devices

The Israeli Customs Administration ("Customs") is authorised, by law to seize counterfeit/infringing goods detected during regular Customs' inspections of goods at the gates, or following a complaint filed by the rights holder of the relevant intellectual property (IP) right or other interests.

4. MANUFACTURING OF PHARMACEUTICAL AND MEDICAL DEVICES

4.1 Requirement for Authorisation for Manufacturing Plants of Pharmaceutical and Medical Devices

Medicinal Preparations

According to the Pharmacists' Regulations (Good Manufacturing Practices), 2008 (the "GMP Regulations"), the manufacturing site of pharmaceuticals must be issued a Good Manufacturing Practice (GMP) certificate. The Institute for Standardisation and Control of Pharmaceuticals (a department of the Pharmaceuticals Division within the MOH) carries out an inspection of the manufacturing site prior to issuing the certificate. For sites located outside Israel, the MOH recognises the GMP certificate issued by the competent authorities of recognised countries. The MOH also carries out periodic inspections to confirm the manufacturer's compliance with the applicable GMP regulations (which are largely based on the European Medicines Agency (EMA) GMP standards). The GMP certificate is valid for five years.

Manufacturers of pharmaceuticals must also possess a valid business licence to operate as such pursuant to the Licensing of Businesses Law, 1968.

Medical Devices

According to the Medical Device Regulations (which, as already noted by us, have yet to enter into effect), the registration of medical devices is subject to demonstrating that the relevant manufacturing site possesses a certificate issued by a health authority (or other competent regulatory body indicating that the manufacturing practices comply with Israel Standard ISO 13485 ("ISO 13485")) as well as a valid business licence.

5. DISTRIBUTION OF PHARMACEUTICAL AND MEDICAL DEVICES

5.1 Wholesale of Pharmaceutical and Medical Devices

The MOH grants authorisation to establishments engaged in the wholesale of pharmaceuticals only. The authorisation is granted by the Pharmacy Division, subject to compliance with Good Distribution Practice (GDP) requirements as specified in MOH Guideline 130.

Activities approved under the authorisation include distribution at the wholesale level only. Retail marketing may only be carried out by a qualified pharmacist in a pharmacy.

The authorisation is valid for up to three years, based on the level of compliance of the warehouse with the requirements stipulated in Guideline 130. In special circumstances, the authorisation will be valid for up to five years.

5.2 Different Classifications Applicable to Pharmaceuticals

See **1.3 Different Categories of Pharmaecuticals and Medical Devices**.

6. IMPORTATION AND EXPORTATION OF PHARMACEUTICALS AND MEDICAL DEVICES

6.1 Governing Law for the Importation and Exportation of Pharmaceutical Devices and Relevant Enforcement Bodies

Medicinal Preparations

The following legislation and guidelines govern the importation and exportation of pharmaceuticals: the Pharmacists' Regulations; the GMP Regulations; the Registration Guideline; MOH Guideline 33 titled "Importation and Marketing of Medicinal Preparations and Pharmaceutical Materials"; MOH Circular 19/07; and the Free Import Order.

Medical Devices

The relevant pieces of legislation are the Medical Device Law and the Free Import Order.

The regulatory bodies having responsibility for applying and enforcing the import regulations covering both pharmaceuticals and medical devices are the MOH and the Customs authorities.

6.2 Importer of Record of Pharmaceutical and Medical Devices

This is not applicable in Israel.

6.3 Prior Authorisations for the Importation of Pharmaceuticals and Medical Devices

Pharmaceuticals

Under the Pharmacists Ordinance, the term "marketing" is broadly defined to include "importing". The following requirements need to be satisfied in order to obtain the requisite MOH approval for importing a preparation into Israel:

- a certificate of pharmaceutical product (CPP) indicating the approval and marketing of the preparation in a recognised country;
- importation may only be performed by a pharmaceutical company, a wholesale pharmaceutical business or a storage facility of a health institute;
- an application for an import certificate may be filed only by a qualified pharmacist appointed by the applicant and approved by the MOH; and
- the preparation must be registered in the Drug Registry, or otherwise should fall within the specified exemptions applicable to preparations that may be manufactured, marketed and used, even if unregistered, or not in accordance with their registration conditions.

The MOH will not issue an import certificate, unless the following conditions are met:

- the preparation was transported into Israel by authorised dealers in recognised countries; and
- en route to Israel, the preparation was stored only in recognised countries.

Specific exemptions to the above conditions may be applied for organ donation purposes, emergency situations, and personal use (see **3.5 Access to Pharmaceutical and Medical Devices without Marketing Authorisations**).

Medical Devices

Similarly, the term "marketing" in the Medical Device Law is defined broadly to include the "importation" of medical devices. Therefore, the principal requirements applicable to the importation of medicinal preparations equally apply to medical devices.

The registration holder is required to identify the importer in the registration application, and the MOH will include the importer's details in the registration certificate, on which basis the importer can then apply for an import permit.

Marketing an imported medical device requires a certificate from the health authority or any other regulatory body of the country in which the device was manufactured, certifying that the manufacturer's GMP standards satisfy the requirements of ISO 13485. Furthermore, carriers of devices must possess a certificate from an entity recognised by the MOH, certifying that their storage and transportation conditions meet the requirements of Israel Standard ISO 9001.

6.4 Non-tariff Regulations and Restrictions Imposed upon Importation

The Free Import Order, 2014 (the "Free Import Order") sets the requirements for certain products upon their release from Customs. The Customs Tariff Order provides the Harmonized Tariff Schedule codes. The importer is responsible for classifying the imported goods in accordance with such schedule.

6.5 Trade Blocs and Free Trade Agreements

Israel is a party to free trade agreements with various countries, such as the United States, the EU, Bulgaria, Canada, the Czech Republic, Hungary, Mexico, Poland, and Romania. These free trade agreements have resulted in increasing trade between the contracting parties, as well as the prevention of trade barriers.

In addition, in October 2012, an ACAA agreement (Agreements on Conformity Assessment and Acceptance of industrial products), between Israel and the EU was ratified. The agreement recognises the Israeli industrial standards as being equivalent to those prevailing in the EU. The agreement comprises an Annex pertaining to the mutual recognition of GMP inspections and the corresponding certificates.

7. PHARMACEUTICAL AND MEDICAL DEVICE PRICING AND REIMBURSEMENT

7.1 Price Control for Pharmaceuticals and Medical Devices

The Supervision of Prices of Commodities and Services Law, 1996 authorises the Ministers of Health and Finance to regulate the prices of services and products by issuing an order to such effect. It should nonetheless be noted that there is no supervision over the profits generated by establishments engaged in the wholesale of pharmaceuticals and pharmacies, nor has any procedure been adopted regarding the supervision of medical devices.

The Order for the Supervision of Prices of Commodities and Services (Application of Law on Preparations), 2001 specifies three means of price regulation that are applied with regard to goods comprising preparations:

- price-fixing by the regulator with regard to prescription preparations – by referencing the prices of several European countries;
- for any price increase above the fixed price with regard to OTC preparations – specific approval will need to be sought in advance; and
- with regard to GSL preparations – the duty to report of prices and profits.

7.2 Price Levels of Pharmaceutical or Medical Devices

See **7.1 Price Control for Pharmaceuticals and Medical Devices**.

7.3 Pharmaceuticals and Medical Devices: Reimbursement from Public Funds

The National Health Insurance Law, 1994 provides for the inclusion of a "healthcare basket" that encompasses the full range healthcare services, pharmaceuticals, medical equipment and devices which sick fund members are entitled to receive (without consideration or subject to a defined co-payment). The "health basket" is updated on a yearly basis. In order to update the healthcare basket, the Public Committee for Expansion of the Health Services Basket (the "Healthcare Basket Committee") submits recommendations to the National Health Insurance Council proposing what changes or additions should be considered included in, or excluded from, the healthcare basket for the coming year. Following approval of the Minister of Health and the consent of the Minister of Finance, the recommendations must then be forwarded to the government for its final approval.

7.4 Cost-Benefit Analyses for Pharmaceuticals and Medical Devices

As part of the process of crystallising its recommendations, the Healthcare Basket Committee (see **7.3 Pharmaceuticals and Medical Devices: Reimbursement from Public Funds**) must assess, classify and grade the pharmaceuticals, medical devices and available technologies, taking into account a list of varying factors, in order to determine the healthcare basket composition. Among these factors, the Healthcare Basket Committee will take into consideration:

- the efficiency of the technology;
- whether the technology is "life saving";
- the existence of therapeutic alternatives and their efficiency;
- financial costs; and
- the anticipated benefit of including the technology in the healthcare basket.

7.5 Regulation of Prescriptions and Dispensing by Pharmacies

See **1.3 Different Categories of Pharmaceuticals and Medical Devices**. In addition, the Pharmacists' Ordinance caters for the possibility of pharmacists being able to dispense pharmaceuticals without a physicians' prescription in situations deemed immediate and urgent.

8. DIGITAL HEALTHCARE

8.1 Rules for Medical Apps

There is no specific regulation with respect to medical applications. However, the definition of "medical device" under the Medical Device Law includes, among others, a device used for medical treatment, as well as a device or computer program required to operate such device ("medical treatment", however, includes diagnosis and prevention of disease).

Thus, a mobile or web application may be considered a medical device when required to operate a medical device.

8.2 Rules for Telemedicine

The provision of digital health services is currently not regulated by law. However, the MOH has published several circulars that specifically address certain areas of digital health and telemedicine.

MOH Circular, titled "Criteria for Operating Telemedicine Services" ("Circular 6/2019"), sets out the principles relating to the provision of telemedicine services. According to Circular 6/2019, the provision of telemedicine services

need not be approved by the MOH. Instead, it is for the management of the sick fund or medical institution operating the telemedicine services to prescribe conditions facilitating their operation, provided that it shall have determined that the quality and safety of the telemedicine services align with those provided in face-to-face consultations with patients. Circular 6/2019 clarifies that telemedicine services are not intended to replace the corresponding face-to-face consultations, and it is thus recommended that both types of consultation services are available for patients to choose at their discretion. Additional rules and guidance are set out in Circular 6/2019.

In addition, MOH Circular 8/19 titled "Access of Personal Health Data for the Patient", contains rules and guidance for broadening the medical data that is available to patients online through the electronic medical records and files maintained on their behalf by the applicable sick funds.

8.3 Promoting and/or Advertising on an Online Platform

The main piece of legislation governing the advertising of medicinal products is the Pharmacists' Regulations. In addition, the MOH publishes guidelines and circulars implementing the criteria adopted in the Pharmacists' Regulations.

The term "advertising" is defined in the Pharmacists Regulations as an act aimed at disseminating information in writing, through the media or by any other means. As a general rule, advertising a preparation cannot contradict its registration, nor can advertising material attribute indications that are not expressly approved as required.

Advertisements aimed at healthcare professionals for prescription and non-prescription preparations are permitted, provided they emphasise the approved indications. Online advertising for healthcare professionals is permitted, subject to certain limitations, such as applying mandatory means to identify users prior to them gaining access to the relevant information.

By contrast, the advertising of prescription preparations directed at the general public is prohibited. Certain non-commercial information, intended for improving the educated use of and compliance with medicinal preparations may be provided to patients prescribed with such preparations, in accordance with MOH Guideline 137. In any event, the information cannot include advertising content or encourage the consumption of preparations.

The advertisement of OTC preparations or GSL to the general public is permitted, subject to the prior approval of the MOH. Such advertising must be accurate, clear and consistent with the registered indications. MOH guidelines specify mandatory data that must be included in such advertising, as well as data that must be excluded.

Advertising of Medical Devices

The MOH is authorised to supervise the advertising of medical devices but, currently, no specific regulation to this effect has been proposed or drafted.

8.4 Electronic Prescriptions

Electronic prescriptions were introduced in Israel as early as 2010, which consequently led to an amendment in legislation permitting physicians to sign prescriptions electronically.

8.5 Online Sales of Medicines and Medical Devices

MOH Guideline 128 allows, subject to certain conditions, the online retail dispensing of medicinal preparations (including prescription preparations).

The online sale of medical devices is not covered by current regulation and guidelines.

8.6 Electronic Health Records

Healthcare providers are obliged to maintain confidential any and all medical records and information relating to a patient coming to their knowledge during the course of the fulfilment of their duties or as part of their ongoing work, and must take all required measures to ensure that their employees similarly maintain the confidentiality of all such records and information. Medical records may contain data classified as sensitive, and information included there may only be used for the express purpose for which they were collected and stored, and cannot be transferred to third parties, unless the consent of the patient was obtained or if otherwise permitted by law.

The Protection of Privacy Law, 1981, and its regulations contain general provisions relating to the ownership, management and holding of databases, as well as data protection, which may also be relevant to healthcare providers (eg, a database owner will be obliged to register same with the Registrar of Databases).

The MOH has issued several circulars and guidelines covering certain aspects of data protection and privacy. Among others, MOH Circular 3/15 titled "Data Protection in Computerised Systems", sets out the principles and standards for the protection of data stored on the computerised health system; MOH Circular 2/2021, titled "Use of Cloud Computing in the Israeli Healthcare System", establishes the criteria for the proper operation of computerised applications using cloud computing by healthcare organisations, in order to encourage the introduction of advanced technologies for use by healthcare organisations.

9. PATENTS RELATING TO PHARMACEUTICALS AND MEDICAL DEVICES

9.1 Laws Applicable to Patents for Pharmaceutical and Medical Devices

In Israel, patents are governed by statute, namely, the Patents Law, 1967 (the "Patents Law"), as well as Secondary legislation enacted in the form of the Patents Regulations (Authority Practice, Rules of Procedure, Documents and Fees), 1968.

The Manual of Patent Examining Procedure, published by the Israeli Patent Office (the "Israeli MPEP"), provides working guidelines for patent examiners. In a nutshell, the Israeli MPEP provides guidance with respect to the examination and prosecution of patent applications and the implementation of pertinent legislation and case law in this regard. From a normative point of view, the Israeli MPEP is considered an administrative guideline.

According to Section 3 of the Patents Law, in order to be eligible for patent protection, an invention must be a product or process in any technological field which is new, non-obvious and susceptible to industrial use; and must satisfy the utility requirement.

In general, patent protection is available for both products and processes in the pharmaceutical field. However, according to Section 7 of the Patents Law, methods for therapeutic treatment of the human body (which are considered processes) are not considered patentable subject matter.

Issues most commonly encountered by pharmaceuticals and medical devices under the Patents Law are novelty, obviousness and utility. As Israel employs a pre-grant opposition system, any person can oppose a patent application,

provided that the opposition is filed within three months from the date of publication of acceptance of the patent application. Where an opposition has been timely filed, the sought patent will be granted only if the opposition is finally rejected. Patent revocation proceedings are also available.

9.2 Second and Subsequent Medical Uses

From a legal perspective, second medical use claims relate to a product or a process which are not deemed novel, but whose novelty resides in the new use itself. Hence, the claims of a patent protecting second medical use must be carefully phrased.

Specifically, the claims may be phrased as purpose-limited product claims.

Swiss-type claims which do not demonstrate novelty and inventive step to perform the claimed process, will not be allowed.

A dosage regimen may be presented as a technical feature in a product claim. Such claim will not be classified as a "method for treating the human body", since it would be considered as mere guidance for the manufacturer without intending to limit the discretion of treating physicians. Like any other invention, a [new] dosage regimen must satisfy the requirements for subject matter eligibility, otherwise the patent will be disallowed.

The Israeli MPEP (Appendix F, Section 6.11), refers to claims for a known medicinal composition, indicated for use by a specific target population. When considering cases of this nature, there will need to be examined whether:

- the composition concerning the claimed indication is known;
- one of the compounds (or a relative portion of them) in the composition is different;
- there is a difference in the claimed dosage regimen or method of administration; and
- the target group defined in the claim was explicitly described (in whole or in part) in the prior art.

The presentation or, as applicable, demonstration of an unexpected effect, such as increased effectiveness in the target group, will not suffice to satisfy the novelty requirement. However, the invention may be considered novel if the mere possibility of treating the target group is unexpected.

The scope of protection of a patent is determined in Section 49 of the Patents Law which provides, among others, that a patentee may exclude others from unlawfully exploiting the invention, subject matter of the patent. The term "use" is included within the framework of the definition "exploitation of an invention", which expression is defined in the Patents Law as follows:

"(1) In respect of an invention that is a product – any act that comprises one of the following: manufacture, use, offer for sale, sale or import for purposes of one of the enumerated acts;

(2) In respect of an invention that is a process – use of the process, and in respect of a product directly derived from the process – any act that is one of the following: manufacture, use, offer for sale, sale, or import for purposes of one of the enumerated acts;

but excluding any of the following:

(1) any act which is not on a commercial scale and does not have a commercial character;

(2) any experimental act in connection with the invention, the objective of which is to improve the invention or to develop another invention;

(3) any act performed under the provisions of Section 54A."

The definition does not include exportation. However, in one case, the Jerusalem District Court expressed the opinion that commercial activity resulting in export may fall within the ambit of such definition, provided that the intended activity is of a commercial scale or nature.

The doctrines of equivalents and variants have both been adopted by the Supreme Court and are generally applicable. No specific case law applies the doctrine of equivalents or variants in relation to second medical use claims.

Second medical use claims may be enforceable on the basis of indirect infringement. However, the question surrounding the indirect infringement of second medical indication patents has yet to be addressed by the Israeli courts.

9.3 Patent Term Extension for Pharmaceuticals

Patent term extension (PTE) is available in Israel, in certain circumstances, for a pharmaceutical product protected by a basic patent. The patentee can select the basic patent to be extended. In general, a basic patent is a patent protecting an active pharmaceutical ingredient (API), a process for manufacturing an API, its use or a pharmaceutical product containing an API, or medical device for which regulatory approval is required in Israel. PTE is available only for the first regulatory approval allowing the use of an active ingredient in a pharmaceutical product in Israel.

In general, the Patents Law provides that subject to the following, the PTE order shall remain valid for a period equal to the shortest extension afforded to the reference patent in a "recognised country" (which term is defined in the Patents Law to mean Italy, the UK, Germany, Spain, France and the US). Nonetheless, the term of the PTE order cannot exceed five years beyond the 20-year period of patent protection granted to the basic patent. In addition, the overall period of the basic patent and related PTE order (if any) shall terminate no later than fourteen years from the date marketing authorisation was first received in a recognised country. Moreover, the PTE order shall expire no later than the first date of expiry of the extension period granted to the reference patent in a recognised country, in which marketing authorisation was obtained, or the revocation of any reference patent.

A PTE application may be challenged or grant of the PTE order can be revoked, regardless of the existence of the basic patent. Where an opposition has been timely filed, PTE will be granted only if the opposition is finally rejected.

9.4 Pharmaceutical or Medical Device Patent Infringement

The scope of protection afforded to a patent (including covering a pharmaceutical or a medical device) is explained in **9.2 Second and Subsequent Medical Uses**.

Applying for marketing authorisation would not amount to patent infringement. The threat of infringement, as opposed to actual infringement, is not actionable.

9.5 Defences to Patent Infringement in Relation to Pharmaceuticals and Medical Devices

The Patents Law provides a broad "Bolar-type" exemption that allows for experimental testing in order to obtain marketing authorisation for a product following expiry of the basic patent. The "Bolar-type" exemption covers, among oth-

ers, research for the purposes of obtaining marketing authorisation in Israel as well as in any other country, in which an experimental act on a patent-protected invention for the purpose of obtaining a licence is permitted before the patent expires.

In addition, any experimental act in connection with an invention aimed at improving the invention or developing another invention, is excluded from the definition of "exploitation of an invention".

If the Registrar of Patents is convinced that a patentee is abusing his or her monopoly, he or she may grant a compulsory licence to exploit the patented invention to a person seeking to use the patented invention, provided that the application is filed following the expiry of three years from the date of grant of the patent, or four years from the date of filing the patent application, whichever is the later. The licence will be granted mainly to satisfy the needs of the domestic market and subject to royalties as the Registrar of Patents shall determine.

9.6 Proceedings for Patent Infringement

Infringement proceedings may be initiated by the patentee or an exclusive licensee, and are conducted before the relevant district court.

Final remedies for infringement include injunctions, damages (including an account of profits), delivery up of infringing material, as well as declaratory judgments, prohibitive orders, orders for specific performance or any other relief, as the court deems fit.

9.7 Procedures Available to a Generic Entrant

A third party (potential generic entrant) may apply to the court seeking a declaratory order that their exploitation of the invention does not amount to infringement of the specific patent. The proceedings are conducted before the district court under the assumption that the patent is valid.

Clearing the way is not a requirement for generic market entry.

Patent linkage does not apply in Israel for the marketing authorisation process.

10. IP OTHER THAN PATENTS

10.1 Counterfeit Pharmaceuticals and Medical Devices

Pharmaceuticals

In addition to general IP law which makes provision for various causes of action that may be relied upon for the enforcement of counterfeit pharmaceuticals, the Ordinance underwent an extensive amendment in 2016 in order to introduce punitive sanctions against the phenomenon of pharmaceutical crime and, particularly, the counterfeiting, theft and use of defective preparations. In addition, a specific provision was incorporated to define activities that may amount to consumers being misled within the context of the Ordinance (which may also serve as a basis for civil and criminal liability). As a consequence of the amendment, the Ordinance now also includes not only a comprehensive punitive chapter, but also additional chapters dealing with the imposition of administrative sanctions and the regulation of supervisory authorities.

Medical Devices

The Medical Devices Law also provides punitive sanctions against various violations of its provisions. However, as the Medical Devices Law has yet to enter into force, no such punitive sanctions can be applied and enforced in practice.

Accordingly, as an administrative tool, the Investigative Committee on Misleading Advertising is authorised to enforce and regulate misleading advertisements of healthcare products, including medical devices (and pharmaceuticals). Said authority can be applied also with respect to counterfeit products.

In addition, the Department for Fighting Crime in the Field of Medical Devices, which forms part of the Division of Enforcement and Inspection within the MOH, acts in order to reduce crime associated with medical devices. For example, the Department:

- investigates the suspected counterfeiting of medical devices;
- prevents the entrance of medical devices into Israel in co-operation with the Customs authorities; and
- locates and investigates healthcare providers who use medical devices absent the proper authorisation or use counterfeit devices.

10.2 Restrictions on Trade Marks Used for Pharmaceuticals and Medical Devices

See **10.3 IP Protection for Trade Dress or Design of Pharmaceuticals and Medical Devices**.

In addition, neither the Trade Marks Ordinance (New Version), 1972 (the "Trade Marks Ordinance") nor its corresponding regulations include specific restrictions regarding the parallel import of pharmaceuticals or medical devices.

10.3 IP Protection for Trade Dress or Design of Pharmaceuticals and Medical Devices

Trade dress or design of pharmaceuticals and medical devices in so far as concerning the visual appearance of the product, its packaging and marketing, are protected by a broad array of IP legislation, such as the Trade Marks Ordinance, the Designs Law, 2017, the tort of passing off by virtue of the Commercial Torts Law, 1999 and the Unjust Enrichment Law, 1979.

Unregistered trade marks can also be protected, in appropriate and rare circumstances, under the doctrine of unjust enrichment or the tort of passing off. Well-known unregistered marks are also protected under the Trade Marks Ordinance in connection with goods for which the trademark is well-known or for goods of the same description.

10.4 Data Exclusivity for Pharmaceuticals and Medical Devices

The Ordinance provides, under certain circumstances, protection to confidential data submitted as part of a marketing authorisation application, provided that its creation entailed considerable effort. New chemical entities (NCEs) registered in Israel are therefore entitled to a period of market exclusivity, during which the MOH will not issue marketing authorisation for a new medicinal product containing said NCE. The market exclusivity period will be capped by the earlier of the following:

- six years from the date of registration in Israel of the medicinal product containing the relevant NCE; or
- six years and six months from the date of registration in a recognised country of the medicinal product containing the relevant NCE.

The Ordinance in its current form makes no reference to biologics. The Israeli government is nonetheless currently assessing and considering the feasibility of amending the Ordinance so as to include the possible grant of exclusivity with respect to data filed in order to obtain regulatory approval for marketing biologics.

11. COVID-19 AND LIFE SCIENCES

11.1 Special Regulation for Commercialisation or Distribution of Medicines and Medical Devices

As part of its emergency powers, the MOH implemented an array of temporary relaxations in relation to the commercialisation or distribution of medicines and medical devices.

In addition, the MOH expedited the approval process for COVID-19 vaccines, medications for treatment of the COVID-19 (eg, Paxlovid and Lagevrio) and for conducting rapid antigen tests.

The MOH also issued a temporary order allowing private pharmacies to dispense medications based on a copy of the prescription received by them either by e-mail or facsimile.

11.2 Special Measures Relating to Clinical Trials

In March 2020, the MOH published several notices setting out adjustments relating to the conduct of clinical trials during the widespread period of COVID-19. These included, eg, the electronic filing of an application to conduct a clinical trial (ie, without requiring a hard copy), home delivery of the investigational product and performing tests at the participant's home (where applicable) and instructions relating to protocol changes and deviations that became necessary due to the widespread and prevailing pandemic. Most of the provisions in the notices were extended to June and December 2020 and were subsequently cancelled during 2021. Home delivery of the investigational product is nonetheless still possible where required and subject to approval of the IRB.

Interventional clinical trials relating to COVID-19 generally require the approval of the MOH (save for clinical trials involving vitamins and nutritional supplements). The progress of those trials should be reported to the MOH.

11.3 Emergency Approvals of Pharmaceuticals and Medical Devices

See **11.1 Special Regulation for Commercialisation or Distribution of Medicines and Medical Devices**.

11.4 Flexibility in Manufacturing Certification as a Result of COVID-19

There is no standalone flexibility or simplification for obtaining certifications in light of COVID-19.

11.5 Import/Export Restrictions or Flexibilities as a Result of COVID-19

See **11.1 Special Regulation for Commercialisation or Distribution of Medicines and Medical Devices**.

11.6 Drivers for Digital Health Innovation Due to COVID-19

In practice, COVID-19 led to both the MOH and healthcare professionals being encouraged to use telemedicine services.

11.7 Compulsory Licensing of IP Rights for COVID-19-Related Treatments

The Minister of Health unprecedentedly exercised his power under the Patents Law (as amended) and approved the exploitation of three Israeli patents assigned to AbbVie, stated as covering its antiretroviral medication KALETRA® (lopinavir/ritonavir), indicated for the treatment of HIV.

This unusual approval was understood to have been granted in light of the potential efficacy of the medication for treatment of COVID-19, in circumstances where AbbVie was unable to meet the exponential demands of Israel's public health system for an urgent and immediate supply of large quantities of the medication.

The approval granted by the MOH was confined to the importation into Israel of a generic version of KALETRA from a specific supplier, for the sole purpose of treating patients infected with COVID-19.

11.8 Liability Exemptions for COVID-19 Treatments or Vaccines

No liability exemptions were introduced in existing or new provisions regarding COVID-19 vaccines or treatments.

11.9 Requisition or Conversion of Manufacturing Sites

There are no existing or new provisions regarding the requisition or conversion of manufacturing sites due to COVID-19.

11.10 Changes to the System of Public Procurement of Medicines and Medical Devices

There was no change to the system of public procurement in light of COVID-19.

S. Horowitz & Co has long been recognised as one of Israel's premier law firms. By adhering to its commitment to provide services of the highest professional standards, the firm has sought to maintain its ingrained tradition throughout its 100-year history, while adapting its needs to take into account 21st-century advanced technologies and developments, all of which have enhanced its reputation and rich experience. The firm's clientele includes reputable and well-established Israeli and international companies, operating in a wide array of fields and industries, including energy, banking and finance, communications and media, aviation, real estate and infrastructure, and consumer products, local authorities and more. The firm has specific and deep expertise in working with clients in the healthcare and life sciences industries. The firm employs more than 200 lawyers and interns, of whom 70 are partners. S. Horowitz & Co is the only Israeli member of Lex Mundi, the leading global network of independent law firms.

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