Chapter 17

MALTA

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I INTRODUCTION

Malta has the second largest pharmaceutical trade balance per capita in the European Union (€614 million in 2016), the tenth in total, and was the EU's fastest growing pharmaceutical exporter between 2001 and 2016 with an unprecedented increase of 45 per cent.[2] More than 30 established international pharmaceutical brand names operate in Malta, including several US mega-cap corporations. In 2019, the Managing Director of Aurobindo Pharma (Malta) Limited, Frederick Schembri, announced the company will invest in oncology research and set up a highly specialised new oncology laboratory in Malta to test oncology medicines destined for the EU and African markets. Aurobindo Pharma, the tenth-largest generic company by sales globally, has been established in Malta for the past 13 years and now employs 150 people.[3]

Companies must adhere to EU requirements in manufacturing, licensing and distribution of pharmaceuticals, active pharmaceutical ingredients and medical devices, and most companies also receive US Food and Drug Administration accreditation.

This chapter summarises the Maltese laws governing medicines and medical devices. Malta is the European Union's smallest Member State and has implemented the EU medicines and medical devices regimes. We will therefore not repeat the substantive content of the EU chapter, but will only focus on unique, different, and significant features of the Maltese regime. This chapter should be read in conjunction with the EU chapter.

The principal regulatory authority to ensure the quality safety, and efficacy of medicines is the Superintendent of Public Health, which is the Licensing Authority for the purposes of the Medicines Act.[4] The Medicines Authority is a body corporate having a separate and distinct legal personality and its functions are delegated to it by the Licensing Authority. It is responsible for assisting and advising the Licensing Authority on any matter relating to the regulation of medicinal products and related activities, as well as establishing licensing and marketing procedures.

The Medicines Authority is headed by a Chief Executive Officer who must be qualified and experienced in the medical, pharmaceutical or medical science sector and who is appointed

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2 Malta Pharma Exports and Trade Snapshot, Pharma Boardroom, 11 July 2018 (accessible at https://pharmaboardroom.com/facts/malta-pharma-exports-and-trade-snapshot/).

3 Aurobindo Pharma Investor Presentation, November 2019 (accessible at https://www.aurobindo.com/wp-content/uploads/2019/11/Aurobindo-Pharma_Investor-Presentation_November-2019.pdf).

4 The Medicines Act (Chapter 458 of the Laws of Malta), Article 3.

by the Minister responsible for public health. The Chief Executive Officer is responsible for the overall management and performance of the Medicines Authority including the management of its day-to-day operations. The Medicines Authority has established five directorates and appoints its own officers and employees. The terms and conditions of employment are set by the Medicines Authority with the 'concurrence' of the Minister responsible for public health, given after consultation with the Minister responsible for finance.[5] Since at least 2019, the Medicines Authority does not receive a government subsidy as its budget is funded exclusively from 'user fees' imposed on the industries it regulates, mainly the pharmaceutical industry. User fees may include registration fees for marketing authorisation applications, annual licensing fees for manufacturing and wholesale dealing facilities, and marketed medicinal products.

In Malta, to date, medical devices are regulated and authorised by the Malta Competition and Consumer Affairs Authority (MCCAA), although medical devices are planned to be regulated by the Licensing Authority and Medicines Authority instead in the future. This change is dependent on the passing of a bill and legal notice that are under way.

'Medicinal products' are defined and regulated by the Medicines Act (Chapter 458 of the Laws of Malta) and its subsidiary legislation. Medical devices are regulated by the Product Safety Act (Chapter 427 of the Laws of Malta), the Active Implantable Medical Devices Regulations (SL 427.10 of the Laws of Malta), the In Vitro Diagnostic Medical Devices Regulations (SL 427.16 of the Laws of Malta), and the Medical Devices Regulations (SL 427.44 of the Laws of Malta).

The Chamber of Commerce, Enterprise, and Industry based in Valletta represents the pharmaceutical industry in Malta through three sections, namely: the Healthcare Business Section, the Professional Community Lead Pharmacists Business Section, and the Pharmaceutical Manufacturers Business Section. The pharmaceutical manufacturers established their stakeholder group in 2003, before Malta's EU accession, to lobby their interests during the transposition of EU legislation. The pharmaceutical industry has evolved considerably to date as Malta was able to leverage foreign investment, especially with English being an official language, and developed a strong reputation in manufacturing, batch-release to the EU market, day-one product launches, good engineering expertise, and favourable economic growth. The Chamber of Commerce members now include active pharmaceutical ingredient (API) manufacturers, finished dosage form manufacturers, repackaging and labelling companies, wholesale dealers, brokers, and pharmacists.

II THE REGULATORY REGIME

i Classification

The Medicines Authority's Borderline Classification Committee distinguishes between medicinal and non-medicinal products.[6] Assessments are made on a case-by-case basis. The Medicines Authority has issued borderline product classification guidelines and application forms. The guidelines explain the information and materials that must be provided for the

5 The Medicines Act (Chapter 458 of the Laws of Malta), Articles 4–8. Professor Anthony Serracino Inglott has served as Chief Executive Officer of the Medicines Authority since 2013.

6 The Medicines Authority Terms of Reference state that the Borderline Classification Committee is composed of the Licensing Director who chairs the group; a quorum of six members representing the Licensing Directorate, the Inspectorate and Enforcement Directorate and the Advertising Committee; a

classification to be undertaken, including dosage form, container type and packaging.[7] The Borderline Classification Committee takes into account the medicinal claims made; intended use; mode of action; pharmacological properties; and similar authorised medicinal products that are on the market.

Medical devices are classified according to the degree of risk the patient is exposed to. Malta's medical devices regulations establish standards to classify a medical device, centred on the level of invasiveness, mode of action, contact duration and impact on the patient. Active implantable devices are generally classified as high-risk medical devices, and the risk of in vitro diagnostic (IVD) medical devices is decided on the basis of use.

ii Non-clinical studies

The Good Laboratory Practice Regulations (S.L. 427.56) state that non-clinical studies must be carried out in conformity with the good laboratory practice (GLP) established by EC Directive 2004/10. The transposed regulations state that the inspection and verification of processes and conditions under which laboratory studies are planned, performed, recorded and reported for non-clinical testing shall be carried out in accordance with the rules and regulations, with respect to all chemicals (e.g., cosmetics, industrial chemicals, medicinal products, food additives, animal feed additives, pesticides) in order to assess the effect of such products on humans, animals and the environment.[8]

The National Accreditation Body–Malta Standards Authority (NAB-MSA) is the competent authority responsible for verifying compliance with the principles of GLP of any testing laboratory in Malta claiming to use GLP.[9]

The Animal Welfare Act (Chapter 439 of the Laws of Malta) establishes a Council for Animal Welfare comprising a chairperson and 11 members who advise the Minister responsible for veterinary services on all matters related to biotechnology in animals and animal experiments, and advise on the issuance of licences under the Animal Welfare Act. The Council, with the concurrence of the Minister, can also establish subcommittees for this purpose.

A licence issued by the Minister, acting on the advice of the Council, in conjunction with the Director for Veterinary Services is required to carry out animal experiments.[10] The licence specifies the practice for which it is required and may include conditions and restrictions. Animal experiments must be authorised by the Council, may only be performed by competent authorised persons, or under the direct responsibility of such a person, and only if the experimental or other scientific project concerned is authorised in accordance with the provisions of the Animal Welfare Act to protect animal welfare.

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member of the Committee on Herbal Medicinal Products (HMPC) and Homeopathic Medicinal Products Working Party (HMPWP); a physician (when necessary); and a secretary, to take minutes, list actions taken and to manage the administrative duties of the committee.

7 The Medicines Authority has issued guidelines on what constitutes a medicinal product, which appears on the Authority's website at http://www.medicinesauthority.gov.mt/classificationborderlineproducts.

8 Good Laboratory Practice Regulations (S.L. 427.56) Article 5.

9 Good Laboratory Practice Regulations (S.L. 427.56) Article 3.

10 Animal Welfare Act (Chapter 439 of the Laws of Malta) Article 32.

The Good Clinical Practice and Requirements for Manufacturing or Import Authorisation of Investigational Medicinal Products (Human Use) Regulations (S.L. 458.47) state that available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.[11]

iii Clinical trials

Medicines

Legislation

In Malta, clinical trials are governed by the Clinical Trials Regulations (S.L. 458.43), transposing European Directive 2001/20/EC regulating clinical trials on human subjects where such clinical trials involve medicinal products in interventional clinical trials. The Good Clinical Practice and Requirements Regulations (SL 458.47 of the Laws of Malta) supplement the Clinical Trials Regulations and outline good clinical practices to ensure the subject's rights and safety. The Medicines Authority has issued guidance notes on good clinical practice, clinical trial applications and notifications, which were last updated in February 2018.

Application and authorisation

A clinical trial may be carried out if its benefits outweigh foreseeable risks. This is a decision that falls on the Ethics Committee set up by the Licensing Authority. A 'sponsor' – the person taking responsibility for the initiation, management and financing of the clinical trial – must be authorised on the basis of the Ethics Committee's opinion. Approvals are granted for one trial at a time. Requests for clinical trial approval must be decided by the Licensing Authority no later than 60 days from the date of the request.

Insurance policy

Insurance or indemnity to cover the liability of the investigator and sponsor is a requisite to be able to carry out a clinical trial, and the adequateness of the insurance taken out is assessed by the Ethics Committee.

Informed consent

The Clinical Trial Regulations define 'informed consent' as a decision written in one of the official languages of Malta (English or Maltese) or in a language understandable to the clinical trial subject or his or her legal representative, dated and signed, to take part in a clinical trial, taken freely after being informed of its nature, significance, implications and risks, and documented by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative. If such person is unable to write, verbal consent may be given in the presence of at least one witness.

11 The Clinical Trial Regulations (S.L. 458.43) define an 'investigational medicinal product' to be 'a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form'.

Medical devices

The Medical Devices Regulations require a mark of conformity (a 'CE mark') to market a medical device. A notified body must have carried out a conformity assessment procedure depending on the class of medical device. A technical file is submitted with documentation showing the medical device's conformity with the regulations. As an EU Member State, the EU's Clinical Trials Regulation (536/2014) will be directly applicable in Malta.

iv Named-patient and compassionate use procedures

Unlicensed medicinal products

The Committee for Unlicensed Medicinal Products was established to permit the use of unlicensed medicines in Malta. The Pharmaceutical Unit within the Ministry for Health is responsible for the processing of individual requests for medicinal products by certified prescribers and for use in public and private hospitals.

The 'Guidelines for the supply of medicinal products for human use through processes which are not covered by the Medicines Act, 2003 and its subsidiary legislation (unlicensed medicinal products)' includes application forms.[12] The supply and use of unlicensed medicinal products is restricted to circumstances where the licensed product cannot be obtained or the patient is not in a position to obtain the product directly from abroad for personal use under a doctor's prescription (Annex 1 of the Guidelines).

'Unlicensed products' do not include products that are: undergoing clinical trials, approved for compassionate use under European Council Regulation 726/04; prepared in a pharmacy under prescription; prepared by division of authorised packs into smaller units in a pharmacy for dispensing to patients within the same pharmacy; reconstituted intravenous preparations and prepared in centralised intravenous additive services; or used outside the clinical indications of their marketing authorisation.

The request for the use of an unlicensed medicinal product must be submitted by a doctor or a dentist registered in Malta to the Superintendent of Public Health. The request must explain why a licensed product is not a suitable alternative and include a declaration that the prescriber takes direct personal responsibility for the use of the unlicensed product.

Requests on a named patient basis must include the patient's signature confirming that he or she is aware that the medicinal product is unlicensed. The absence of the patient's signature has to be justified.

Exceptional medicinal treatment

In March 2018, the Maltese legislature passed the Exceptional Medicinal Treatment (EMT) Committee Regulations (S.L.528.08). These regulations cater for medicinal treatment provided to patients suffering from diseases for which medicinal treatment is not listed on the Government Formulary List; or listed on the Government Formulary List but not according to protocol, indication or prescribed criteria; specifically branded medicines; or medicines for the treatment of rare diseases. The Exceptional Medicinal Treatment Committee (EMTC) assesses requests submitted to the Directorate for Pharmaceutical Affairs of the Health

12 Form I: request for the use of an unlicensed medicinal product on a named patient basis, for a specific patient (applies to both the government health services and the private sector); Form II: request for the use of an unlicensed medicinal product by a hospital department within the government health services; Form III: request for the use of an unlicensed medicinal product by a hospital or clinic in private practice.

Ministry by medical consultants by a prescribed application form. Department of Health Circular 15/2018 (DH 417/2018) comprises the policy addressed to healthcare professionals outlining the procedures, the EMT Request Form, the EMTC Terms of Reference, and the Schedule of Review Criteria.

v Pre-market clearance

Medicines

Medicinal products are approved and authorised for commercial distribution in Malta through the legal supply chain as follows:

a marketing authorisation according to Article 20 of the Medicines Act (Chapter 458 of the Laws of Malta) and Legal Notice 387 of 2004 as amended;

b marketing authorisation by centralised procedure (Regulation 726/2004);

c parallel import licence according to Legal Notice 437/2004;

d authorisation on the ground of public health according to Article 4(2) of the Medicines Marketing Authorisation Regulations (Legal Notice 387 of 2004) in accordance with Article 126a of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use, as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004; and

e Licensing Authority approval of medicine to be put on the market in exceptional cases, subject to such conditions as the Licensing Authority may attach to it (Article 20(1) of the Medicines Act, 2003) on the ground of public health.

In the past seven years, the Licensing Directorate of the Medicines Authority processed 4,400 licensing applications that were granted a marketing authorisation in Malta. There are approximately 2,000 medicines in Malta licensed under the Article 126a procedure mentioned in (d) above. The Medicines Authority has set eligibility criteria for an Article 126a application, stating that 'this procedure should in no way be considered as an easy way of circumventing the current procedures stipulated by the EU legislation'. However Malta, because of its small market size and availability challenges, has proven itself to be the biggest user of the Article 126a marketing authorisation. From around 5,400 national authorisations (inclusive of parallel importation licences), more than one-third have been licensed through the Article 126a procedure. A total of 572 new authorisations for medicinal products were issued in 2018; 372 of these authorisations were made under Article 126a. Malta is also a Reference Member State (RMS) or a rapporteur in European registration procedures. In 2018, Malta led 38 authorisation procedures, an increase of 12 procedures from 2017.[13]

A study published by senior authorised officers of the Medicines Authority identifying pharmaceutical issues encountered during regulatory review in European marketing authorisation application procedures found that applicants would benefit from following published guidelines to avoid delays in the registration of medicines.[14]

EU laws apply for the licensing of biologics, biosimilars and generic medicines, and the validity of marketing authorisations. In the case of homeopathic and herbal medicines,

13 The Medicines Authority Annual Report, 2018.

14 Chetcuti M et al. (2018) Pharmaceutical issues during the review of European Marketing Authorisation Applications in Malta, Pharmaceutical Development and Technology, 23:6, 561–572.

the authorisation procedure is simplified and applications are received and reviewed by the Medicines Authority. The quality issues and regulatory challenges the pharmaceutical industry needs to consider when developing and producing biosimilars and in the submission of dossiers for marketing authorisations were studied and published by senior authorised officers of the Medicines Authority.[15]

Medical devices

The European Medical Device Regulation 2017/745 repealed the directives on medical devices: the European Medical Devices Directive 93/42 and the European Active Implantable Medical Device Directive 90/38. The Medical Device Regulation was published on 5 May 2017 and came into force on 25 May 2017. Approved medical devices have until 26 May 2020 to meet the new Medical Device Regulation requirements. At the time of writing, the Malta Competition and Consumer Affairs Authority Technical Regulations Division is responsible for the approval and authorisation of commercial distribution of medical devices.

vi Regulatory incentives

Malta applies European pharmaceutical law, including data and market exclusivity, orphan medicines and paediatric medicines. The EU and the US in particular have adopted regulations, incentives and policies targeted at improving orphan drug access to patients suffering from rare diseases.[16] Malta has no additional national regulatory requirements beyond the EU requirements so as not to hinder the pharmaceutical industry.

Data exclusivity

The Medicines Act regulates the period of data exclusivity. The Medicines Act data protection and exclusivity provision arises from the derogation of Article 10 of European Council Directive 2004/27.

Generic medicines and Roche Bolar

Malta is one of the few EU Member States that has a broad interpretation of the Roche Bolar provision, which has been incorporated in the Maltese Patents and Designs Act, and fully recognises the research exemption of the Patent Cooperation Treaty and European Patent Convention, by which generic companies can undertake development, but not commercialisation, of drugs prior to patent expiry.[17]

15 Cilia M et al. (2018) Quality Issues Identified During the Evaluation of Biosimilars by the European Medicines Agency's Committee for Medicinal Products for Human Use, AAPS PharmSciTech 19: 489.

16 In a University of Malta (Pharmacy Department, Faculty of Medicine and Surgery) study published as a research paper, out of 24 countries only 16 countries were found to have a national orphan drug (OD) or rare disease (RD) policy. Malta was found to have no national OD or RD plan, financial incentives or non-financial incentives. Malta's pricing of OD is 'free' 'upon passing HTA through therapeutic programme scheme'. Abbas, Amar & Vella, Janis & Azzopardi, Lilian & Serracino-Inglott, Anthony (2019) Orphan drug policies in different countries. Journal of Pharmaceutical Health Services Research. 10.1111/jphs.12305.

17 The Patents and Designs Act (Chapter 417 of the Laws of Malta), Article 27.

Joint/multilingual labelling

The Medicines Authority recognises joint/multilingual labelling with other countries to be an incentive for retaining medicinal products on the Maltese market. The Medicines Authority has facilitated joint/multilingual labelling with the UK, Ireland and other markets, and continues to pursue collaboration opportunities with other European competent authorities for multilingual labelling.

Day zero mutual recognition procedure (simplified procedure)

To address medicines availability challenges in Malta, the Medicines Authority accepts the assessment of the RMS or the national competent authority (where the product had been authorised nationally), without any comments or questions. The approved product information will also be accepted without any comments. The Medicines Authority does not request any update of the assessment report or the dossier, nor are there any changes related to such procedure, except that in this simple way Malta joins a mutual recognition procedure (MRP). These procedures are finalised once the application has been accepted by the RMS and the Medicines Authority, known as an 'MRP day zero procedure'. Day zero licensing procedures have already been executed successfully with various RMS countries.

vii Post-approval controls

Medicines

Pharmacovigilance

Pharmaceutical companies and regulatory authorities must honour their pharmacovigilance obligations according to EU law. The Medicines Act (Chapter 458 of the laws of Malta), and its subsidiary legislation namely the Pharmacovigilance Regulations S.L. 459.35, transpose the European Council Directive 2001/83 (as amended). The Medicines Authority has also published Guidance Notes for Pharmaceutical Companies on Pharmacovigilance Obligations and Adverse Drug Reaction (ADR) Reporting Requirements for Medicinal Products for Human Use (last amended in December 2019). There are no significant country-specific obligations provided for by Maltese law.

The Medicines Authority ensures patient safety by communicating with healthcare professionals, evaluating safety reports and conducting pharmacovigilance inspections to assess marketing authorisation holders' (MAH) compliance with pharmacovigilance obligations. MAHs must comply with their pharmacovigilance obligations to maintain the marketing authorisation of a medicines product.[18]

If there are concerns affecting the risk-benefit balance of an authorised medicinal product, the Medicines Authority may impose an obligation on a MAH to operate a risk management system and to submit a detailed description of the risk-management system that the MAH intends to introduce for the medicinal product concerned. The imposition of such obligations shall be duly justified, notified in writing and shall include the time frame for submission of the detailed description of the risk management system.[19]

18 The Medicines Authority website, Pharmacovigilance: http://www.medicinesauthority.gov.mt/safety?l=1.

19 The Pharmacovigilance Regulations, Article 8.

Staffing requirements for MAHs – the QPPV

MAHs in Malta must appoint a qualified person for pharmacovigilance (QPPV). The MAH shall submit the name and contact details of the QPPV to the Medicines Authority and the European Medicines Agency. The Medicines Authority may request the nomination of a contact person for pharmacovigilance issues in Malta (at national level) who reports to the QP responsible for pharmacovigilance activities.

Variations and transfer of ownership of product approvals

Post-authorisation procedures are handled by the Medicines Authority and include variations, notifications, renewals and withdrawals. Variations of marketing authorisations are governed by European Variation Regulation 1234/2008, amended by European Regulation 712/2012, which introduced work-sharing of different types of procedures, timelines, and takes into account the new European pharmacovigilance regulations. European Council Directive 2009/53 applies to variations submitted for nationally authorised medicines. The transfer of ownership of the marketing authorisation is made by filing the relevant request forms to the Medicines Authority depending on whether the marketing authorisation has already been issued or not.

Medical devices

The Medical Devices Regulations impose post-market surveillance obligations. Medical devices that compromise the health and safety of patients may be withdrawn from the market or prohibited or restricted by the Director of Market Surveillance after interim measures are taken. The Market Surveillance Directorate may carry out inspections, including the technical documentation and the CE conformity declaration. The Medical Devices Regulations specify that regulatory data must be uploaded to the European databank and made accessible to the national competent authorities.

viii Manufacturing controls

The main applicable legal instruments are the Manufacture and Importation of Medicinal Products for Human Use Regulations (S.L. 458.36); Good Manufacturing Practice in Respect of Medicinal and Investigational Medicinal Products for Human Use Regulations (S.L. 458.42); and the Good Clinical Practice and Requirements for Manufacturing or Import Authorisation of Investigational Medicinal Products (Human Use) Regulations (S.L. 458.47).

The manufacture of any dosage form of a medicinal product must be in conformity with the EU Good Manufacturing Practice (EU GMP) throughout the entire manufacturing process until the its release on the market. The applicant must hire qualified staff, particularly the qualified person (QP) responsible for manufacturing. The Medicines Authority Inspectorate and Enforcement Directorate carries out inspections to verify that the technical facilities and equipment is in place and that the manufacturing site fulfils all legal and EU GMP requirements.

The authorisation timeline is as follows: the application is vetted within 10 days of being submitted by the applicant; the assessment is then expected to take six months (unless further information or clarifications are needed); and the approval is issued within five days of conclusion of the assessment. The decision is then delivered within the following two days.

The list of licensed manufacturers is published on the Medicines Authority website.[20]

Medical devices

The production or manufacture of medical devices in Malta and the importation of medical devices into Malta are required to be in compliance with the Product Safety Act (Chapter 427 of the Laws of Malta) under penalty of law. Producers are obliged to only place safe medical devices on the market.[21]

ix Advertising and promotion

Medicines

The advertising of medicinal products is governed by the Medicinal Products (Advertising) Regulations (S.L. 458.32), which transpose European Directive 2004/27 into Maltese law and regulate advertising to the general public and to healthcare professionals. The Medicines Authority has also issued guidelines, last updated in 2017. The system of medicines advertising is based on self-regulation as the Medicines Authority does not review advertising prior to its publication, but offers guidance and monitors advertisements. No advertising complaints were made to the Medicines Authority in 2018.

It is unlawful to advertise medicinal products that have not been granted marketing authorisation. The Licensing Authority may prohibit advertising of reimbursable medicinal products to the general public. The advertising to the general public of prescription-only medicines, and medicines that contain substances defined as psychotropic or narcotic under the First Schedule to the Dangerous Drugs Ordinance (Chapter 101 of the Laws of Malta) and the Third Schedule to the Medical and Kindred Professions Ordinance (Chapter 31 of the Laws of Malta), is forbidden.

Compliance orders issued by 'qualified entities' as defined by law, administrative penalties, and other administrative sanctions are made under the Medicines Products (Injunction to Advertising) Regulations (S.L. 458.51), which transpose European Directive 92/28 implementing it into Maltese law.

20 List of licensed pharmaceutical activities, Medicines Authority website http://www.medicinesauthority.gov.mt/licensed-pharmaceutical-activities.

21 Article 2 of the the Product Safety Act gives a wide definition of 'producer': '(a) the manufacturer of the product, when he is established in Malta, and any other person presenting himself as the manufacturer by affixing to the product his name, trade mark or other distinctive mark, or (b) the person who reconditions the product; or (c) the manufacturer's representative, when the manufacturer is not established in Malta or, if there is no representative established in Malta, the importer of the product; or (d) others in the supply chain, in so far as their activities may affect the safety aspects of a product placed on the market'.

Medical devices

The Product Safety Act (Chapter 427 of the Laws of Malta) contains a definition of 'advertisement' and states that in the interest of public safety, the Director General (Technical Regulations) of the MCCAA may impose, by order in writing, conditions on product marketing, advertising, labelling and marking.

Other laws

The Broadcasting Act (Chapter 350 of the Laws of Malta) includes rules on the broadcasting of medicinal products advertising. The Commercial Code (Chapter 13 of the Laws of Malta) applies to all advertising in Malta.

x Distributors and wholesalers

Medicines

The applicable legal instrument is the Wholesale Distribution and Brokering of Medicinal Products and Active Substances Regulations (S.L. 458.37). These Regulations also apply to homeopathic medicinal products. The Medicines Act (Chapter 458 of the Laws of Malta) defines 'wholesale distribution'. The Medicines Authority publishes a list of licensed wholesale dealers in Malta, last updated in December 2019.[22]

Application

The national competent authority (the Licensing Authority) shall grant the applicant a wholesale distribution licence (WDL) within 90 days of the date of receipt of the application provided the requirements listed in Article 8 of SL458.37 are met. This timeline is suspended if the applicant is asked to provide additional information. The application must also include the pharmaceutical forms of the medicinal products to be distributed, in particular whether they are sterile, require storage below 8º centigrade, details on whether they are narcotic or psychotropic substances, blood, immunological medicinal products or radiopharmaceuticals.

Responsible person

One of the requirements is that the applicant must engage a responsible person (RP). The RP is a registered pharmacist with the Malta Pharmacy Council and recognised as suitable by the national competent authority. The RP must be knowledgeable of proper conditions for the storage and distribution of medicinal products and have an understanding of good distribution practice (GDP) and must comply with the duties assigned to the RP as described

22 List of licensed pharmaceutical activities, Medicines Authority website http://www.medicinesauthority.gov.mt/licensed-pharmaceutical-activities.

in the Regulations. The RP can be a full-time employee, a part-time employee or work on a contract basis for the wholesale dealer. The Medicines Authority publishes a list of pharmacists accepted by the Medicines Authority to act as RPs.

Marketing authorisation holder letter of access

For each medicinal product distributed in Malta, the wholesale dealer must provide the Licensing Authority with an authenticated copy of the marketing authorisation together with a letter of access issued by the MAH granting the wholesale dealer the use of such marketing authorisation. The only exception is if the wholesale dealer is in possession of a valid parallel import licence.

Patients' needs and medicines supply obligations

The Regulations also require every wholesale dealer, within the limits of their responsibilities, to ensure that 'an appropriate and continuous supply of medicinal products is provided to pharmacies and persons authorised to supply medicinal products' to satisfy patients' needs.

Good distribution practice

The Licensing Authority requires full traceability of product quality throughout the entire supply chain and the wholesale dealer's conformity with the EU Good Distribution Practice (EU GDP) standards. The Medicines Authority carries out EU GDP inspections. The licensed entity is given a list of findings after the Medicines Authority inspection, which they are required to respond to with proposals for corrective action within 28 days. Once all findings have been addressed with a satisfactory corrective action plan and measures, the renewal of the wholesale dealer's licence is recommended to the Licensing Authority. Site re-inspection is performed at a frequency determined by the Medicines Authority by a systematic risk-based assessment.

Medical devices

The Product Safety Act (Chapter 427 of the Laws of Malta) regulates the wholesale dealing of medical devices. Wholesale dealers are obliged to cooperate in monitoring the safety of products on the market. Knowingly distributing unsafe medical devices is unlawful. The Director General (Technical Regulations) of the MCCAA may impose restrictions.

xi Classification of products

Medicines

The Borderline Classification Committee classifies borderline products into medicinal or non-medicinal products in line with the EU pharmaceutical law definition of medicinal product.

In Malta, medicines can only be dispensed to a patient from a licensed pharmacy. Medicinal products are either 'prescription-only medicines (POM)' (dispensed by a pharmacist to the patient under a physicians' prescription) or 'over-the-counter products (OTC)' (dispensed by a pharmacist to the patient without a prescription).

Classifying medicines as prescription-only or over-the-counter is part of the Marketing Authorisation process that licenses and ensures the quality, safety and efficacy of the

medicinal product. The Medicines (Marketing Authorisation) Regulations (S.L. 458.34) specify the POM classification criteria. The Prescription and Dispensing Requirements Rules (S.L. 458.49) stipulate the content of the prescription and the dispensing regulations.

The Prescription Forms for Free Medicinals Rules (S.L. 458.24) govern the provision and prescription of medicinal products and medical aids to the patients at no cost to the end-user through the national health service (NHS) under the Social Security Act (Chapter 318 of the Laws of Malta).

Medical devices

Medical devices are classified in line with European law, on the basis of their risk to patients.

xii Imports and exports

Maltese legislation governing the import and export of medicinal products and medical devices generally reflects EU rules. Import regulations are enforced by the Customs Authority, and the Commissioner for Revenue also plays a part. Import tariff regulations are established by the Import Duties Act (Chapter 337 of the Laws of Malta). Product classification in Malta is made under the Harmonised Standard (the HS code number). The Dual-Use Items (Export Control) Regulations (S.L. 365.12) control dual-use export goods. European Council Regulation 428/2009, which governs the EU's export control regime, applies to Malta.

Medicines

The main applicable legal instrument is the Manufacture and Importation of Medicinal Products for Human Use Regulations (S.L. 458.36). In Malta, an importer's licence (IL) is required for the importation of medicinal products.[23] 'Imported medicinal products' means medicinal products obtained from a source outside the European Union or the European Economic Area.[24]

All medicinal products for human use imported into Malta and the EU from a non-EU or non-EEA country, including medicinal products intended for export outside the EU and not intended for the Maltese market, are to be manufactured in accordance with the principles and guidelines of European Good Manufacturing Practice (EU GMP).[25] It is the importer's duty to ensure that medicinal products imported from third countries have been manufactured in accordance with standards equivalent to the EU GMP standards by authorised manufacturers.[26]

In Malta any licence holder (whether the holder of a manufacturing or importation licence, a wholesale dealing licence) must be a natural person or a legal person. 'Licensee' means any person who is the holder of a licence for a particular activity granted under the Medicines Act.[27] Whichever entity within the EU or EEA first physically receives medicinal products entering the EU or EEA market from a non-EU or non-EEA country must be in possession of an IL.

23 S.L. 458.36, Article 3(3).

24 S.L. 458.36, Article 2.

25 'Good practice' in relation to manufacturing practice, laboratory practice, distribution practice, clinical practice and dispensing practice means the standards for the proper execution of the relative activity as established by or under the Medicines Act, Chapter 458 of the Laws of Malta, Article 2.

26 S.L. 458.36, Article 7(5)(a)&(b).

27 The Medicines Act, Chapter 458 of the Laws of Malta, Article 2.

The IL is issued by the national competent authority following verification of the contents of the application, but no later than 90 days from the date of receipt of the application. This time period is suspended when additional information is requested from the applicant. The national competent authority may grant a conditional licence subject to the applicant's fulfilment of the legal requirements. The IL shall only apply to the premises, medicinal products and pharmaceutical forms specified in the application.[28]

There must be a qualified person (QP) approved by the Maltese national competent authority for batch release, who ensures that each batch complies with the law, the GMP, the importer's or manufacturer's authorisation and the marketing authorisation.[29]

The Wholesale Distribution and Brokering of Medicinal Products and Active Substances Regulations (S.L. 458.37) state that wholesale distributors of active substances must comply with EU GDP, including active substances intended for export.

Falsified medicines

The Licensing Authority is responsible for taking the necessary measures to prevent medicinal products that are brought to the EU, but are not intended to be placed on the EU market, from entering into circulation if there are sufficient grounds to suspect that those products are falsified. These measures include applying the S.L. 458.37 regulations to warehouses in the free trade zones and customs bonded warehouses used to store medicinal products.[30]

Medical devices

The import and export of medical devices is regulated by the Product Safety Act (Chapter 427 of the Laws of Malta).

xiii Controlled substances

Malta ratified the Single Convention on Narcotic Drugs in 22 February 1990.[31] The Single Convention has 186 state parties.

The importation, manufacture, exportation, purchasing and selling of any controlled drug is subject to the Drugs (Control) Regulations (S.L.31.18). These activities need to be authorised by the Superintendent of Public Health and registered and reported to the Superintendent at specified time frames. Importation and exportation procedures including details to be submitted and labelling requirements are at the Superintendent's discretion. Dispensing of controlled must follow the applicable protocols.

According to the Medical and Kindred Professions Ordinance, the Health Minister, after consultation with the Council of Health, can amend, add to, revoke or substitute the list of psychotropic drugs. The Health Minister can also make regulations for controlling the manufacture, exportation, importation, possession, distribution and sale of psychotropic drugs, in the public interest.

28 S.L. 458.36, Article 5.

29 The qualifications for designation of a QP are outlined in S.L. 458.36 Articles 9 and 10. The QP's responsibilities are listed in S.L. 458.36 Articles 11 and 12. The requirements of Directive 2001/83/EC as transposed into national legislation (the Medicines Act, Chapter 458 of the Laws of Malta, Article 38(1e) and S.L. 458.36, Article 9) must be fully complied with.

30 S.L.458.37, Article 12.

31 https://treaties.un.org/doc/Treaties/1975/08/19750808%2006-05%20PM/Ch_VI_18p.pdf.

xiv Enforcement

The Licensing Authority has delegated its enforcement powers to the Medicines Authority. A dedicated Inspectorate and Enforcement Directorate within the Medicines Authority is tasked with enforcement and market surveillance.[32] Article 101 and 101A of the Medicines Act (Chapter 458 of the Laws of Malta) establishes broad enforcement powers including right of entry, inspection, taking of samples, and seizure of goods and documents of any person duly authorised in writing by the national competent authority.

On production of his or her authorisation or credentials, such authorised person shall have a right to enter and carry out repeated and unannounced inspections at any premises (including any building, place or means of transport) at any reasonable time for the purposes of ascertaining whether there is, has been or is likely to be any breach of the provisions of the Medicines Act and its subsidiary legislation.

An authorised officer shall, on the production of his or her authorisation, have a right to board any ship or aircraft at any reasonable time to ensure that no substance or article is imported in contravention of the Medicines Act and its subsidiary legislation.

Offences and penalties

Article 99 of the Medicines Act establishes the penalties, in the form of fines and terms of imprisonment, in the event of conviction for failure to comply with any of the provisions of the Medicines Act or any regulations or rules made thereunder.

III PRICING AND REIMBURSEMENT

Malta has a unique 'split' medicines market, with two separate and distinct regimes:

i The National Health Service

Patients' entitlement to medication on the public health market (national health services) outside a Maltese government hospital setting is based on the principle of social solidarity. Entitlement is assessed on the basis of disease or means by virtue of the Social Security Act (Chapter 318 of the Laws of Malta).

National health services are funded by taxpayers and managed by the Maltese government (responsible directorates within the Ministry of Health). Medicinal products listed in the government formulary are provided free of charge to eligible patients (end user). Under the entitlement programme, patients have no freedom of choice but are prescribed the medicinal products included in the government formulary.

Requests by medical practitioners (consultants) for medicinal products not included in the government formulary are made on a named-patient basis and may be accepted provided conditions are met and the medicinal product holds a valid marketing authorisation in an EU Member State.

32 According to the Medicines Authority 2018 Annual Report, in 2018 the Medicines Authority investigated four enforcement cases, coordinated by the Enforcement Committee (chaired by the Licensing Authority), and resulted in two court sittings concerning pharmacy issues, and two other court cases in which the Medicines Authority's employees were summoned as witnesses.

Malta has transposed and implemented the EU transparency laws which apply to medicinal products procured via national health services (i.e., the national formulary). The applicable Maltese law is the Availability of Medicinal Products within the Government Health Services Regulations (S.L. 458.31).

ii The private market

This essentially services those areas of the healthcare sector that are not covered and supported by the Malta National Health Service. Medicinal products purchased on the private market (i.e., from a pharmacy at retail level) are an out-of-pocket cost to the patient or consumer and, in the case of prescription medicines, are prescribed by a doctor (prescriber) in private practice.

The Maltese private market enjoys a free-market pricing policy. There are no statutory price controls. Private market medicines prices (purchased by the consumer from a pharmacy at retail level) are not fixed by the government, but are determined by the licensed market players in the legal supply chain (pharmacy, wholesale dealer, manufacturer or MAH). A number of privately owned hospitals are licensed to operate in Malta.

The price of medicines at retail level are monitored by the MCCAA via a referencing mechanism aimed at benchmarking an average consumer price across 12 EU Member States and there have been negotiations between the Maltese government and the pharmaceutical industry that have led to price reductions of certain medicines.

iii Health technology assessment

In January 2018, the European Commission published a Proposal for a Regulation on Health Technology Assessment (HTA) amending Directive 2011/24/EU. The proposal establishes a Member State Coordination Group on HTA (Coordination Group) composed of representatives from national HTA authorities and bodies. The Coordination Group will be responsible for overseeing the joint clinical assessments. Joint clinical assessments (of medicinal products and medical devices) are limited to the most innovative technologies with the most potential EU-wide public health impact. A Maltese pharmaceutical expert, former Medicines Authority CEO Dr Patricia Vella Bonanno, spearheaded and significantly contributed to a paper that presents the consolidated views and considerations of policymakers, payors, pricing and reimbursement authorities, and academics on the original European Commission proposal.[33]

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

The matter of legal interest is of paramount importance in litigation and judicial remedies. In Malta legal standing is apportioned based on legal interest (i.e., the test for being an interest party). Interest must be direct and personal, meaning that the right claimed or alleged should belong directly to the patrimony of a person. Interest has to be legal, meaning it must find a legal basis and be qualified as being based and founded on a legal principle or legal provision.

33 Vella Bonanno P, et al. (2019) Proposal for a regulation on health technology assessment in Europe–opinions of policy makers, payers and academics from the field of HTA, Expert Review of Pharmacoeconomics & Outcomes Research, 19:3, 251-261.

Interest must be actual, meaning that the party must demonstrate some actual benefit from the proceedings. This need not be economic benefit but it could be intangible such as reputation.

The Medicines Review Board hears appeals submitted by the applicant of a marketing authorisation on any recommendation of the Medicines Authority in relation to the safety, quality and efficacy of a medicinal product and to provide advice and make its recommendations to the Licensing Authority in this regard. An appeal may be filed with the Medicines Review Board within 14 days of receipt of a copy of the Medicines Authority's recommendations and findings. The timelines and stages of the process are established by the Medicines Act. The Medicines Review Board appoints the matter for public hearing within 30 days of the day of filing the appeal or review request and shall decide the matter as expeditiously as possible. It is possible to file a warrant of prohibitory injunction as an interim measure provided certain conditions are met. It is also possible to file other civil law proceedings on the basis of unlawful government action, for example under the Administrative Justice Act (Chapter 490 of the Laws of Malta), or the judicial review of administrative action under Article 469A of the Code of Organisation and Civil Procedure (Chapter 12 of the Laws of Malta).

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYORS

The Medicinal Products (Advertising) Regulations (S.L. 458.32), which transpose European Council Directive 24/2007, lay down a regulatory framework for the promotion of medicinal products and gift provisions to healthcare professional (HCP) prescribers.

Gifts to HCPs must be inexpensive and related to the practice of medicine or pharmacy. Hosting HCPs is restricted to events organised around a scientific theme and the same invitation should not be extended to non-HCPs. The provision of free samples to medical prescribers needs to be documented and is conditional to a number of provisos, such as having to be in their smallest presentation on the market and prohibiting the prescriber from using the free samples in any commercial transactions.

According to the Ethics of the Medical Profession Regulations (S.L. 464.17), practitioners cannot publicly endorse any particular commercial product or service.[34] Moreover, conducting commercial enterprise of medicines can result in erasure from professional registers.[35] S.L. 464.17 stipulates that doctors ensure their professional independence and must not accept conditions that could jeopardise it.[36]

The Pharmaceutical Research-Based Industry Malta Association (PRIMA) is a member of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and has established a national code applicable to all its members, based on the EFPIA HCP Code of Practice.

Anti-bribery and anti-corruption laws are governed by the Criminal Code (Chapter 9 of the Laws of Malta) and the Prevention of Money Laundering Act (Chapter 373 of the Laws of Malta).

34 S.L. 464.17, Paragraph 7(a).

35 S.L. 464.17, Paragraph 4(f).

36 S.L. 464.17 Paragraph 8.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

The European Council Product Liability Directive was transposed into Maltese law by introducing the principle of strict liability to the Consumer Affairs Act (Chapter 378 of the Laws of Malta), enabling consumers to claim compensation when a product causes death, personal injury, loss, damage or destruction of any item of property. The producer is also able to raise defences under the provisions of the Act.[37] Under Maltese law, liability may arise either in contract or in tort. Private actions for damages suffered as a result of a breach of competition law would usually be founded on tort. Tort is based on fault. The Maltese Civil Code (Chapter 16 of the Laws of Malta) states that every person shall be liabile for the damage that occurs through his or her fault.[38] A person shall be deemed to be at fault if in his or her own acts he or she does not use prudence, diligence, and attention of a *bonus paterfamilias*.[39] Any person who, with or without intent to injure, voluntarily or through negligence, imprudence, or want of attention, is guilty of an act or omission constituting a breach of duty imposed by law, shall be liable for any resulting damage.[40]

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

The Competition Act (Chapter 379 of the Laws of Malta) governs competition law in Malta. As an EU Member State, Malta subscribes to the EU competition law regime. National antitrust or competition law litigation in Malta of special relevance to the life sciences sector in Malta is not commonplace.

ii Transactional issues

Transactional issues in the pharmaceutical and medical device sectors, including mergers and acquisitions, joint ventures, and licensing and strategic collaborations, inevitably have a regulatory impact, especially in the transfer of marketing authorisations and meeting pharmacovigilance requirements. The complex interplay of provisions of Maltese codified legislation, including but not limited to the Product Safety Act, the Medicines Act, the Commercial Code, the Civil Code, the Companies Act, the Competition Act, the Data Protection Act, the Patents and Designs Act, the Trademarks Act and the Copyright Act, would feature prominently in any transaction.

37 Consumer Affairs Act, Chapter 378 of the laws of Malta, Article 62 and 'Pharmaceutical Law in the EU and USA: The impact on Public Health and the Pharmaceutical Industry', University of Malta, Faculty of Laws, 2010.

38 Civil Code (Chapter 16 of the Laws of Malta), Section 1031.

39 Civil Code (Chapter 16 of the Laws of Malta), Section 1032.

40 Civil Code (Chapter 16 of the Laws of Malta), Section 1033.

VIII CURRENT DEVELOPMENTS

i Brexit

As a small island EU Member State, Malta has experienced medicines access and availability challenges in its national healthcare service.[41] Malta's national market is also expected to be affected by Brexit.[42] The Medicines Authority has also seen a recent surge in applications to act as the RMS in medicines authorisation applications, partly due to the UK's impending exit from the EU as Malta takes over as RMS in applications where it is the only EU CMS.

ii EU–US FDA mutual recognition of inspections of medicines manufacturers

On 1 November 2017, Malta became one of the first of eight EU Member States to begin mutual recognition of inspections of manufacturing sites for human medicines between the US and the EU.

iii Medical cannabis

The Production of Cannabis for Medicinal and Research Purposes Act (Chapter 578 of the Laws of Malta) and its subsidiary legislation were enacted in 2018, legalising the production of cannabis for medicinal and research purposes. This initiative was led by the Medicines Authority's Advanced Scientific Initiatives Directorate.[43]

Licensed medical practitioners are able to prescribe cannabis-based medicinal products with a valid marketing authorisation, and other cannabis products for medicinal use that are manufactured under EU GMP. The Medicines Authority reviews applications for the importation or wholesale distribution of such products. The first application was received in March 2018.

iv Medicines pricing – the Valletta Group

Headlined by the Deputy Prime Minister and Health Minister the Honourable Christopher Fearne, Malta hosted a Valletta Group meeting in July 2019 with a mandate to move forward on a collaborative framework for price-information sharing to undertake collective negotiations on regional prices for bulk purchases of medicinal products in Europe, with the ultimate objective of reducing prices. The Valletta group is named after the 2017 Valletta Declaration in which 10 EU countries, representing 160 million citizens, agreed to work together to leverage pharmaceutical industry negotiations.

41 P Vella Bonanno, International Conference, Competition and Pharmaceutical Policy in European Law, 'Availability of Medicines: A Case Study for Malta' (Iceland, 12 September 2008).

42 The Medicines Authority has published a regulatory update regarding Brexit on its website: http://www.medicinesauthority.gov.mt/brexit?l=1.

43 AnthiaZammit Legal was engaged by the Medicines Authority, Malta's national competent authority, to draft the General Guidelines on the Production of Cannabis for Medicinal and Research Purposes: http://www.medicinesauthority.gov.mt/file.aspx?f=4137, the Production for Cannabis for Medicinal and Research Purposes (Fees) Regulations 2018: http://justiceservices.gov.mt/DownloadDocument.aspx?app=lp&itemid=29382&l=1, and the Application for a Licence in accordance with the Production of Cannabis for Medicinal and Research Purposes Act: https://servizz.gov.mt/en/Pages/Health-and-Community-Care/Health/Medicines/WEB2427/default.aspx and the respective memos addressed to the Cabinet of Malta, the collective decision-making body of the government of Malta. The agricultural science and scientific EUGMP section (Appendix 1) of the General Guidelines was written by Professor Everaldo Attard.

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Anthia A Zammit LLB, LLD is an advocate admitted to practise law in Malta (EU) and is a licensed legal consultant in the State of New York (US). Anthia advises multinational mega-cap, private and publicly listed companies and institutions in the healthcare, life sciences, biotechnology, and pharmaceutical industries. Anthia drafts, reviews and negotiates contracts related to regulated products. She provides advice on market access, EU and national licensing and marketing authorisations, including EU regulatory data protection, EU risk management plans, pricing and reimbursement, compliance matters, advertising and labelling, R&D, clinical trials, and pharmacovigilance agreements. Anthia drafted the commercial agreements and terms introducing and implementing anti-corruption and anti-bribery provisions and procedures for leading pharmaceutical companies. Anthia has extensive experience in European regulatory law and compliance of medicinal products, pharmaceuticals, biologics, biosimilars and medical devices. She worked in-house and on a consultancy basis with and for the Medicines Authority (Malta's national competent authority responsible for the regulation of medicinal products and the pharmaceutical industry), and was recently engaged to draft Malta's medical cannabis regulations, general guidelines, and licence application. She served as legal counsel to the Malta Chamber of Commerce's Healthcare Business section and was a member of the Policy Advisory Group of the European Patients Forum (EPF), a not-for-profit, non-government organisation that represents the interests of an estimated 150 million patients in public health and health advocacy across Europe. She has participated as a keynote speaker in high-level healthcare conferences on invitation of the European Commission. Anthia earned her LLB (Bachelor of Laws) and LLD (Doctor of Laws) from the University of Malta.