2022

MALTA
MEDICINES
AUTHORITY

Annual Report

2022 Statistics at a Glance

117

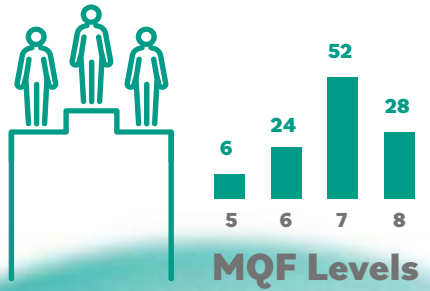
Total number of employees

Females: 80 I Males: 37

115

Academic qualifications of MMA employees

Females: 79 I Males: 36



15 International Fellowship Programme students

Research publications **25**

194

QMS internal documents
(SOPs, Policies and Guidelines)

Audit performed **11**

754

New medicinal products authorised

77 Finalised MRP/DCP procedures with MT acting as RMS

Scientific advice **19**

EMA SAWP Procedures

147 ICSRs registered

393

Reports of suspected ADRs

EU-GMP inspections

Local: 21 I 3rd country: 23

36 EU-GDP inspections

QP approved **15**

64 Free sale certificates for MDs

169

MDs registrations received

29

Approved cannabis-based products

Formulation of approved cannabis-based products

Oil: 14

Dried flowers: 14

Purified extract: 1

783

Article 20 exemption applications approved

30 Matters requiring legal advice

Acronyms

AA	Authorisation according to Article 126(a)
ADR	Adverse Drug Reaction
AI	Artificial Intelligence
API	Active Pharmaceutical Ingredient
ASID	Advanced Scientific Initiatives Directorate
AT	Austria
BCC	Borderline Classification Committee
BE	Belgium
BG	Bulgaria
CA	Canada
CAT	Committee for Advanced Therapies
CB1	Cannabidiol receptor type 1
CBD	Cannabidiol
CEO	Chief Executive Officer
CH	Switzerland
CHMP	Committee for Medicinal Products for Human Use
CMDh	Co-Ordination Group for Mutual Recognition and Decentralised Procedure-Human
CMRU	Cannabis for Medicinal and Research Purposes Unit
CMS	Concerned Member State
COVID-19	Coronavirus Disease
CPPs	Certification of Pharmaceutical Products
CPSU	Central Procurement and Supplies Unit
CTIS	Clinical Trials Information System
CTR	Clinical Trial Regulation
CU	Cuba
CY	Cyprus
CZ	Czechia
DCP	Decentralised Procedure
DE	Germany
DG INTPA	Directorate General for International Partnership
DHPCs	Direct Healthcare Professional Communications
DK	Denmark
DPU	Data Protection Unit
EAFP	European Association of the Faculties of Pharmacy
EC	European Commission
ECA	European Competent Authority
EDP	Entrepreneurial Discovery Process
EDQM	European Directorate for the Quality of Medicines and Healthcare
EE	Estonia
EEA	European Economic Area
EL	Greece
EMA	European Medicines Agency
EMRN	European Medicines Regulatory Network
EPAD	Educational Planning and Academic Development
ES	Spain
EU	European Union
EUCD	EU Coordination Department
EU-GMP	EU-Good Manufacturing Practice
EU-NTC	EU-Network Training Centre
EURD	European Union Reference Dates
EVDAS	EudraVigilance Data Analysis System
FEBS	Fellowship of the European Board of Surgery
FI	Finland
FMD	Falsified Medicines Directive
FOI	Freedom of Information
FOICU	FOI Coordination Unit
FR	France
FRCS(ed)	Fellow Royal College of Surgeons England
FSCA	Field Safety Corrective Actions
GACP	Good Agricultural and Collection Practices
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
HCPs	Healthcare Professionals

HERA	Health Emergency Preparedness and Response Assessment
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HR	Croatia
HTA	Health Technology Assessment
HU	Hungary
IACS	International Academic Conference Scheme
ICSRs	Individual Case Summary Reports
ICT	Information and Communications Technology
IE	Ireland
IED	Inspectorate and Enforcement Directorate
IFP	International Fellowship Programme
IN	India
IPAS+	Internationalisation Partnership Awards Scheme Plus
IPS	Institute of Public Service
IRG	Inspections Review Group
IS	Iceland
ISO	International Organization for Standardization
IT	Italy
IVD	In-Vitro Diagnostics
LA	Licensing Authority
LD	Licensing Directorate
LI	Liechtenstein
LT	Lithuania
LU	Luxembourg
LV	Latvia
Lvl	Level
M.D.	Doctor of Medicine and Surgery
M.Phil	Master of Philosophy
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder
MCAST	Malta College of Arts, Science and Technology
MCM	Medical Counter Measures
MCST	Malta Council for Science and Technology
MD	Medical Devices
MDH	Mater Dei Hospital
MDR	Medical Device Regulation
MDRP	Medical Device Registered Person
MDSSG	Medical Devices Shortages Steering Group
ME	Malta Enterprise
ME	Montenegro
MEYR	Ministry for Education, Sport, Youth, Research and Innovation
MFAA	Minister for Active Aging
MFHEA	Malta Further and Higher Education Authority
MHRA	Medicines and Health Regulatory Agency
MIAU	Medicines Intelligence and Access
MLN	Malta Laboratories Network
MMA	Malta Medicines Authority
MoUs	Memorandum of Understandings
MP	Member of the Parliament
MQF	Malta Qualifications Framework
MRCS	Member of the Royal College of Surgeons
MRP	Mutual Recognition Procedure
MS	Member States
MSSG	Steering Group on Shortages and Safety of Medicinal Products
MT	Malta
NAT/LE	National and Line Extension
NBs	Notified Bodies
NCA	National Competent Authority
NL	Netherlands
NO	Norway
NOT	Notifications
OMCL	Official Medicines Control Laboratory
PAES	Post-Authorisation Efficacy Studies
PASS	Post-Authorisation Safety Studies
PDPID	Policy Development and Programme Implementation Directorate

Pharm.D	Doctorate in Pharmacy
PhV	Pharmacovigilance
PI	Parallel Import
PL	Poland
PPE	Pharmaceutical Products Entrepreneurship
PPPs	Pregnancy Prevention Programmes
PSRs	Product Safety Recalls
PSURs	Periodic Safety Update Reports
PSUSAs	Periodic Safety Update Report Single Assessments
PSWG	Prescription Status Working Group
PT	Portugal
QIs	Quality Improvements
QM	Quality Management
QMS	Quality Management System
QP	Qualified Person
RAs	Rapid Alerts
RAT	Rapid Antigen Test
RCA	Regulatory Competent Authorities
REN	Renewals
RIS3	Research and Innovation Smart Specialisation Strategy
RMMs	Risk Minimisation Measures
RMPs	Risk Minimisation Programmes
RMPs	Risk Management Plans
RMS	Reference Member State
RO	Romania
ROMAD	Regulatory Operations, Medicines Intelligence and Access Directorate
RWD	Real-World Data
RWE	Real-World Evidence
SAWP	Scientific Advice Working Party
SE	Sweden
SI	Slovenia
SK	Slovakia
SMART	Specific, Measurable, Achievable, Relevant, and Time-bound
SMS	Short Message Service
SOC	System Organ Class
SOPs	Standard Operating Procedures
SPH	Superintendent of Public Health
SPOC	Shortages Single Point of Contact
SUSARs	Suspected Unexpected Serious Adverse Reactions
SVP-LTCF	St. Vincent de Paul Long Term Care Facility
THC	Tetrahydrocannabinol
TOPRA	The Organisation for Professionals in Regulatory Affairs
UK	United Kingdom
UOM	University of Malta
USA	United States of America
VARS	Variations
VPN	Virtual Private Networks
WHO	World Health Organisation
WP	Working Party
YoY	Year on Year

Contents

Foreword from the Minister

It is my honour and privilege to be writing this foreword. The Malta Medicines Authority is Malta's flagship in the pharmaceutical sector. Its mission is to ensure that every pharmaceutical product and Medical Device that is put to use in our country is safe, of good quality and proven efficacy. Therefore, there can be no doubt about the utmost and grave sensitivity and consequences of its operations. As such, the Malta Medicines Authority epitomises the quintessential requirements of a modern scientific regulatory body that is steeped in education, training and research. The Malta Medicines Authority proudly employs a team one hundred and seventeen (117) personnel out of which, eighty (80) are in possession of post-graduate qualifications.

The Malta Medicines Authority carries out a significant number of third country inspections. This enhances the accessibility of quality medicines in Europe in addition to assisting in the establishment and functioning of the pharmaceutical industry in Malta. By being an important Reference Member State and its performance in rapporteurship for centralised procedures, Malta plays a significant role in the licensing of medicines for use in Europe.

True to its mission, the Authority is heavily involved in a wide variety of international and European Union entities such as the European Medicines Agency, Heads of Medicines Agencies, Committee for Medicinal Products for Human Use, Committee for Advances Therapies, Executive Steering Group on Shortages and Safety of Medicinal Products, Medical Devices Shortages Steering Group and the Medicines Shortages Single Points of Contact Working Party.

Within it, the Medicines Intelligence and Access succeeded in improving the accessibility to medicines and keeping shortages to the barest minimum. Affordability is another crucial aspect which will grow further in its remit. The Pharmacovigilance, Medicines Safety and Support Senior Headship ensures safety through adverse drug vigilance, signal detection, risk minimisation measures and other pharmacovigilance activities. The Medical Devices and Pharmaceutical Collaboration Directorate, on the other hand, ensures that Malta procures Medical Devices of the highest order. This Directorate is also processing the first application for the establishment of a Notified Body in Malta which will not only enhance Malta's image on the international stage, but it will benefit countless operators and patients both locally and abroad. It is no coincidence that the Malta Medicines Authority is held in such high regards that it has been designated as a model for similar entities in countries aspiring to join the European Union.

I must admit that the Authority's academic and research endeavours are very close to my heart. The Malta Medicines Authority in collaboration with the Department of Pharmacy of the Faculty of Medicine and Surgery at the University of Malta, spearheads a veritable trove of Masters, Doctoral and now even post-Doctoral research degrees. The Advanced Scientific Initiatives Directorate and the Pharmaceutical Products Entrepreneurship Unit bring the Authority close to the patient and to stakeholders. These are bearing fruit in establishing a clinical pharmacy service at St. Vincent de Paul Long Term Care Facility and the organisation of scientific conferences such as the Med-In Pharma Symposium and the first Maltese Multi-Disciplinary Conference on Continence. In the latter initiatives, the Malta Medicines Authority is working with the University of Malta, the Association of Surgeons of Malta, the European Association of Endoscopic Surgery, the Royal College of Surgeons of Edinburgh and the Royal College of Physicians and Surgeons of Glasgow.

The Malta Medicines Authority has an excellent track-record in reliability, efficiency and sustainability. I take this opportunity to wholeheartedly thank all of our employees for their sterling work and faultless professionalism. I wish them every success.

Hon Jo Etienne Abela MD MPhil MRCS FRCSEd FEBS MP
Minister, Ministry for Active Aging

Message from the Chief Executive Officer

The Malta Medicines Authority is the National Competent Authority responsible for the safeguarding of the safety, quality and efficacy of medicinal products and Medical Devices. In order to address recent challenges, the Malta Medicines Authority is reflecting on the addition of two (2) additional parameters namely accessibility and environment.

In 2022, the Authority contributed to the outstanding results of dealing with one of the greatest challenges ever faced by society in recent history. The Malta Medicines Authority joined global efforts, and the excellent local actions, to tackle the COVID-19 pandemic. The contribution by the Superintendent of Public Health was supported by Malta Medicines Authority through continuous technical assistance and intelligence. The Medicines Intelligence and Access had already shown its prowess in expanding the Malta Medicines Authority vision to a patient-centred approach. The Malta Medicines Authority was instrumental in the timely accessibility to vaccines and pharmaceutical products including medicines and Medical Devices. The Pharmacovigilance Directorate kept a very close eye on the safety of new vaccines and treatments, acting swiftly when required during an unparalleled successful campaign for vaccination. The Authority kept society informed in a transparent manner on health aspects including safety recommendations based on data and communication with European and international authorities. Personnel within the Authority worked tirelessly throughout the pandemic, to approve medicines and supplies coming both from the European Union and globally whilst ensuring the quality, safety, and efficacy of all products that reached our shores. In parallel, while tackling problems related to COVID-19, excellence was shown by the Authority in performing significant progress in other areas through teamwork. The extended mandate to the Authority in regulating Medical Devices provided challenges that go beyond systems related to medicines.

The support for innovative initiatives provided by the Authority was found to be particularly useful in crisis situations and in the preparations for other emerging health threats. Of note, is the global threat on the shortages of medicines, which was particularly pronounced in Europe. The response by the Malta Medicines Authority on this occasion was bold and ambitious. I am confident in stating that the hard work of the staff of the Authority led to accessibility to medicines unparalleled in many other countries. In 2022, the Malta Medicines Authority has issued several recommendations for Article 20 exemptions, where due diligence was exerted to ensure that patients' needs are met.

I would also like to highlight the progress made in the implementation of two important new legislations: the change from Directives on Medical Devices to Regulations which was introduced in an extraordinary smooth manner and the Clinical Trials Regulation which lays the foundation for introducing the framework to be able to carry out clinical trials in Malta as per the new European Union requirements.

Digitalisation is another priority to ensure that in line with government policy, new tools are devised to tackle future challenges. Our ambitious vision to deliver in this area has already been put into practice whereby we have embarked on the introduction of a significant IT programme namely the Medical Device Management System.

Over the past ten (10) years, the Authority's collaborations with European Medicines Agency and European Union Member States, through participation in several committees ensure important contributions to European regulatory sciences which have been paramount. Through this network, the Malta Medicines Authority was able to deal efficiently with the core regulatory activities, particularly the activities which form the heart of regulation needed to protect the public, namely the activities of the Licensing and Inspectorate and Enforcement Directorates.

The Authority continued to show a patient-centred environment in the field of cannabis for medicinal use and is an example of the co-operation that the Malta Medicines Authority continuously maintains with public and private stakeholders.

Maintaining a highly skilled workforce is at the forefront of the Malta Medicines Authority's strategy. The extension of the International Fellowship Programme to a Postdoctoral level continues to be an example of capacity building and a means of matching competencies with local needs in line with the Electoral Manifesto Measures.

The Authority is proud of its sustainability mainly due to its highly qualified and competent staff which lead to innovative activities outside the core functions of the Authority. These included the establishment of a Directorate for Advanced Scientific Initiatives with its flagship, the Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences, and this year's forward-looking initiative in the establishment of the outstanding Pharmaceutical Products Entrepreneurship Unit.

Professor Anthony Serracino-Inglott
Chief Executive Officer, Malta Medicines Authority

1. The Malta Medicines Authority - Background

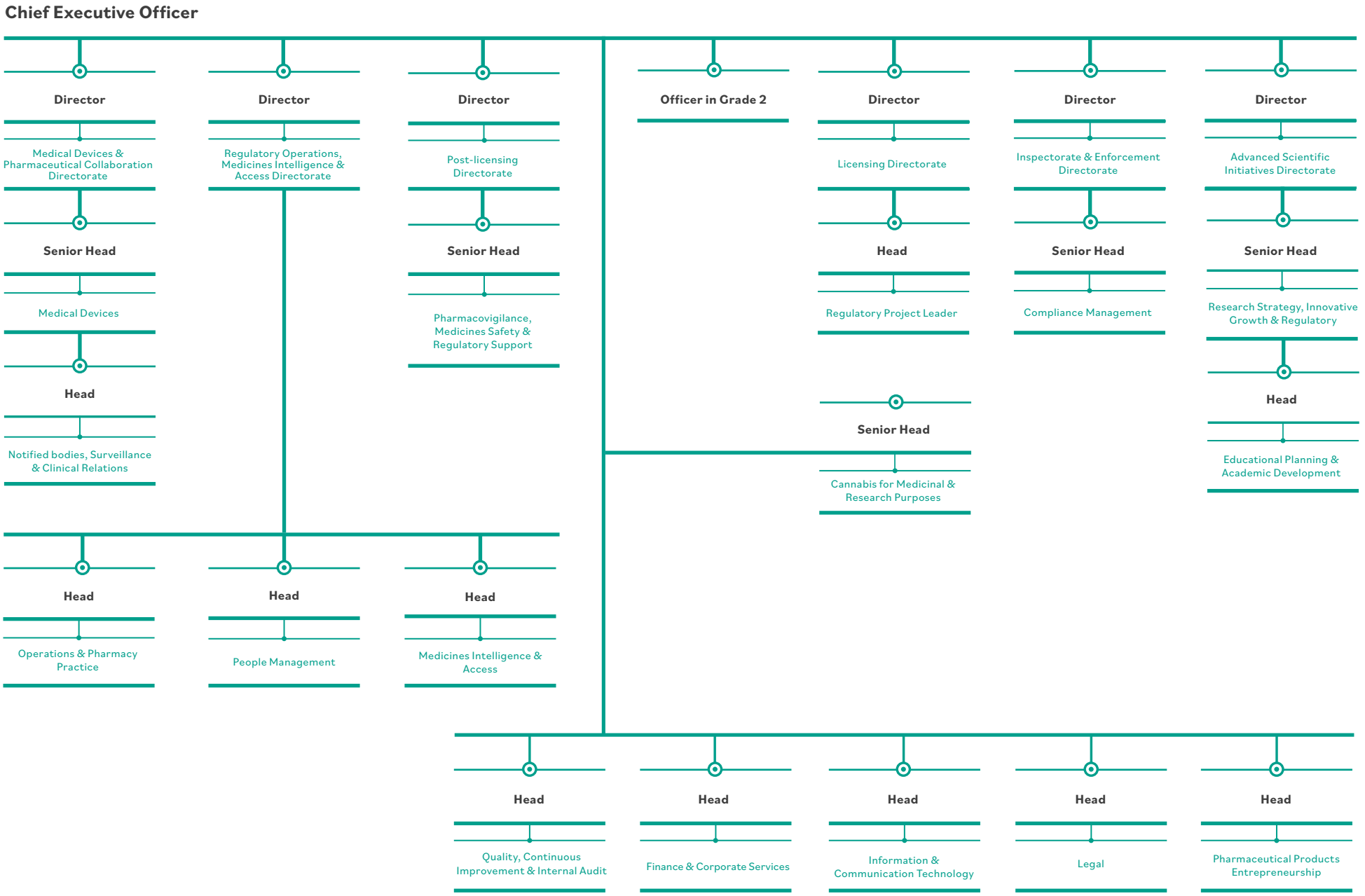
The Malta Medicines Authority (MMA) was established by virtue of the Medicines Act 2003, and has developed into an autonomous body that implements scientific decisions in the best interest of patients. It is committed to provide high quality licensing, Pharmacovigilance (PhV), pharmaceutical inspections and enforcement services to its stakeholders for the ultimate benefit of the public.

The MMA is established by six (6) Directorates under the guidance of the Chief Executive Officer (CEO). These are the Licensing Directorate (LD), the Post-licensing Directorate (PLD), the Inspectorate and Enforcement Directorate (IED), the Advanced Scientific Initiatives Directorate (ASID), the Regulatory Operations, Medicines Intelligence and Access Directorate (ROMAD) and the Medical Devices and Pharmaceutical Collaboration Directorate. Their core work is supported by six (6) Senior Headships, namely the Medicine Regulation and Coordination, the Pharmacovigilance, Medicines Safety and Regulatory Response, the Compliance Management, the Research Strategy, Innovative Growth and Regulatory Response, the Medical Devices, five (5) Headships, namely the Educational Planning and Academic Development (EPAD), the Medicines Intelligence and Access (MIAU), the People Management, the Operations and Pharmacy Practice, and the Notified Bodies, Surveillance and Clinical Relations.

The Authority is also supported by the continuous collaboration of six (6) Units which fall within the Office of the CEO, namely the Finance and Corporate Services Unit (FCS), the Information and Communications Technology Unit (ICT), the Quality, Continuous Improvement and Internal Audit Unit, the Legal Unit, the Pharmaceutical Products Entrepreneurship Unit (PPE), and the Cannabis for Medicinal and Research Purposes Unit (CMRU).

In view of the expansion of its regulatory portfolio, the MMA was re-engineered to enable the broadening of its scope of operations, fulfil new obligations and cope with the increasing volume of activity, entailing the Authority to sustainably invest in manpower.

Organogram


Chief Executive Officer
Director
Medical Devices & Pharmaceutical Collaboration Directorate
Senior Head
Medical Devices
Head
Notified bodies, Surveillance & Clinical Relations
Director
Regulatory Operations, Medicines Intelligence & Access Directorate
Director
Post-licensing Directorate
Senior Head
Pharmacovigilance, Medicines Safety & Regulatory Support
Officer in Grade 2
Director
Licensing Directorate
Head
Regulatory Project Leader
Senior Head
Cannabis for Medicinal & Research Purposes
Director
Inspectorate & Enforcement Directorate
Senior Head
Compliance Management
Director
Advanced Scientific Initiatives Directorate
Senior Head
Research Strategy, Innovative Growth & Regulatory
Head
Educational Planning & Academic Development
Head
Operations & Pharmacy Practice
Head
People Management
Head
Medicines Intelligence & Access
Head
Quality, Continuous Improvement & Internal Audit
Head
Finance & Corporate Services
Head
Information & Communication Technology
Head
Legal
Head
Pharmaceutical Products Entrepreneurship

Main Roles and Responsibilities

The MMA works to sustain its reputation as a recognised centre of excellence for European regulatory sciences through the highest quality and scientific rigour with which it undertakes the core functions outlined below in a patient-centred approach.

I. To perform duties delegated to the MMA by the Licensing Authority (LA) through the Medicines Act;

II. To assist and advise the Licensing Authority on any matter relating to the regulation of medical products and related activities;

III. To ensure in so far as possible and consistent with current medical and scientific knowledge, that medical products marketed in Malta (MT) and the European Union (EU) are of good quality and have a favourable risk-to-benefit profile through independent, science-based assessment, post-authorisation activities and participation in decision-making at European level;

IV. To scientifically evaluate requests and monitor clinical trials carried out in Malta;

V. To ensure, that the medical products supplied on the local market through the regulated supply chain are of good quality, safe for the public, and as per the intended use;

VI. To provide high-quality monitoring and inspection services for pharmaceutical activities, local Medical Device (MD) economic operators, and the performance of Notified Bodies (NBs) registered in Malta;

VII. To monitor the safety of medical products;

VIII. To monitor and enforce the relevant legislation through investigation of potential breaches of regulations and a range of measures;

IX. To enhance the effective, safe and rational use of medical products through the provision of objective and unbiased information which helps prescribers, healthcare professionals (HCPs) and patients make informed decisions on the choice and use of medicines;

X. To support the availability of medical products on the local market;

XI. To support the competitiveness of the local market through scientific and regulatory advice and the implementation of principles of SMART Regulation;

XII. To utilise and develop tools, standards, and approaches to assess and ensure the safety, quality and effectiveness of medical products, and pharmaceutical activities;

XIII. To enhance the standard of medicinal products and pharmaceutical activities for medicines for human use in Malta;

XIV. To manage developments related to scientific research, innovation, and academic initiatives, in line with the strategy of the MMA;

XV. To support the regulation of cannabis for medicinal and research purposes through guidance, technical review, and stakeholder engagement among other areas;

XVI. Process and investigate complaints received regarding advertised medicinal products and provide guidance as laid down in the advertising regulations;

XVII. To participate on European fora of the European Medicines Agency (EMA), Council, working groups, and the Commission and perform assessment and give scientific and regulatory positions in various areas.

Mission and Vision

"Our mission is to safeguard public health through the regulation of medical products and pharmaceutical activities for human use."

"Our vision is to be a centre of excellence in advancing effective and innovative regulation and promoting quality and scientific rigour in the work we do. We strive to be a best in class regulator for the benefit of patients and stakeholders. We endeavour to be an internationally recognised, efficient entity and promoter of people development and sustainable growth."

Values

People

Our people are our most valued resource. We are committed to sustain our ongoing efforts to improve our workforce through educational advancements and most importantly a healthy work life balance.

Quality

We are committed to provide high quality licensing, Pharmacovigilance, inspections, enforcement, and advisory services to our stakeholders in the best interest of consumers.

Integrity

Discipline and fairness are the utmost priciples which guide us to do what is right. The intergity of our officers lies at the very heart of our mission to uphold the best interests of Maltese consumers and beyond.

Innovation

In an everchanging environment, innovation is what drives us forward and keeps us up to speed with the constant technological and scientific advancements. This ensures we remain both valid and effective.

Strategic Goals and Objectives

The new strategic goals and objectives of the MMA include:

1. Resilience against current and potential market disruptors

- **1.1.** To act in coherence with partners in designing supply chain strategies
- **1.2.** To optimise the allocation of the Authority's resources in response to major events
- **1.3.** To monitor developments related to the COVID-19 pandemic
- **1.4.** To sustain support structures in the areas of Brexit and falsified medicines

2. Enhancing the accessibility framework

- **2.1.** To gather intelligence systematically and expediently
- **2.2.** To operate in a global context to address shortages
- **2.3.** To maintain current regulatory approaches to accessibility

3. A robust regulatory system that adapts to new realities

- **3.1.** To further bolster the surveillance for the safety and quality of medicines
- **3.2.** To spur initiatives related to the clinical development of medicinal products
- **3.3.** To reinforce the regulation of Medical Devices
- **3.4.** To instil change in pharmacy practice

4. Organisational growth and sustainability

- **4.1.** To offer workspaces with in-built ergonomics
- **4.2.** To monitor performance targets and achieve proper people and financial management
- **4.3.** To continue acting as a global player
- **4.4.** To implement a forward-looking Information and Communications Technology (ICT) Governance system
- **4.5.** To enhance the Quality Management System (QMS) and auditing functions

5. Leading through science, innovation, and expertise

- **5.1.** To intensify the research arm by leveraging on collaborations
- **5.2.** To instil a professional acumen in tomorrow's pharmaceutical leaders
- **5.3.** To venture further into the Authority's innovative regulatory activities

6. Advancing communication norms

- **6.1.** To implement internal engagement initiatives
- **6.2.** To uphold professional communication approaches with external stakeholders
- **6.3.** To enhance public knowledge on the MMA and the appropriate use of medicines

Quality Management, Simplification Measures and Good Governance

As an internationally certified institution according to International Organization for Standardization (ISO) 9001:2015, the MMA upholds the highest standards of governance and is fully committed to improved Quality Management (QM).

By the end of 2022, the foundation of the Quality Management System at the Authority, that ensures uniform and high-quality operations, consisted of thirty-eight (38) Policies, one hundred and twenty-two (122) Standard Operating Procedures (SOPs) and thirty-four (34) Guidelines. In 2022, five (5) Policies, forty-eight (48) SOPs, and twenty (20) Guidelines were revised or introduced through the annual Management Review process and periodic internal audits which are both an integral part of the ongoing efforts to continuously improve the MMA's Quality Management System (***Figure 1.1***).

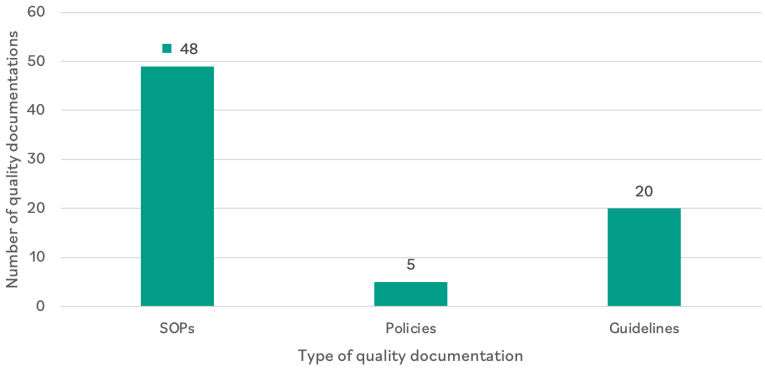


Figure 1.1: SOPs, Policies and Guidelines of the MMA that were revised or introduced in 2022

The MMA implemented eleven (11) internal audits throughout 2022, in line with the five (5)-year audit strategy which was extended to a six (6)-year programme due to COVID-19 interruptions.

Overall, a total of seventy-five (75) Quality Improvements (QIs) were submitted to the Quality, Continuous Improvement and Internal Audit Unit. These QIFs arose from internal audits and other internal initiatives by the respective Directorates and Units. Consequently, this led to the introduction of new Policies and SOPs or the systematic review of existing ones with a cross-cutting aim of reducing red tape and unnecessary bureaucracy.

The annual Management Review examined the operations of each Directorate and the respective Units within the MMA, evaluated the results of stakeholder (internal and external) feedback, analysed the results of previous audits (internal and external) and studied the outcome of the previously identified QIs, in a comprehensive exercise to strengthen the QMS.

In line with the Government direction to simplify the Public Sector system and processes, the MMA identified and implemented one (1) simplification measure. A Standard Operating Procedure for the assessment and risk-based prioritisation of exemption requests in accordance with Article 20 of the Medicines Act, 2003 (Chapter 458 of the Laws of Malta) was developed to enhance the efficiency of processing of exemptions while ensuring the continuous provision of medicinal products on the Maltese market. Article 20 exemptions are considered in response to exceptional basis and justified public health reasons. This measure ensures formalisation of the process and prioritise requests based on the risk associated to the patient.

The MMA endured its commitment to the budgetary measure studying the feasibility of setting up a national reference laboratory in Malta. This measure was initiated in 2021 and extends over a six (6)-year period to ensure the protection and safety of medicinal products and patients. The planning and development of the national laboratory covers important considerations including logistical matters as well as financial, technical, legal, and quality issues.

The MMA pledged its commitment to four (4) Electoral Manifesto Measures with the scope of:

1. Sustaining the growth of the pharmaceutical industry in Malta by introducing certifications for the production of biosimilars;
2. Enhancing affordability and accessibility to medicines;
3. Supporting increased expertise in the pharmaceutical scenario by extending the International Fellowship Programme to Post-Doctoral degrees;
4. Attracting the establishment of Notified Bodies in Malta.

The MMA attaches utmost importance to good governance practices which are embodied in three (3) primary measures of transparency based on information disclosure, clarity and accuracy. In compliance with the Freedom Of Information (FOI) Act, categories of documents and manuals held by the Authority together with the full audited financial statements were published on the Authority's official website. Privacy by design is a concept brought about by data protection regulations that is fully embedded within the Authority's operational framework for processes handling personal data. The MMA continued to process FOI and data protection access requests and queries in a timely and supportive manner, where necessary liaising with the Government Data Protection Unit (DPU) and FOI Coordination Unit (FOICU). Members of the public can submit their FOI requests through the portal www.freedomofinformation.gov.mt and forward any queries related to data protection on communications.medicinesauthority@gov.mt.

2. Organisational Development, A Positive Working Environment, A Patient-Centred Ethos, and A Proactive Approach

Throughout 2022, the Authority maintained its focus on the implementation of the MMA Strategy to 2025 as well as the National Framework for Education Strategy 2014-2024. This is achieved through a cross-cutting patient-centred approach across all Directorates and Units.

Team-building activities, capacity building courses and sustained work-life balance measures all contributed towards a positive working environment without which we would not have reached the highest goals which are expected of a reputable scientific regulatory authority. The positive working environment equips employees of the MMA with the best tools to implement our patient-centred ethos, where the patient is put at the core of each and every decision made.

The solid internal structure and philosophy enabled the MMA to improve its engagement with all stakeholders and the public in general through several meetings, seminars, conferences, social media campaigns, and the distribution of informative material on a wide spectrum of topics; ranging from the use of cannabis for medicinal and research purposes, the safety of medicines, the Medical Device Regulation (MDR) and accredited courses which are organised by the MMA.

By the end of 2022, one hundred and seventeen (117) employees were engaged, with the MMA (***Figure 2.1***). This represents an increase of 69% from the year 2013 (***Figure 2.2***) which effectively caters for the increased regulatory activities.

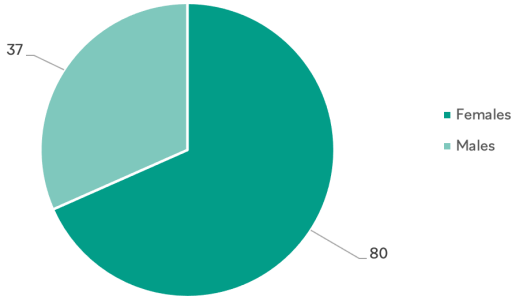


Figure 2.1: Total number of employees at the MMA at the end of 2022 (N=117)

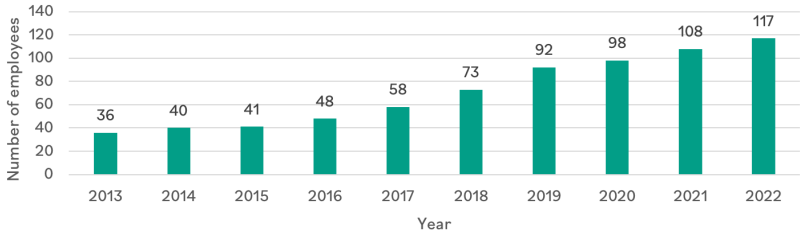


Figure 2.2: Number of employees at the MMA (2013-2022)

Education and Professional Development

The education and professional development of the MMA's workforce is the key towards its continued regeneration and relevance to the ever-evolving pharmaceutical industry. In 2022, its employees successfully attained two hundred and sixty-two (262) certificates related to training initiatives which were offered internally (n=173) and externally (n=89). These comprised a wide range of subjects including Pharmacovigilance, regulatory sciences related to good practices and Cannabis for Medicinal and Research Purposes (***Figure 2.3***).

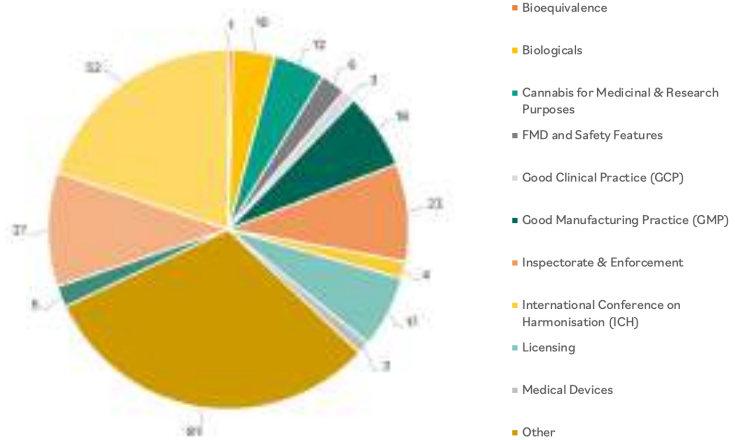


Figure 2.3: Number of training certificates attained by employees at the MMA (N=262)

Besides the ongoing internal training across all the respective scientific fields of operation, the MMA spearheads various initiatives which continuously strengthen its most valued resource.

The flexible working conditions for officers undergoing scientific and corporate studies are a fine example of the above-mentioned commitment. This is clearly portrayed in the number of employed graduates in 2022, whereby one (1) employee attained the Doctorate in Pharmacy degree (Pharm.D).

The MMA offers the new International Academic Conference Scheme (IACS) whereby employees tap into financial support to attend international conferences. This scheme further enhances the scientific image of the Authority through the presentation of papers as listed in Section 6.

The International Fellowship Programme (IFP) may be described as a flagship initiative that attracts local and foreign students to join the MMA's team while reading for a Doctorate, Master or a comparable and equivalent qualification in line with the Malta Qualifications Framework (MQF) in Pharmacy, Leadership, Management, Administration, and Finance.

Till the end of 2022, fifteen (15) students from across the globe were following the MMA's IFP (***Figure 2.4***). Through this initiative, which is intended to overcome skills mismatches in the local pharmaceutical sector by increasing the capacity and level of research, young professionals actively contribute to the ongoing functions and day-to-day running of the Authority in exchange for a financial grant which covers the tuition fee or facilitates the living expenses of the participants. Graduates are often engaged on a full-time contract with the MMA following their successful completion of the Fellowship Programme.

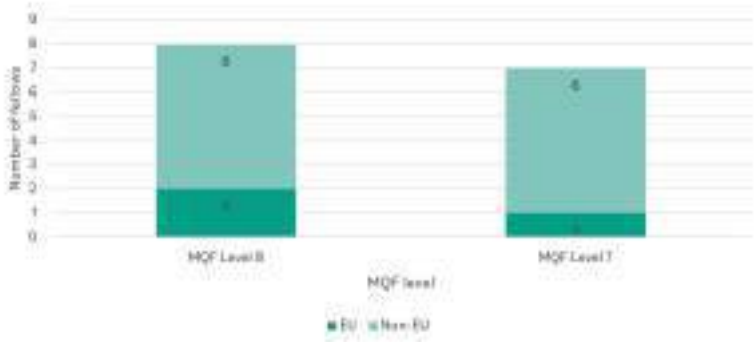


Figure 2.4: Number of students following the IFP in 2022 (N=15)

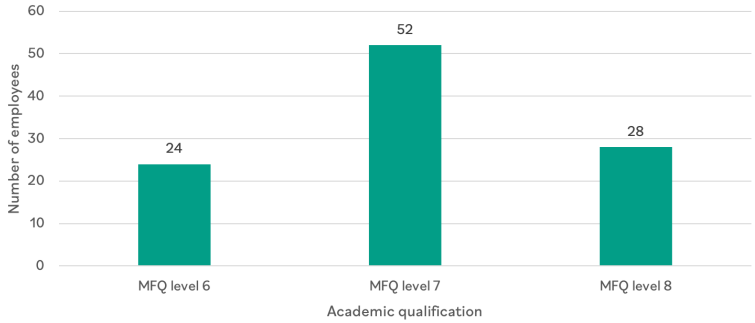


Figure 2.5: Academic qualifications for employees at the MMA in 2022 (N=104)

The above represents a concerted effort to improve the overall capacity of the MMA while reinforcing its scientific prowess. As it currently stands, twenty-eight (28) employees hold Doctoral degrees, whilst fifty-two (52), nearly half of the Authority's workforce, hold an academic qualification at a Master level (***Figure 2.5***).

The MMA's commitment towards the professional development of its human resources was augmented by the increased investment in cross-border opportunities for its employees, allowing the exchange of best practices with European and International bodies. Such professional exposure secures the Authority's ability to adapt to the constantly-evolving landscape of pharmaceutical regulation.

Furthermore, the MMA maintains strong ties with the University of Malta (UOM) by hosting student placements. In 2022, the Authority also welcomed students on summer placements from the Malta Enterprise (ME) and through the Students' Summer Work Opportunities' Scheme within the Ministry for Education, Sport, Youth, Research and Innovation (MEYR), in collaboration with Institute for Public Service (IPS). Such initiatives set the benchmark for future cooperation with other national and international institutions such as the Malta College of Arts, Science and Technology (MCAST) and the University of Illinois in Chicago.

A European and Global Player

The MMA maintained its active role at the highest European and international fora, with officers participating in diverse technical and management meetings, conferences and training opportunities. During 2022, the extent of the Authority's representation in professional bodies was sustained and surpassed the Authority's engagement of 2021. By the end of year, MMA delegates were involved in a total of fifty-one (51) strategic and scientific expert groups, committees and boards (***Figure 2.6***).

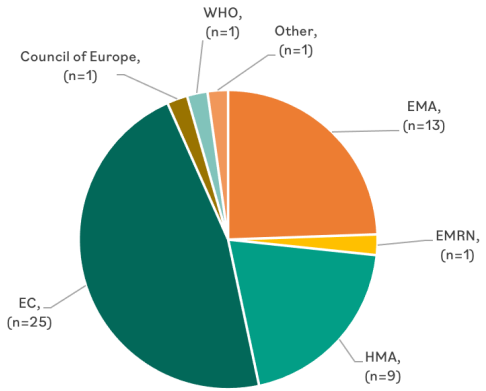


Figure 2.6: Representation by the MMA in European institutions and professional bodies (N=51)

The MMA was consulted on a number of established and proposed EU legislative files and any relevant outputs from the EU institutions, which mostly concern the regulation of medical products, and pharmaceutical activities. In liaison with the line Ministry Policy Development and Programme Implementation Directorate (PDPID), the Government EU Coordination Department (EUCD) and the Permanent Representation of Malta to the EU, the Authority provided feedback, following the necessary internal and external consultations, on diverse regulatory policy areas (***Figure 2.7***), keeping the interest and safety of patients and consumers at the core of all positions put forward.

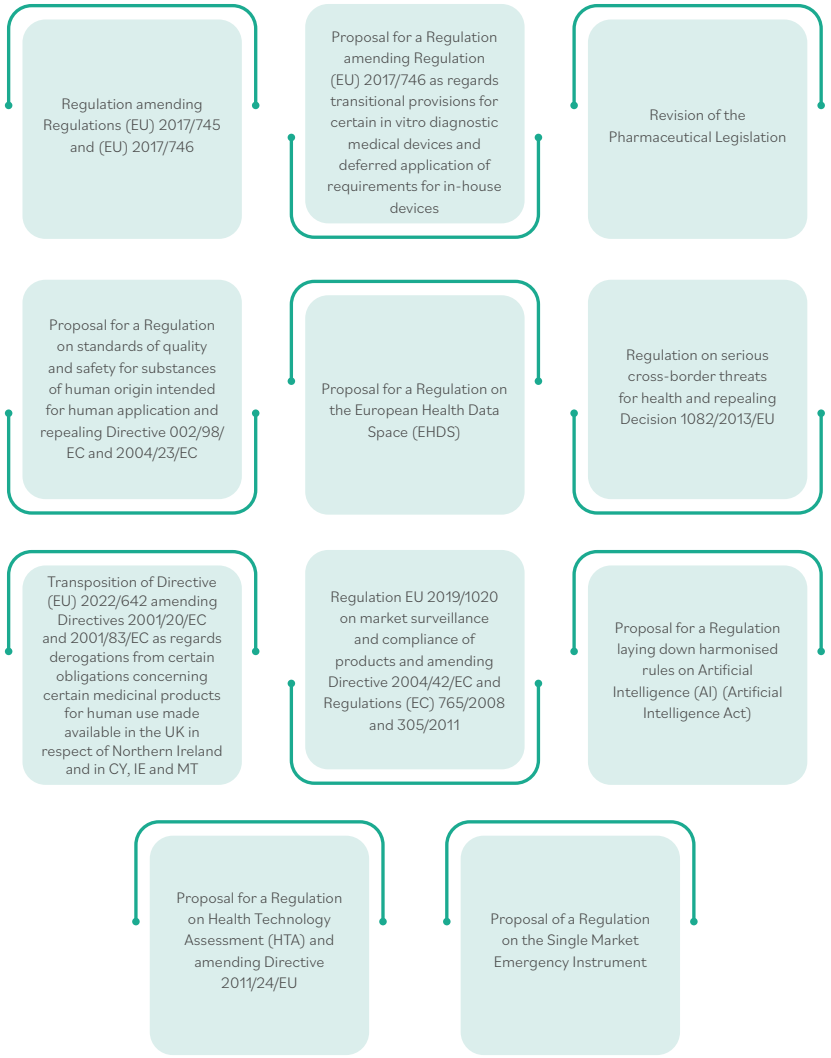


Figure 2.7: EU legislative files and any relevant outputs from the EU institutions on which the MMA was consulted in 2022

In view of the withdrawal agreement concerning United Kingdom (UK) and Northern Ireland (IE) from the European Union, the EU Commission issued a Notice in December 2020 on the application of the pharmaceutical ***acquis*** in markets historically dependent on medicines supply from or through Great Britain after the end of the transitional period. To prevent shortages of medicinal products and ensure a high level of public health protection, Directive 2022/642 introduced amendments to Directives 2001/20/EC and 2001/83/EC with regards to derogations from certain obligations concerning certain medicinal products for human use made available in the UK in respect of Northern Ireland, Cyprus (CY), Ireland and Malta. The Authority actively transposed the Directive in the Maltese legislation and continuously provided guidance to stakeholders.

Through the tenets of knowledge dissemination and training in advanced pharmaceutical research, the MMA reaches out to its counterparts in third country states with the objective of consolidating the quality of medicines imported in the EU and to spur the accessibility of medicinal products. The Authority has sustained the impetus in the area of international affairs through a number of networking initiatives that consolidate the role of Malta as a global player. The Authority interfaced with officials from the Commission Directorate General for International Partnerships (DG INTPA) to identify emerging opportunities for collaboration with African states. The Authority also contributed towards the Malta Government Policy Framework for collaboration with the regions of Asia, Latin America and Montenegro (ME). Bilateral collaborations were tabled with India (IN) and Cuba (CU) on sharing scientific insights and possible capacity building in the area of COVID-19 vaccine development.

Through these agreements, the Authority foresees the development of industrial cooperation between pharmaceutical bodies of participating countries and the eventual exchange of experience and knowledge. The Authority has also pledged its support to the pharmaceutical sector in these international states by providing training to obtain EU Good Manufacturing Practices (EU-GMP) certification. The agreements are also intended to promote collaboration on capacity building with regards to pharmaceutical product registration, pharmaceutical quality control, and pharmacovigilance.

Members of the Authority have also contributed into other related platforms, including the Task Force for Industrial Scale-up of COVID-19 vaccines, EU Executive Steering Group on Shortages of Medicines and of Medical Devices and the EMA/HMA Communications Working Group, on the impact of accessibility to medicines and communication updates.

The MMA is also contributing to the EU4Health Programme by leading working packages of the Joint Actions on reinforced market surveillance of Medical Devices and In Vitro Diagnostics Medical Devices and increasing capacity building of the EU medicines regulatory network.

Assessment and Marketing Authorisation Applications

One of the main priorities of the MMA is that of ensuring that a comprehensive range of medicinal products are authorised and accessible to Maltese patients. In addition, through life-cycle management, the Authority ensures that the information for all authorised medicinal products available in Malta is always updated and in line with scientific advancements, for both Healthcare Professionals and patients.

Applications for National Marketing Authorisations

The number of applications for authorisations for the approval of new products finalised in 2022 is shown in ***Figure 3.1***. These submissions include applications for national Marketing Authorisations (MAs) as a result of purely national procedures (n=15), three hundred and fifteen (315) Marketing Authorisations through European procedures (DC and MR procedures, both with Malta as Reference Member State (RMS) and Concerned Member State (CMS)), authorisations in accordance with Article 126(a) (AA) of Directive 2001/83/EC (n=342), and Parallel Import (PI) licenses (n=82). A total of seven hundred and fifty-four (754) new product authorisations were issued in 2022.

Data 2022		
2022 new products according to route	**New Applications (products)**	**Number of MAs issued**
RMS	102	140
CMS	248	175
Authorisation 126(a)	655	342
NAT/LE	6	15
PI	98	82

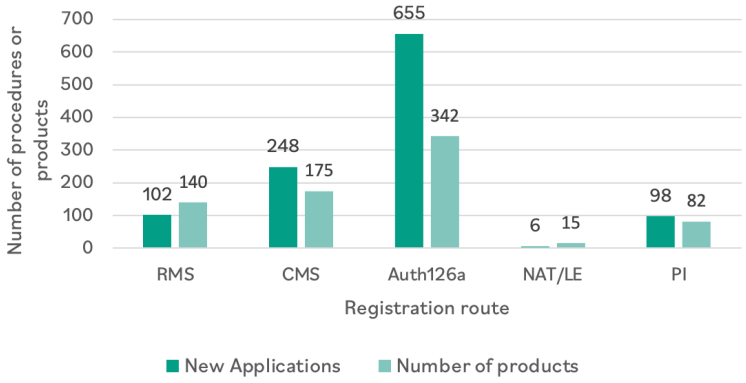


Figure 3.1: Total number of product applications and resulting product authorisations through all routes in 2022 (N=754)

Authorisations in accordance with Article 126(a) of Directive 2001/83/EC

The total cumulative number of authorisations in accordance with Article 126(a) of Directive 2001/83/EC standing at end 2022 were two thousand seven hundred and ninety-three (2,793). In 2022, six hundred and fifty-five (655) applications were received. There was an 87% increase in the number of applications received when compared to the previous year. As a result of Brexit, a shift in source countries in 2022 was observed, with most products originating from Ireland, followed by France (FR) and Germany (DE). The Licensing Directorate continued to support companies to apply for Marketing Authorisations through the Mutual Recognition Procedure (MRP). As a result, forty-four (44) products that had been previously authorised on the basis of Article 126(a) of Directive 2001/83/EC, are now authorised through the Day 0 MRP. Companies are always supported to use this procedure, through sound regulatory advice, reduction of bureaucracy and by enabling communication channels with other competent authorities such that this route is made more feasible.

Figure 3.2: Distribution of authorisation holders of applications in accordance with AA in 2022

Malta as a Lead in European Procedures

In this area, the MMA sustained its reputation as a key player in the European network for the regulation of medicinal products to provide greater accessibility for patients in Malta and beyond. This was primarily achieved through its role as a Reference Member State via the European Decentralised Procedure (DCP) and the Mutual Recognition Procedure, and by acting as co-/rapporteur for authorisation of medicinal products through the centralised procedure. The Malta Medicines Authority is steadily increasing the portfolio and embarking on the assessment of more complex products. The MMA continues to receive numerous requests to act as Reference Member State in the DCPs. In 2022, the requests in this regard increased considerably and every effort was made to grant the slots at the required time, but this was not always possible. In its effort to service the industry, recruitment, and training of staff to be able to handle more procedures is currently under way.

The number of authorisation procedures led by Malta as RMS in the DCP received in 2022 was fifty-two (52) procedures with a resulting one hundred and two (102) Marketing Authorisations granted. The resulting number of products authorised through this route in 2022 was one hundred and forty (140). The other procedures are still ongoing. The procedures in 2022 were more challenging, mainly because companies had to face the issues resulting from problems posed by COVID-19 and its effect on the conduct of Good Manufacturing Practice (GMP) inspections in third countries and also to overcome the new challenges brought about by the outcome of the European referral on nitrosamines. These issues will continue to have an impact on procedures for the next few years. By the end of 2022, Malta ranked eighth (8^{th}) as a Reference Member State for the number of started MR and DC procedures and sixth (6^{th}) (***Figures 3.3 and 3.4***) in the number of finalised procedures with Malta as Reference Member State.

In 2022, Malta was rapporteur for four (4) applications submitted to the EMA, leading assessments of medicinal products eligible for a single authorisation throughout the EU. This brings the portfolio of centralised procedures where Malta is rapporteur to forty-three (43). This set the tone for more involvement in such assessments in the future which will effectively enable the MMA to expand its visibility as a reputable scientific body while improving its expertise in this field of operation. Malta also participates in multi-national teams with other Member States (MS) where there is available expertise to contribute, through internal staff and external international experts engaged with the Malta Medicines Authority. This enhances collaboration with other European countries and also allows for these internal and external experts in the organisation to work with counterparts in other agencies.

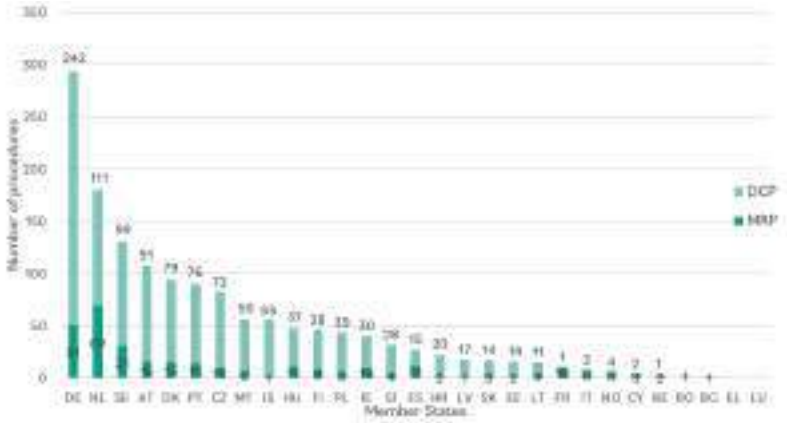


Figure 3.3: 2022 started MR/DC procedures by RMS

Figure 3.4: 2022 Finalised DC/MR procedures by RMS

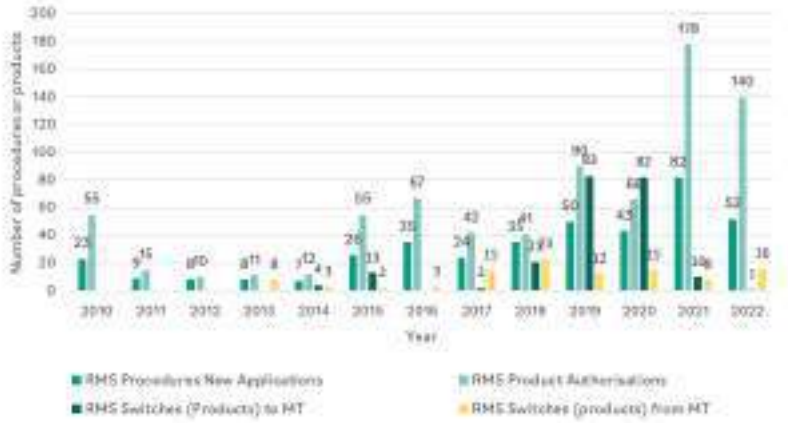


Figure 3.5: A non-cumulative overview of applications as number of procedures (and resulting product authorisations) with MT as RMS, inclusive of RMS switches (2010-2022)

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Figure 3.5 gives a year-on-year (YoY) overview of the number of procedures handled by the Malta Medicines Authority over the period 2010-2022. In 2021 a record number of duplicate procedures were received, and this explains the very high number of procedures. In 2022, the number of duplicates year stabilised to previous numbers but there was an overall increase of procedures received over the previous years.

Malta as a Contributor in European Procedures

The number of MA applications received in 2022 in the MRP and DCP with Malta as CMS were two hundred and forty-eight (248), whilst one hundred and seventy-five (175) MAs were issued. ***Figure 3.6 and Figure 3.7*** show the applications started and finalised by Malta through this route compared to other Member States. As can be seen from both ***Figures***, the size of the market and economies of scale determine the extent that smaller Member States are included as CMS in European procedures by pharmaceutical companies. However, during the last year, Malta has seen an increase in the number of European Marketing Authorisations applications received, also resulting from the increasing use of the Day 0 MRP by companies, following discussions between the MMA, and both industry and other National Competent Authorities. The MMA continues to have talks with companies and other Member States to facilitate this process and make it possible for companies to use it for products that are already authorised in one or more Member States.

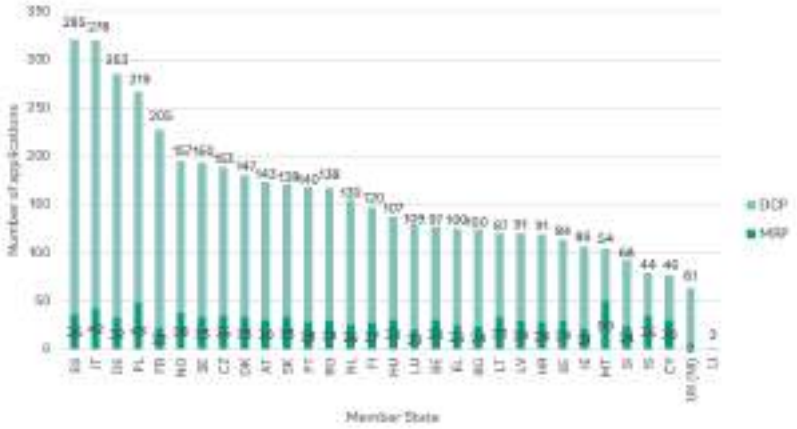

Figure 3.6: The number of MRPs and DCPs started in 2022 by CMSs
[SOURCE CHART: CMDh 2022 Statistics]

Figure 3.7: The number of MRPs and DCPs finalised in 2022 by CMSs

[SOURCE CHART: CMDh 2022 Statistics https://govmt.sharepoint.com/:x:/r/sites/LicensingDirectorateLD-5/_layouts/15/Doc.aspx?sourcedoc=%7BD1F249B8-B8BF-4090-905B-98137455F6A0%7D&file=STATS%20LD%20COMBO%202021%20FORMAT.xlsx&action=default&mobileredirect=true Mapping EU Procedures YoY]

Figure 3.8 gives an overview of the registration of medicinal products over the period 2010-2022 by the MMA (finalised procedures). The relatively constant number of authorised products was due to an increase in the number of MR and DC procedures and authorisations in accordance with Article 126(a) of Directive 2001/83/EC, especially during 2021. Therefore, in spite of the loss of medicinal products that were withdrawn because (mainly) of Brexit, the number of authorised products was maintained. The years 2019 and 2020 were exceptional for the number of applications for authorisations in accordance with Article 126(a) from the UK. This has helped to maintain a number of authorisations in place until alternatives from other European Member States are being identified by companies. The products can continue to be made available on the basis of the derogations granted by the European Commission until end of 2026, in case of no availability of alternatives from the European Union.

Figure 3.8: A 12-year overview of products registered in MT by route of registration

Post-authorisation Procedures

Post-authorisation procedures mainly include Variations (VARS), Notifications (NOT), Renewals (REN), and withdrawals. As the product portfolio, in particular resulting from European procedures, increases so does the number of post-authorisation procedures, mainly variations. These constitute a considerable workload for the MMA and ensure that the life-cycle management of products is maintained so that the latest information with respect to quality, safety and efficacy of all products is always available to the Authority, Healthcare Professionals and patients.

Post-authorisation activities, especially for procedures where Malta is a RMS, maintained a robust increase, also as a result of the additional procedures taken over by Malta from the United Kingdom. This is expected to subsist in the coming years (***Figure 3.9***). As the RMS portfolio increases, this results in a consistent increasing trend in the number of post-authorisation procedures. The MMA received five hundred and fifty-two (552) variation applications in this category with resulting updates to one thousand one hundred and eighty-seven (1187) products in procedures where Malta is the RMS (***Figure 3.9***).

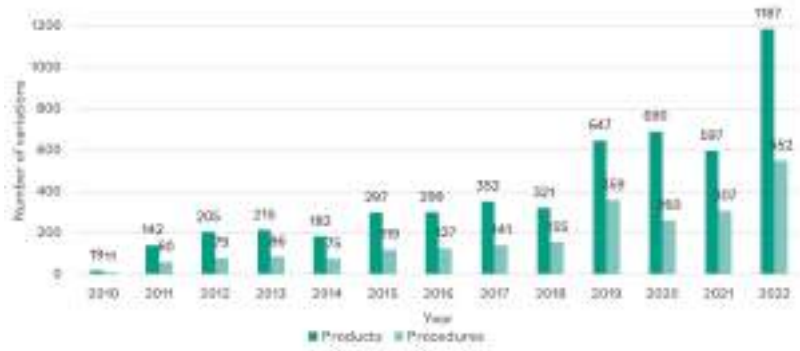

Figure 3.9: An overview of the number of VARS applications (with resulting product information changes) received for procedures with MT as RMS

Figure 3.10 gives a breakdown of variation applications received by type and applications for the renewal of Marketing Authorisations.

Figure 3.10: The number of post-authorisation applications received by MMA for procedures where MT is RMS (2010-2022)

The portfolio of procedures where Malta is the rapporteur or co-rapporteur in the centralised procedures also continues to increase as Malta takes on more new procedures each year. Thirty-three (33) post-authorisation activities for centralised procedures where Malta is rapporteur were reported for 2022. Twenty-four (24) were variations, including Type 1B and Type II variations, while nine (9) were renewal of MAs (***Figure 3.11***).

Figure 3.11: Cumulative number of post-authorisation procedures with MT as co/rapporteur in the centralised procedure (2011-2022)

In 2022, the MMA received two thousand nine hundred and eighty-one (2981) variation applications and other post-authorisation procedures including sixty seven (67) Renewals and fifty-two (52) Article 61(3) notifications (***Figure 3.12***), for products authorised through the MRP with Malta as CMS.

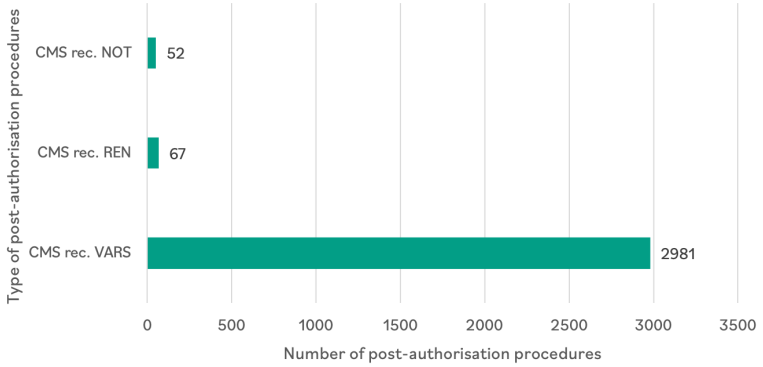

Figure 3.12: Post-authorisation procedures received by MT as CMS in the MRP in 2022

Figures 3.13, 3.14 and ***3.15*** show the number of national post-authorisation procedures, including Renewals, Variations, Marketing Authorisation Holder (MAH) transfers and Notifications in accordance with Article 61(3) of Directive 2001/83/EC.

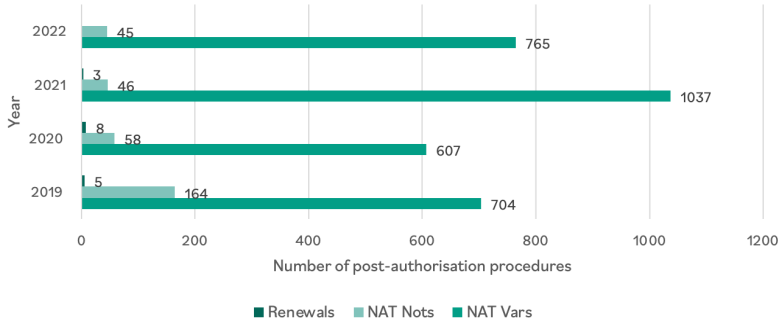

Figure 3.13: Number of post-authorisation procedures for NAT MAs received in 2022 (N=810)

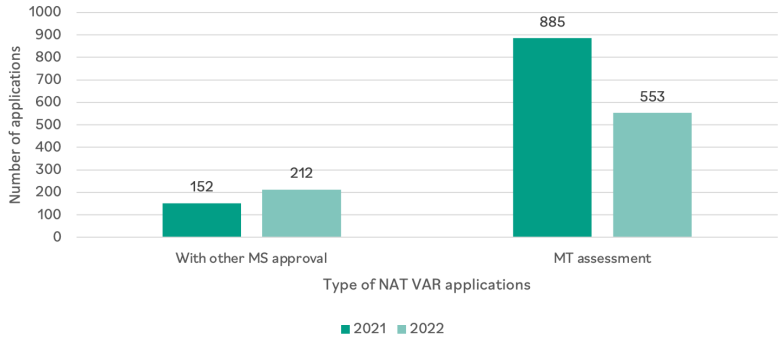

Figure 3.14: Number of NAT VARS with assessment for 2022 (N=765)

Over the previous year the number of post-authorisation procedures decreased for these products because of the reduction in number of nationally authorised medicinal products, mainly withdrawn because of Brexit. This has been offset by the increase in the number of procedures authorised through other routes, mainly European procedures, with Malta acting as both RMS and CMS.

Figures 3.15 and ***3.16*** show the number of post-authorisation procedures for authorisations in accordance with Article 126(a) of Directive 2001/83/EC and Parallel Import licenses, including Notifications of change and Renewals. It has been noticed that holders of authorisations in accordance with Article 126a of Directive 2001/83/EC are not submitting Notifications of change when the product changes in the source country. It is important that product information is kept up to date and in line with that authorised in the source country, to ensure complete information for patients and Healthcare Professionals. There are ongoing discussions on how to support local authorisation holders to submit these Notifications.

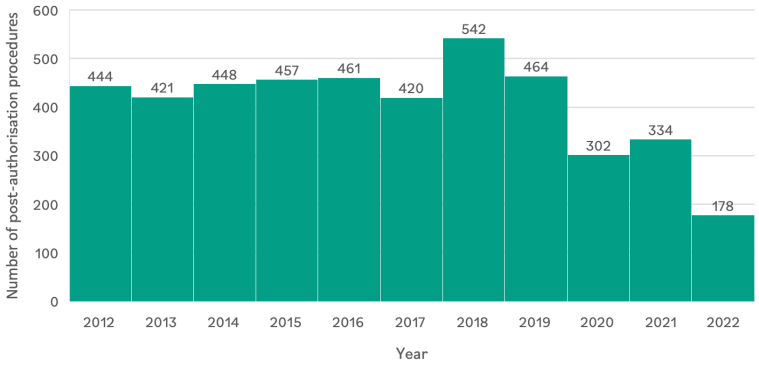

Figure 3.15: Number of post-authorisation procedures received for authorisations in accordance with AA of Directive 2001/83/EC in 2022 (N=178)

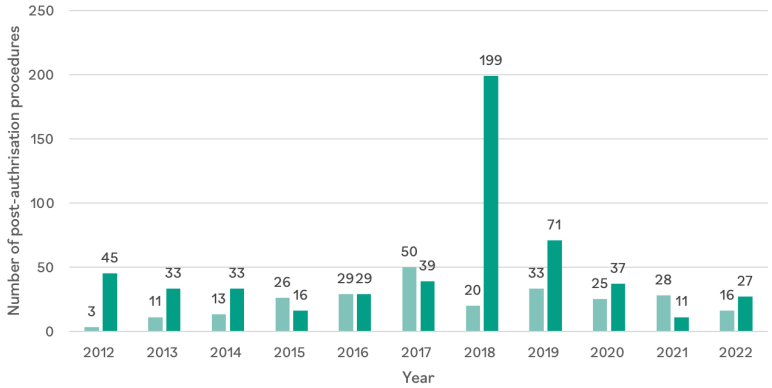

Figure 3.16: Number of post-authorisation procedures received for PI licences in 2022 (N=43)

Brexit

Since Brexit, it has been a priority for the Licensing Directorate, to assist stakeholders in ensuring continuity of supply by providing support for them to carry out the necessary regulatory changes to come in line with EU legislation.

In April 2022, the European Commission published Directive (EU) 642/2022 extending further the derogations previously covered by Commission Notices, allowing for the granting of authorisations in accordance with Article 126(c) on the basis of Marketing Authorisation granted in the UK.

The Licensing Directorate continued to receive further exemptions for products authorised before Brexit, which resulted in the continued availability of over seven hundred (700) products, which can continue to be made available to the Maltese market, in particular to the National Health Service, which were granted previous to Brexit date.

In addition, until end of 2022, one hundred and seventy-two (172) new authorisations were granted on the basis of UK Marketing Authorisations, where availability from other Member States was not possible, on the basis of Article 126(c) as amended by Directive (EU) 642/2022. Other derogations were granted, mainly to derogate from the need of batch testing or batch release of products in the European Union. Over sixty products are benefitting from these derogations.

Reports on the derogations granted on Directive (EU) 642/2022 are reported to the EC on a 6-monthly basis and are published on the MMA website.

Committees, Working Groups and National Advisory Services

Advisory Committee

The Advisory Committee continues to meet regularly to discuss the public health need of product applications in accordance with Article 126(a) of Directive 2001/83/EC and Article 20 of the Medicines Act. Wherever this is possible, companies are invited to use the Mutual Recognition Procedure to place their products on the Maltese market. The members of the Advisory Committee, together with the Medicines Intelligence and Access, also discuss each application and investigates the availability of other authorised products on the market. The Advisory Committee met thirty-four (34) times in 2022 to discuss these applications. The agendas and relevant outcomes from the discussions are published on the MMA website for enhanced transparency.

Prescription Status Working Group

During 2022, the Prescription Status Working Group (PSWG) continued to work on the harmonisation of the legal classification of medicinal products (prescription versus non-prescription). Apart from the legal classification of medicinal products, the PSWG worked to harmonise classification by therapeutic class and discussed several cases relating to the availability of medicinal products in view of the new requirements of prescription-only medicinal products due to the Falsified Medicines Directive (FMD).

Borderline Classification Committee

The Borderline Classification Committee (BCC) of the MMA classifies products into either medicinal products or non-medicinal products when requests for classification are received from companies or from other sources. The Committee meets regularly, and feedback is sought from all members including national experts such as herbal and paediatric experts. International experts are also consulted. The BCC also participates in the European Directorate for the Quality of Medicines and Healthcare (EDQM) Borderline Products Network Meeting which in 2022 was held in Strasbourg. In 2022, forty-one (41) applications for the classification of borderline products were received, out of which thirty-one (31) were considered as non-medicinal and three (3) were considered medicinal.

Scientific Advice

The objective of Scientific Advice procedures is to discuss with the MMA scientific matters regarding the development and licensing of medicinal products. In this context applicants have the opportunity to obtain input with regard to questions related to procedures which are in the remit of the Malta Medicines Authority.

On a national level, the MMA is continuously seeking to expand its remit as a reputable scientific advisory centre.

Scientific Advice Working Party (SAWP)

Since 2018, the Authority has also been engaging in scientific affairs regarding the development and licensing of Medicinal products through the active participation in the EMA SAWP advice. Experts of the Malta Medicines Authority continue to receive training through the European network. This is important to maintain a high level of expertise required for the assessment activities to assess company data of diverse products and maintain life-cycle management of medicinal products. Each month, the Authority receives a list of procedures and bids for products it would like to assess. Both external and internal assessors are engaged in assessing these products. In 2022, the Authority fully participated in SAWP activities assessing nineteen (19) SAWP requests.

Patient safety is a priority area for the MMA as it continues to strengthen its efforts to ensure the safe use of medicinal products on the local market. The Pharmacovigilance role of the MMA includes the evaluation, monitoring and communication of safety related data and, where appropriate, implementation of regulatory action to maximise benefit and minimise risks associated with medicinal products.

The collection, investigation and transmission of Adverse Drug Reaction reports to EudraVigilance comprises a major Pharmacovigilance activity carried out by the MMA. In 2022, the Authority continued to receive ADR reports from local Healthcare Professionals as well as from patients and consumers.

The Authority continued the implementation of its ADR promotion strategy, which for 2022, included the participation in a face-to-face seminar targeting HCPs on vaccinology and participation in the annual ADR awareness week social media campaign (#MedSafetyWeek). During the seminar on vaccinology, MMA staff delivered a session about vaccine safety where participating HCPs were advised on how to report ADRs following COVID-19 vaccine administration. In 2022, #MedSafetyWeek was held between 7th and 13th November 2022 and aimed to increase awareness on the importance of monitoring of side effects and encouraging reporting of side effects by both Healthcare Professionals and patients.

The MMA has direct access to all reports in the EU EudraVigilance database for signal detection activities. Furthermore, European IT applications such as EudraVigilance Data Analysis System (EVDAS) allows for detailed analysis of ADR data.

A total of one hundred and forty-seven (147) Individual Case Summary Reports (ICSRs) were registered in 2022. These cases detailed at least one (1) ADR to the medicinal product concerned and together these 147 ICSRs resulted in three hundred and ninety-three (393) suspected ADRs. ***Figure 3.17*** gives a breakdown of these ADRs according to System Organ Class (SOC) classification.

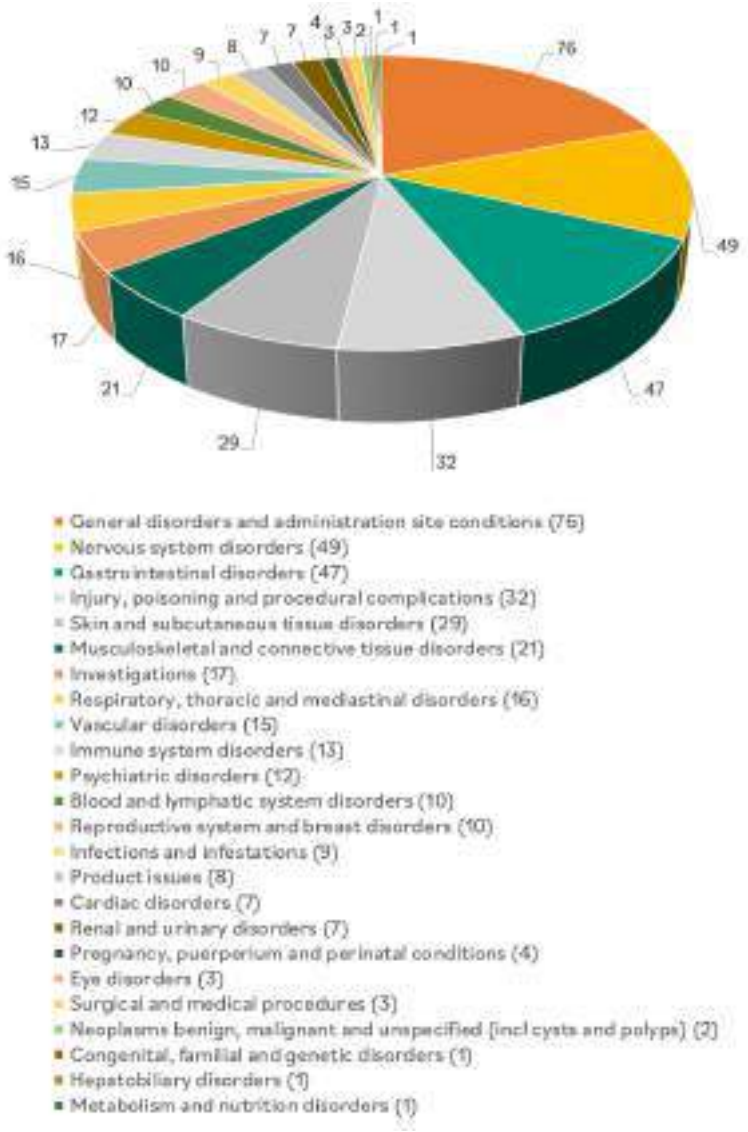

Figure 3.17: Distribution of ADRs according to SOC in 2022 (N=393)

Each case report received at the MMA was assessed and reported electronically to the EMA and the World Health Organisation (WHO) as the central ADR repositories.

Figures 3.18 and ***3.19*** further classify the adverse ICSRs (as received over 2022) according to seriousness and patient age respectively. The severity of the adverse reaction is normally assigned by the reporting Healthcare Professional or by the MMA following careful assessment and consideration of applicable factors such as dose of the medicinal product, indication for use, concurrently administered drugs and underlying patient disease.

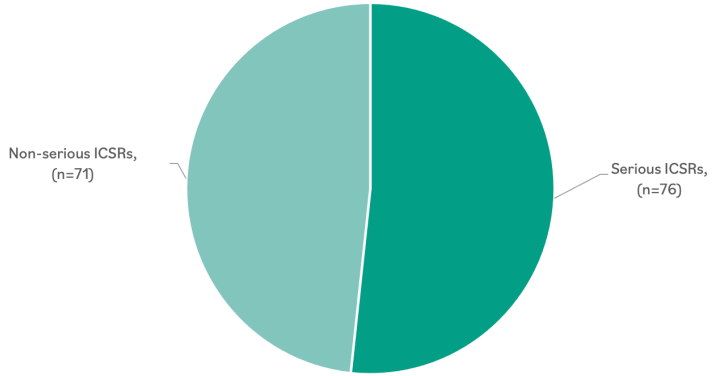

Figure 3.18: Frequency of ICSRs according to seriousness in 2022 (N=147)

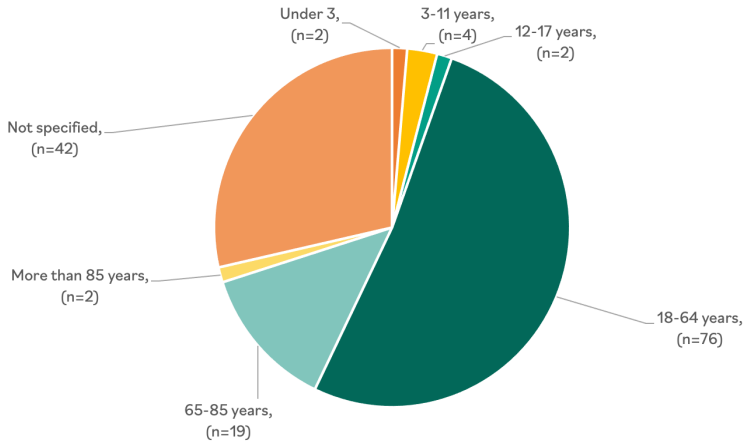

Figure 3.19: Distribution of ICSRs according to patient age in 2022 (N=147)

In addition to the management of ADRs and routine safety signal management as relevant, several other activities were undertaken nationally by the Authority in 2022 for purposes of attaining effective product safety surveillance. Such activities (amongst others) include the:

- Approval of Direct Healthcare Professional Communications (DHPCs) detailing safety/risk changes to scientific information and recommendations on product administration methods, and where necessary co-ordinating joint DHPCs when several MAHs are involved;
- Investigation of newly identified emerging safety issues, Rapid Alerts (RAs) and Product Safety Recalls (PSRs), which where necessary, can lead to immediate product suspension and/or recall;
- Approval and monitoring of Risk Minimisation Programmes (RMPs) and educational material relating to high risk medicinal products as well as approving Pregnancy Prevention Programmes (PPPs) as proposed in relation to potentially teratogenic medicinal products;
- Issue of Safety Circulars and Media Statements addressed to Healthcare Professionals and the general public respectively. Safety Circulars give recommendations on medicinal product use and applicable cautionary and precautionary measures. Throughout 2022 the Authority continued implementing the SMS notification service that allows subscribed medical and HCPs to receive alerts and links to the safety circulars as soon as they are published on the website;
- Initiation and subsequent approval of variations to scientific medicinal product information relating to identified novel or increased risk (Urgent Safety Restrictions);
- Assessment of Periodic Safety Update Reports (PSURs) for nationally authorised products containing active substances or active substance combination not included in the list of European Union Reference Dates (EURD list) and Periodic Safety Update Report Single Assessments (PSUSAs) work-sharing at a EU level;
- Assessment of risk management plans during national and centralised procedures.

Table 3.1 gives the distribution of Safety Communications and Risk Minimisation Measures (RMMs) approvals which the MMA handled over 2022:

Activity	Number of safety communications and RMM approvals
DHCPs	9
Joint DHPCs	4
Safety Circulars	10
RMMs	107

Table 3.1: Safety Communications and RMMs approvals in 2022

An additional stakeholder service performed by the MMA is that of responding to any queries related to Pharmacovigilance activities in a timely manner. In 2022, queries received were mostly related to:

- Submission requirements of PSURs/PSUSAs;
- Qualified Person (QP) for Pharmacovigilance/Local Contact Person for pharmacovigilance; and
- National Pharmacovigilance legislation and requirements locally (***Table 3.2***).

Area Queries	Number (n)
Submission requirements of PSURs	5
QP for Pharmacovigilance/Local Contact Person for Pharmacovigilance	4
National Pharmacovigilance legislation and requirements locally	4
Literature monitoring requirements	3
Risk Management Plans/Risk Minimisation Measure/Educational Material	3
Post-Authorisation Efficacy Studies (PAES) and Post-Authorisation Safety Studies (PASS)	3
Development safety update report	3
Direct Healthcare Professional Communication	2
ADR Reporting/ICSR transmission requirements	2
Safety Signal Detection	1
Clinical Trial Suspected Unexpected Serious Adverse Reactions (SUSARs)	1
Others	1
Total	**32**

Table 3.2: Pharmacovigilance related queries in 2022 (N=32)

Clinical Trials

The role of the MMA with respect to clinical trials is to evaluate both the quality of the investigation and the patient safety of clinical trials and provide recommendations to the Licensing Authority who provides authorisation based on the Authority's and the Health Ethics Committee's recommendations. For 2022, no clinical trial assessment procedures are pending.

The new Clinical Trials Regulation (Regulation (EU) (CTR) No 536/2014) came into application on 31st January 2022. The Regulation is part of a broad initiative to transform the EU/EEA clinical trials environment in support of large clinical trials in multiple European countries, to the benefit of medical innovation and patients. The Regulation introduces an authorisation procedure based on a single submission via a single EU online portal (the Clinical Trials Information System (CTIS)) an assessment procedure leading to a single decision for multinational trials, improved rules on the protection of subjects and informed consent, and new transparency requirements. Currently a three (3)-year transition period is in effect.

Advertising of Medicinal Products

The MMA monitors the advertising of medicinal products and the issue of any promotional material related to such medicinal products being presented either to the public or to Healthcare Professionals. Regulation of promotional material such as the provision of medicinal product samples to Healthcare Professionals and the sponsoring of promotional activities or scientific congresses is also regularly undertaken. Advertising and promotional material regulatory control is implemented according to the criteria set out within the Medicinal Products (Advertising) Regulations. Control of advertising is also implemented via the ad hoc selection and investigation of local advertisements as presented within the major media formats. This activity principally aims at ensuring public health protection via the affirmation that the applicable legislation is constantly being upheld and rigorously adhered to. Monitoring is mainly implemented via the application in accordance with European legislation of a self-regulatory approach whereby medicinal product advertising complaints as reported by external stakeholders are assessed and investigated in detail for purposes of verifying claims of breaches to the Advertising Regulations. For 2022, no advertising complaint procedures are pending.

The patient-centred ethos is the foundation of the functions of the Medicines Intelligence and Access. The Headship liaises with the health authorities, wholesale distributors and Healthcare Professionals to ensure that the medicines needs of the patients are met. To counteract the risk of shortages secondary to Brexit and maintain accessibility to medicinal products on the local market, the Licensing Authority has delegated the assessment of Article 20 exemption requests to the MMA, where the latter has invested in a competence infrastructure within the MIAU to fulfil these duties.

The Article 20 exemption of the Medicines Act (Chapter 458 of the Laws of Malta) allows the Licensing Authority to place medicinal products on the Maltese market in the absence of a Marketing Authorisation in response to exceptional and justified public health reasons. The Article 20 exemption is reserved solely as a measure when registration options through a Marketing Authorisation, authorisation in line with Article 126(a) of Directive 2001/83/EC and parallel importation have been exhausted as possible sourcing routes. The Authority liaises with the concerned public and private stakeholders during the vetting process. Following a thorough review, recommendations and conditions to the Licensing Authority to grant or refuse the request are provided.

In 2022, seven hundred and eighty-three (783) applications were approved. ***Figure 3.20*** describes the classification of medicines approved according to therapeutic class.

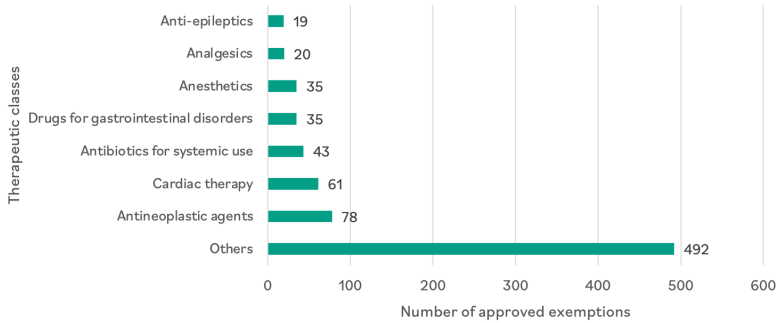

Figure 3.20: Most common therapeutic classes approved under Article 20 exemption in 2022 (N=783)

The reliance of the availability of medicines on the Maltese market which are sourced from the UK is depicted in ***Figure 3.21***. This dependence is multifactorial and could be the result of the lack of interest from EU pharmaceutical operators to market their products in small Member States like Malta, but also due to issues of labelling where packs sourced with product information in the English language are deemed acceptable for the local market without the need of over/re-labelling. Only 28% of the approved Article 20 requests are sourced from EU markets (***Figure 3.21***) which aligns with principles of best regulatory practice to promote the registration of products on the market prior to resorting to the Article 20 exemption. The Article 20 exemption was also granted to medicinal products sourced from UK, Canada (CA) and the United States of America (USA).

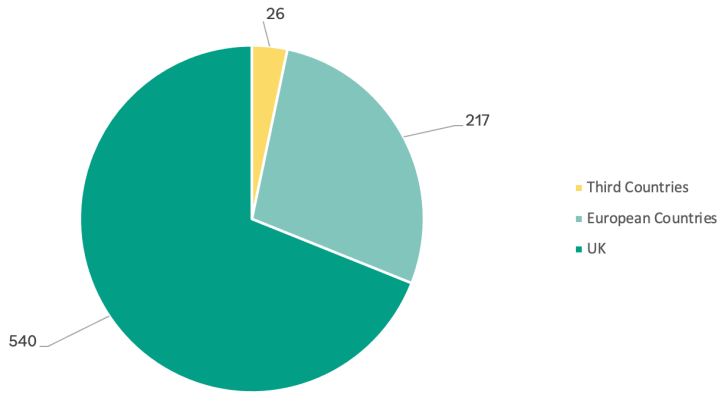

Figure 3.21: Country of source of medicinal products approved under article 20 exemption in 2022 (N=783)

Patients, HCPs and patient organisations are supported in their queries with targeted recommendations from the Headship, to ensure sustainable access to medicines through added value therapeutic interventions. In 2022, the MIAU handled on an individual basis ninety (90) queries related to shortages, pharmacoeconomic, registration and safety issues which included cases such as availability of rabies vaccine, introduction of new innovative medicines and supporting the Licensing Directorate with regards to investigating availability of medicines on the Maltese market as shown in ***Figure 3.22.***

The Headship proactively addresses emerging medical needs by assisting in the sourcing and supply of new medicines. To ensure continuity of supply and access to medicines, eleven (11) Named Patient Basis forms were processed by the Headship's and a positive recommendation was sent to the Licensing Authority.

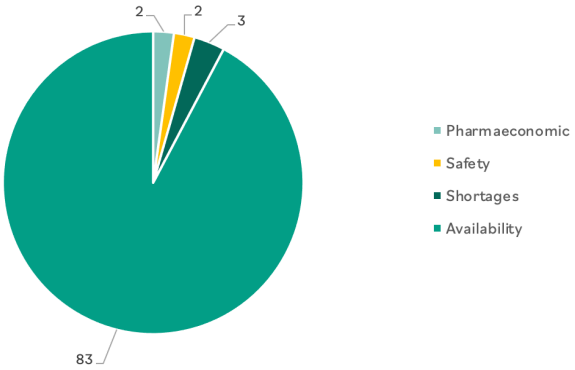

Figure 3.22: Number of interventions in 2022 (N=90)

During the year 2022, members of the Headship attended seven (7) teleconference meetings of the Medicines Shortages Single Point of Contact (SPOC) Working Party which was formally established in May 2022 in accordance with the Regulation on EMA's Reinforced Role (Regulation (EU) 2022/123). Intelligence on medicines including shortages was gathered during these meetings to prepare for disruptions in supply of medicines that may impact Malta.

The MMA is the National Competent Authority for Medical Devices through its Medical Devices and Pharmaceutical Collaboration Directorate. The Directorate reinforces the Authority's commitment in placing patient safety at the centre of all its regulatory activities by applying the robust regulatory principles diagnostics in line with national and European Union legislation and best practices to the field of Medical Devices and In-Vitro Diagnostics (IVD). The overarching aim of the Directorate is to enhance patient safety by overseeing procedures relating to registration of economic operators, notification of Medical Devices/In-Vitro Diagnostics, vigilance and market surveillance and assisting the national stakeholders in ensuring that Medical Devices placed on the local market are safe for the public and function as intended.

Stakeholder Focus: a Patient-centred approach

The Directorate strives to improve stakeholders' access to its services by actively addressing the queries whilst encouraging communication with stakeholders in the area of Medical Devices and In-Vitro Diagnostics adopting a patient-centred approach. In 2022, the Directorate addressed a total of two hundred-thirty (230) queries. The Directorate proactively contributed and shared their expertise by participating in the accredited course "*Award in Good Distribution Practice in Medical Devices*" held in collaboration with the Malta Laboratories Network (MLN) Institute for Scientific Development. The course was designed at addressing knowledge lacunae and strengthening comprehension of EU regulations as applicable in daily practice.

On an international level, the Directorate actively participated at eighty-five (85) international meetings and European Commission working groups meetings. On a national level, a total of one hundred and forty-four (144) meetings involving local governmental entities, such as Central Procurement and Supplies Unit (CPSU), Mater Dei Hospital (MDH), the line Ministry and stakeholders involved in the Medical Device industry coming from the national front and/or international front were held.

Authorisation Activities

The Directorate is responsible for the processing of applications in relation to regulatory operations of Medical Devices and In-Vitro Diagnostics. The ***Medical Devices Registration application form*** refers to the registration of Medical Devices placed on the EU Market, by applying through the MMA. Economic operators and entities intending to carry out operations related to Medical Devices and IVD in Malta are to register with MMA through the ***Organisation Registration form.*** In addition, in line with national legislation, a distributor or importer should appoint a Medical Device Registered Person (MDRP) responsible for regulatory compliance and who should be registered with the MMA. This is done through the ***Medical Device Registered Person application form***. These processes provide easier coordination of surveillance and activity allowing increased transparency and accountability in the field. ***Certificate of Free Sales*** are issued by a European Competent Authority (ECA), in this case by the MMA, upon technical regulatory consideration following a request by a manufacturer or an authorised representative.

Tthe Directorate embraced challenges brought about by COVID-19 and put forward a regulatory framework to safeguard public safety. The COVID-19 related applications provided an oversight and surveillance on a point-of-care COVID-19 test or device for self-testing for COVID-19 on the local market. In addition, point-of-care COVID-19 tests need to be performed on designated premises certified by the Malta Medicines Authority.

Application Type	Number Received
Medical Device registration	169
Organisation registration	58
COVID-19 designated premises	46
COVID-19 Rapid Antigen Test (RAT) notification	47
Medical Device Registered Person Registration	46
Certificate of free sale	64

Table 3.3: Applications processed in relations to operations of stakeholders in the MD and IVD field (N=430)

Notified Bodies, Surveillance and Clinical Relations

The Notified Bodies, Surveillance and Clinical Relations within the Medical Devices and Pharmaceutical Collaboration Directorate is responsible for the designation of conformity assessment bodies' to become Notified Bodies under the Medical Device Regulations and for their subsequent oversight in monitoring the operations of the designated Notified Bodies. Market surveillance is proactively provided for Medical Devices and In-Vitro Diagnostics and the economic operators. It promotes a patient-centred clinical relations approach by co-ordinating vigilance through the evaluation of reported incidents and complaints. The Headship contributes to establishing a patient-centred clinical investigations hub in Malta by assessing applications for clinical investigations and performance studies for the safety, clinical performance and/or effectiveness of a device. These operations ensure safeguarding the safety, efficacy and quality of Medical Devices on the local market and within the European market.

Designation of Notified Bodies

The Directorate is proactively addressing the international challenge of shortages in Notified Bodies in the area of Medical Devices and In-Vitro Diagnostics in accordance with the European Union regulations through its commitment to designate and subsequently continuously monitor the performance of Notified Bodies registered in Malta. Two joint assessment audits led by the Directorate in collaboration with the joint assessment team composed of European experts were undertaken for the two respective conformity assessment bodies which applied in Malta to become designated as Notified Bodies. The designation process is a continued procedure set to continue in 2023.

Clinical Relations: Vigilance

In 2022, a total of one hundred and fifty-three (153) incident reports were processed. The incident reporting system was reviewed and updated with a pilot project being undertaken in collaboration with MDH and the CPSU. A total of one hundred and thirty-two (132) Field Safety Corrective Actions (FSCA) were received and processed.

Continuous Professional Development Training

Technical capacity was increased by the addition of four (4) personnel each undergoing internal induction training. The Directorate is committed to keep abreast with the dynamic advancements in the field of practice and professional development in order to enhance the Directorate service in the interest of the patients we serve. In 2022, the Directorate actively participated in twenty-one (21) academic training courses and seminars at international and national level. Two onsite visits at Regulatory Competent Authorities (RCA) for Medical Devices in Finland (FI) and Denmark (DK) respectively were undertaken in addition to site visit to an Official Medicines Control Laboratory (OMCL) in Switzerland (CH).

New Initiatives and Challenges

The Directorate has been designated as a work package leader in one (1) of the technical packages pertaining to the *EU4 Health Joint Action on Market Surveillance: Direct grants to Member States' authorities: reinforced market surveillance of Medical Devices and in vitro medical device – Joint Action.* The Directorate is leading Work Package 5 focusing on Signal Detection in the area of Medical Device Vigilance with a total of twenty (20) participating countries including Malta. The Directorate is also actively participating in two other Work Packages namely Work Package 6 focusing on Inspections and Work Package 8 focusing on *Academic Training of Experts in the Area for Medical Devices and In-Vitro Diagnostics.* Through its collaborative arm, the Directorate is undertaking a feasibility study for establishing an Official Medicines Control Laboratory in Malta taking into consideration innovation and best practices within a sustainable framework.

4. Maintaining and Ensuring the Highest Standards for Pharmaceutical Activities in the Best Interest of Patient Safety

The MMA is responsible for inspecting and recommending the issue of licences for manufacturers and wholesale dealers according to national legislation, EU-Good Manufacturing Practice and EU Good Distribution Practice (GDP) respectively, while pharmacies are inspected against national legislation and standards. The MMA also carries out Good Clinical Practice (GCP) inspections of clinical trials on a risk-based approach and Pharmacovigilance inspections.

Pharmaceutical Inspections: Manufacturing, Importation and Distribution

Manufacturing and Importation

All medicinal products for human use manufactured or imported into Malta and the EU, including medicinal products intended for export, are to be manufactured in accordance with the principles and guidelines of GMP. The Inspectorate and Enforcement Directorate within the MMA manages and maintains a portfolio of seventy-nine (79) licensed/certified entities, local and in third countries, involved in the manufacturing, importation or other GMP related activities of medicinal products for human use.

During 2022, the MMA carried out twenty-one (21) local GMP inspections for new, renewal or follow up of GMP licences/certificates. These included:

- Seven (7) inspections for full-line non-sterile solid dosage forms manufacturers;
- Two (2) inspections for Active Pharmaceutical Ingredients (API);
- Four (4) GMP inspections for manufacturing authorisations of repackaging and re-labelling/partial manufacturing operations;
- Eight (8) GMP inspections for manufacturing authorisations of importation activity.

Moreover, in 2022 the MMA:

- Processed forty-two (42) manufacturing authorisations administrative variation applications for manufacturers and importers;
- Processed four (4) application variations which required a GMP inspection.

There were no Inspections Review Group (IRG) meetings necessary to be held throughout 2022.

During 2022, the MMA received four hundred and eighty-nine (489) rapid alert and GMP non-compliance notifications, which were investigated and out of which five (5) resulted in a recall of medicinal products from the local market.

Distribution

A distributor of medicinal products sources the products from within the EU/EEA. Distributors are required to follow good practice guidelines known as GDP in order to ensure that the quality of the medicinal products is not compromised in the supply chain and in order to be in a position to carry out a recall of any defective product. The Inspectorate and Enforcement Directorate within the MMA currently manages and maintains a portfolio of ninety-nine (99) licensed/certified local entities involved in wholesale-dealing and brokering activities of medicinal products for human use, and of API distribution and importation.

During 2022, the MMA has also fulfilled its GDP inspection plan where thirty-six (36) GDP inspections were carried out. Also, eight (8) applications for new wholesale dealing licences were submitted, of which four (4) were eventually licensed by the end of the year. Another three (3) applications submitted in 2021 were licenced during year 2022. Forty-four (44) variation applications for wholesale dealing authorisations for medicinal products and active ingredients were processed in 2022, out of which six (6) required an inspection. In 2022, two (2) new applications for brokerage activity were received, out of which none (0) was eventually registered. Three (3) applications for API Registration were submitted and none of them where eventually registered.

Third Country Inspections

During the year under review, the MMA carried out eighteen (18) onsite GMP Inspections in countries outside the EU, whilst another five (5) GMP inspections in countries outside the EU were carried out through distant assessment/virtual inspections due to safety and travel restrictions being in place because of the ongoing COVID-19 Pandemic (***Figure 4.1***). These distant assessment/virtual inspections were carried out for sites already previously inspected in order to vary or renew existing GMP certificates issued by the MMA. However, Good Manufacturing Inspections in countries outside the EU were generally interrupted due to COVID-19 pandemic travel restrictions in the first quarter of 2022. Incoming applications in that time were still validated and put on hold so as these can be processed, and inspections carried out onsite afterwards when travel restrictions were uplifted, according to priorities at that time. Through this process, the MMA is facilitating the possibility that more companies would be in a better position to import medicinal products within the EU. Additionally, these procedures attract new revenue to the Authority and provide exposure to different manufacturing facilities to the inspectors of the MMA.

Figure 4.1: Number of third country EU-GMP inspections carried out in 2022 (N=23)

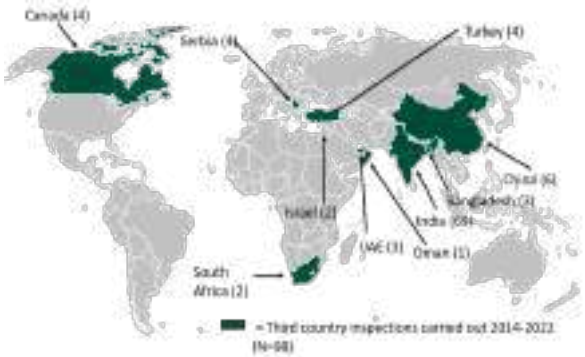

Figure 4.2: GMP third country inspections carried out between 2014-2022 (N=98)

Clinical Trials and Pharmacovigilance Inspections

During 2022, in view that no new Clinical Trials applications were submitted to the MMA, no inspections for this activity were required.

Four (4) Pharmacovigilance inspections were carried out in 2022, for local entities.

Pharmacies, Pharmacovigilance and Surveillance of the Local Market

The Regulatory Operations, Medicines Intelligence and Access Directorate regulates and manages and maintains a portfolio of two hundred and fifty-one (251) licensed pharmacies, which include two hundred and thirty-four (234) pharmacies serving patients in the community, eleven (11) hospital and two (2) government pharmacies.

In 2022, two (2) spot-check pharmacy inspections were carried out, nine (9) pharmacy relocations were inspected and approved, two (2) new pharmacy licences were issued and fifty-three (53) administrative variations for pharmacy licences were processed.

The MMA continued its collaboration with the Inspection Coordination Office towards the automation of a risk assessment model and the launch of the Certificate of High Standard of Compliance. The MMA invited all pharmacies to enrol in the K2 software and perform a self-assessment checklist through the inspection portal. A total of one-hundred and ten (110) pharmacies carried the online self-assessment form in 2022.

Moreover, in 2022 the MMA pursued its collaboration with the Medicines and Health Regulatory Agency (MHRA UK) so that the latter carries out testing in an Official Medicines Control Laboratory for the MMA of any medicinal products sampled during inspections and from the local market as part of the market surveillance programme. In this regard, the Local Market Surveillance Plan for 2021 was closed positively. In 2022, five (5) products were sampled from the local market and were sent for analysis for the Market Surveillance.

Enforcement of Legislation

During 2022 the MMA worked upon four (4) enforcement cases/investigations which were related to receiving complaints. The Enforcement Committee (a specific committee which discusses enforcement cases, chaired by the Licensing Authority) was not required to meet in 2022.

In 2022, the MMA attended one (1) court case sitting in which the Authority's employees were summoned as witnesses.

Granting of Qualified Persons Status and Certification of Pharmaceutical Products (CPPs)

In 2022, the MMA received twenty-two (22) new applications for the Qualified Person status eligibility which were processed. Fifteen (15) of these applicants were interviewed during 2022 and were approved as eligible for QP status. Seven (7) other applicants that submitted the application in 2021 were interviewed and also approved in 2022.

The MMA received two hundred and ninety-five (295) Certificate of Pharmaceutical Products applications which were processed with all certificates being issued.

5. Translating Regulation into Patient-Centred Science

The MMA is a significant player in Europe and globally, promoting the sharing of successful strategies and influencing policies for the benefit of patients. To maintain its achievements and promote further development, the MMA is continuously expanding its ability and capabilities to adapt to changes in global regulations. The MMA encourages professional training and ongoing development by providing access to training resources, tools, and opportunities for knowledge sharing which is vital for capacity building of a skilled workforce. The Educational Planning and Academic Development (EPAD), established within the ASID, is dedicated to conceptualisation, development and implementation of academic programmes that draw on multiple disciplines. This Headship is responsible for designing and delivering courses and activities that integrate knowledge and skills from different fields of study with the goal of providing a well-rounded and holistic education to MMA employees and relevant stakeholders.

The ASID fosters research, thought and analysis, whilst contributing to the consolidation of EU expert views on emerging topics relevant to innovative therapies and technologies. International collaboration with academia is encouraged through fellowship programmes and by encouraging local stakeholders to invest in research opportunities. The MMA is working on the extension of the International Fellowship Programme, spearheaded by the MMA for the past nine (9) years, to the postdoctoral level. The postdoctoral Fellowship Programme will provide training opportunities for doctoral graduates to develop their research skills further and gain additional experience in the field of pharmaceutical regulatory sciences. The MMA is exploring the possibility of collaboration with the Department of Pharmacy at the University of Malta on the launch of the Fellowship Programme on the basis of reciprocity and mutual benefit. The development of a postdoctoral programme is a complex process that requires careful planning and consideration of the needs and goals of both the fellowship recipients and the host institution. During the planning stage, a number of criteria were established such as the goals, duration, number of fellowships and funding opportunities.

Research Strategy, Innovative Growth and Regulatory Response

The research team within the ASID conducted an internal educational needs analysis to determine the training needs within the MMA and to promote and increase involvement in the EU-Network Training Centre (EU-NTC). The needs analysis aimed to identify and address any gaps in skills and knowledge and evaluate the utility and success of available training resources. Internal information sessions on the EU-NTC Learning Management System were developed and delivered, in collaboration with the EU-NTC, to increase awareness and enhance participation in scientific, regulatory and telematics training.

The ASID, through its research arm, conducts horizon scanning for key areas of innovation in pharmaceutical regulatory sciences to identify and evaluate emerging trends and technologies that have the potential to impact the regulation of pharmaceuticals. One key area of focus is the use of Real-World Data (RWD) and Real-World Evidence (RWE) in regulatory decision-making. RWD and RWE can provide valuable insights into the safety and effectiveness of medical products in actual clinical practice but research on the quality and reliability of this data is lacking. Research was also conducted on the possibility to establish a specialised Medical Counter Measures (MCM) unit within the Authority that would be responsible to ensure that sufficient quantities of MCMs are available and can be readily deployed in the case of a public health emergency. This research aims to identify the areas of expertise, potential resources, and potential collaborations required to support the development of innovative treatments, cooperation and sharing of knowledge, coordination of the distribution of MCMs and provision of training and guidance on their use. Outcomes included improved skills and knowledge through the participation in training workshops on the regulatory aspects of vaccines and meetings held by the European Medicines Regulatory Network (EMRN) on COVID-19 vaccines.

The research team within the ASID collaborated with the Malta Council for Science and Technology (MCST) with the aim of exploring funding opportunities for specific research projects through Horizon Europe, the EU flagship programme for research and innovation. Relevant Work Programmes identified include the 'Widening participation and strengthening the European Research Area' and the 'Health Work Programmes'. The research team also collaborated on Malta's Research and Innovation Smart Specialisation Strategy (RIS3) 2021-2027 to help identify research areas of interest within the Health and Well-being thematic area, which focuses on cancer therapy, drug development, digital tools to support healthcare, e-health and bioinformatics, and biomedical engineering. Smart Specialisation is a place-based approach that help regions become more competitive and innovative by identifying strategic areas for development and growth, based on the analysis of strengths, research and innovation potential and an Entrepreneurial Discovery Process (EDP) with wide stakeholder involvement.

Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences

The MMA is committed to progress training and education whilst sustaining a strong knowledge-base, enhancing the scientific acumen, and sharing best practices for a continuous improvement. In 2022, the EPAD, within the ASID, prioritised bolstering of the framework for the MMA Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences, encompassing the apposite elements of accreditation, collaboration and optimisation. Pursuant to the official accreditation of the Award in GDP at Level 5 on the MQF through the Malta Further and Higher Education Authority (MFHEA), the programme was delivered online, between February and March 2022, in collaboration with The Organisation for Professionals in Regulatory Affairs (TOPRA).

The uptake was notable with the course being fully subscribed by national and international stakeholders seeking to broaden their knowledge, skills, and competences to enrich their expertise in the field of GDP. Through this educational initiative, forty-eight (48) participants attained solid grounding on core aspects of GDP, crucial for upholding quality including GDP regulations and guidelines in the European Union, Quality Management personnel, storage requirements, computerised systems and their validation, equipment, integrity and security, returns and recalls, self-inspection, maintaining oversight and interactions with the license holder and regulator. Ninety-eight percent (98%) of the participants successfully completed the course and were granted a certificate.

The drive towards continued education, professional development and scientific exposures enables the identification of innovative strategic areas and tapping into funding opportunities, while supporting academic endeavours that enhance internal competence and meet stakeholder needs. The Seminar on Vaccinology as relevant to COVID-19 and the Workshop on the Dimension of Cannabis for Medicinal and Research Purposes were spearheaded by the MMA Academy in March and September 2022 respectively. Both initiatives were part financed by the Internationalisation Partnership Awards Scheme Plus (IPAS+) of the MCST.

The Seminar on Vaccinology as relevant to COVID-19 brought together over fifty (50) national and international participants working in the public and private health sectors for interdisciplinary exchange of expertise and real-world evidence about the landscape of COVID-19 vaccines. Keynote speaker Dr Marco Cavaleri, Head of the Office of Biological Health Threats and Vaccine Strategy at the European Medicines Agency and CEO of the EMA COVID task force together with local specialists in the fields of public health, paediatric infectious diseases and post-licensing delved into the development process of COVID-19 vaccines, the EUs regulatory process for evaluation and approval of vaccines, COVID-19 vaccines under investigation, evaluation and approved in the EU, therapeutics, adaptation of COVID-19 to variants, COVID-19 infection and vaccines in children, safety monitoring of COVID-19 vaccines and the local challenges and confidence with respect to COVID-19 vaccines. A panel comprising of four prominent local Healthcare Professionals discussed response to the COVID-19 pandemic, future perspectives and preparedness.

Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences

The Workshop on the Dimensions of Cannabis for Medicinal and Research Purposes enabled over one hundred and thirty (130) participating stakeholders with an interest in the dynamic field of medicinal cannabis to scrutinise, debate and constructively grasp scientific acumen delivered through the sharing of first-hand expert opinions and experience. Keynote speakers Professor Robert Nistico from the University of Rome "Tor Vergata", acclaimed in the field of pharmacology, and Professor Roger Guy Pertwee from the University of Aberdeen in Scotland, recognised for outstanding contributions, including the discovery of the endocannabinoids and the characterization of a Cannabidiol receptor type 1 (CB1) receptor allosteric site, explored the synaptic and molecular effects of cannabinoids and the potential therapeutic uses of some cannabis-derived and synthetic cannabinoids. Their contribution synergised well with that of local experts who covered diverse topics, including controversies surrounding the use of cannabis for medicinal and research purposes, legal aspects, the regulatory sciences landscape, analysis, and research initiatives conducted by the MMA on the subject.

Circumstantial exigencies and imminent national, international and organisational priorities influence the activities of the MMA in this dynamic area. The unprecedented outbreak of a disease caused by the monkeypox virus prompted an initiative intended to support preparedness, interdisciplinary exchange of expertise, response plans and ideas. In June 2022, the Monkeypox Seminar for Healthcare Professionals, led by the MMA Academy brought together multiple Healthcare Professionals working in the public and private health sectors for cooperation and dialogue on key aspects in relation to the monkeypox infection, including epidemiology, case notification and surveillance, laboratory diagnosis, clinical diagnosis, management, transmissibility, and prevention.

Wide dissemination of results and deliverables pertaining to initiatives organised by the MMA Academy was accomplished for the year 2022. These include publication of outcomes about the Seminar on Biosimilars and the Implementation of a Framework for the MMA Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences at the European Association of the Faculties of Pharmacy (EAFP) Annual Conference in May 2022, the Seminar on Vaccinology as relevant to COVID-19 at the 80th FIP World Congress of Pharmacy and Pharmaceutical Sciences in September 2022, and the MMA Academy as a gateway to advanced education at the Med-In Pharmacy Conference in November 2022.

Going forward, the EPAD Headship shall continue to build on the momentum achieved for the MMA Academy for Patient-Centred, Excellence and Innovation in Regulatory Sciences in the field of education, in partnership with local, European and international institutions, thematic experts alongside internal experts in the relevant fields. It will strive to design, develop and implement novel programmes, prospectively even online, that provide a platform where national and international participants exchange views, discuss opportunities, enhance competence and overcome challenges through collaborative reasoning for mutual benefit.

Cannabis for Medicinal and Research Purposes

Regulatory Activities

Two (2) legal frameworks principally govern the regulation of medicinal cannabis in Malta where through Article 10 of the Drug Dependence (Treatment not Imprisonment) Act (Chapter 537 of the Laws of Malta) patients may access medicinal cannabis preparations that either have a Marketing Authorisation in line with the requirements of the Medicines Act or have been produced under EU-Good Manufacturing Practice standards, as per the relevant provisions and prescribing protocols established by the Superintendence of Public Health (SPH). The MMA reviews applications for the sourcing of finished cannabis-based products, intended for the local market, ensuring the fulfilment of a number of requisites, such as EU-GMP certification, batch release specifications, certificates of analysis, stability studies and labelling. Chapter 578 of the Laws of Malta provides a legal basis for the production of cannabis for medicinal and research purposes. The regulatory framework, as published in the respective MMA Guidelines, involves a number of aspects, such as EU-GMP and Good Agricultural and Collection Practices (GACP) compliance, product-specific considerations including analytical data, security screening of personnel and security audits of the manufacturing facilities.

Twenty-nine (29) products with varied pack sizes have been approved for commercialisation through both wholesaling and production routes, where the charts in ***Figures 5.1*** and ***5.2*** respectively characterise their formulation and cannabinoid concentration. Equal distribution is noted for cannabis products in their inflorescence and oil formulation. Upon further stratification according to their tetrahydrocannabinol (THC) and cannabidiol (CBD) content, it is observed that nearly three quarters of the products fall in the THC-rich category. The cannabinoid concentration for the approved oils and extracts ranges from 25mg/ml for the most CBD-dominant product to a THC concentration of 8.7mg/10µL present in the purified extract. The most potent THC approved flower product has a concentration of 22 %w/w.

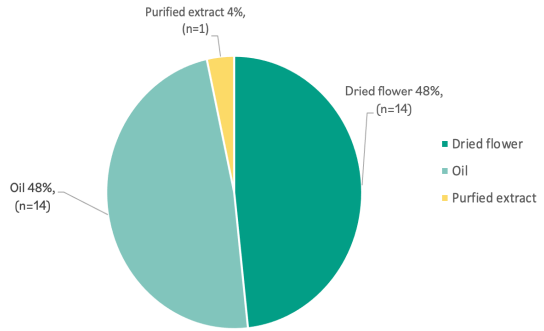

Figure 5.1: Characterisation of the approved cannabis-based products according to their formulation (N=29)

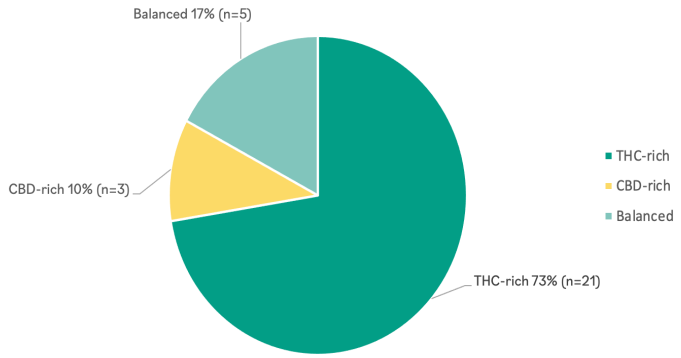

Figure 5.2: Characterisation of the approved cannabis-based products according to their formulation (N=29)

The Authority continuously safeguards the integrity of medicinal cannabis by instilling the notions of reconciliation and traceability with its stakeholders. For the purposes of security and product authenticity, approved wholesalers and production licence holders are provided with unique serialisation codes that are displayed on the packaging of the cannabis units. More than fifty thousand (50,000) serialisation codes were issued by the Authority to local operators throughout 2022 for product units intended to be marketed, surpassing the 2021 global amount by 51% (***Figure 5.3***). This same graph also denotes the relative proportions of commercialised units in terms of the destination market and product formulation. Traceability and reconciliation records are maintained accordingly and submitted to the Authority at stipulated intervals in line with international reporting obligations to track and quantify the movement of imported, processed, disposed and exported cannabis material from authorised suppliers to licensed clients and service providers across the supply chain.

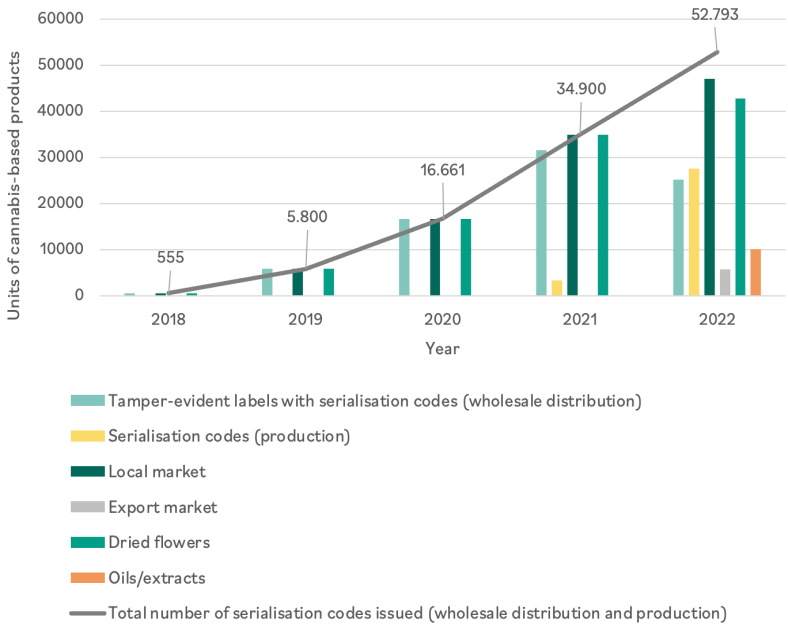

Figure 5.3: Units of cannabis-based products for medicinal use issued with a serialisation code, characterised by licensed/approved operation, destination market and product formulation

Since the first product approval in 2018, two (2) Adverse Events were reported and assessed accordingly. The portfolio of approved cannabis-based products is followed up with annual renewal, including review of emerging data in updated studies.

- **Wholesale Distribution**

  Three (3) operators have been approved for wholesale distribution activities, two of which source cannabis in its dried inflorescence form and another approved to source standardised oils in their finished state. A total of thirty-four (34) new and sixteen (16) renewal applications for cannabis-based products were received and reviewed by December 2022. A notification of approval was issued for seven (7) dried flower products and two (2) oils.

- **Production and Research**

  The total number of companies issued with a positive recommendation for the grant of a licence for the production of cannabis for medicinal and research purposes by end 2022 stood at five (5) from the seven (7) applications received, where one facility produces oils and purified extracts, another three (3) produce flowers, with the remaining company manufacturing products in both inflorescence and oil formulations. Fourteen (14) applications for a variation to the production licence were received. The variations which requested amendments to the conditions of the licence are broadly categorised in ***Figure 5.4.***

Through liaison with relevant bodies, eleven (11) local inspections were co-ordinated, including five (5) for EU-GMP and six (6) for facility/physical security. The licensed operations include the production of seven (7) products in dried flower form, twelve (12) oils and one (1) purified extract, eight (8) of which are intended for export in destination markets and twelve (12) for domestic consumption.

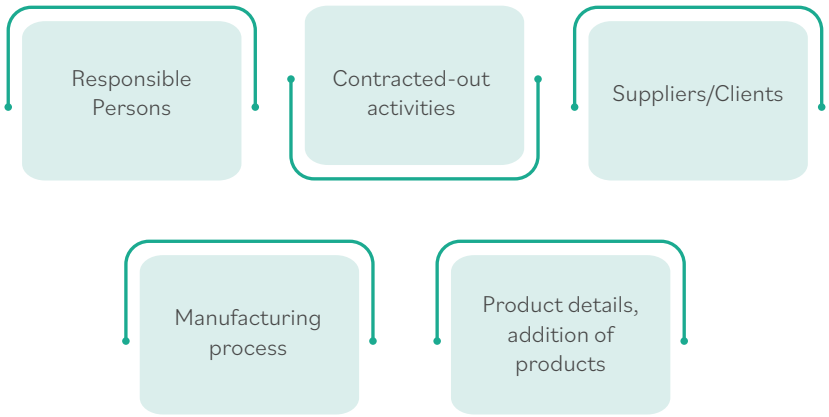

Figure 5.4: Types of VARS applications received requesting changes/introductions to the production licences

Driving Quality-based Decision-making

In the face of an ever-changing medicinal cannabis arena, policy and regulatory decision-making are guided by global horizon scanning for the identification of evolving evidence on the use and management of cannabis-based products and related activities. The Authority consults, collaborates and engages with interested parties and relevant bodies in its sustained efforts to re-engineer internal quality documents, the regulatory framework and legislative aspects at large. Since the inception of the medicinal cannabis regulatory framework, twenty (20) Quality Improvements have been documented to streamline, facilitate and consolidate processes. Cannabis regulatory procedures were also appraised through a series of audits, three (3) internal and one (1) external, which ensured conformity by the concerned personnel, thereby maintaining a high quality service provision to stakeholders.

Research Initiatives and Capacity Building

In its ongoing endeavour to spur and strengthen the research and educational arm, the CMRU capitalises on the acumen and capacity of other structures within the Authority, and also externally. Members from the Unit presented research conducted internally on the interpretation of stability data for cannabis-based products with varied composition and formulation at the Cannabinoid Conference in Basel, Switzerland and the International Annual Congress on Controversies of Cannabis-based Medicines in Copenhagen, Denmark. There was also participation with key interventions at locally-organised fora and high-level meetings including the MedCann World Forum 2022, the MMA Workshop on the Dimensions of Cannabis for Medicinal and Research Purposes, the Czech Presidency of Council of the EU European Medicines Agency Committee on Herbal Medicinal Products (HMPC) Meeting and the Med-In Pharma 2022 Conference. These exposures have served as sterling opportunities to disseminate and network on knowledge and experience with professional peers in the field of medicinal cannabis and beyond.

Pharmaceutical Entrepreneurship

The Pharmaceutical Products Entrepreneurship Unit, established in January 2022, is responsible to co-ordinate synergy in entrepreneurship processes within the MMA. The Unit spearheads projects of relevance to the Authority, especially in the area of pharmaceutical entrepreneurship. It enhances and collaborates with stakeholders on key players' projects which require entrepreneurship skills, relating them to regulatory sciences whilst keeping patients' interests and good governance at the centre of all its activities, with attention to possible conflict of interest. To this end, the Unit collaborated with twenty-two (22) stakeholders by holding twenty-nine (29) meetings to discuss pharmaceutical entrepreneurship initiatives on key projects including services in support of special groups of patients, advanced therapies and nanomedicines.

The Unit undertook an entrepreneurial initiative by collaborating with stakeholders in the organisation of a conference held in Malta which aimed to attract enterprises to Malta. The conference was attended by two hundred (200) professionals, academics and students. Topics discussed included medical technology, Medical Devices and the pharmaceutical industry. The conference provided an opportunity for discussions on policy-making and regulation, health inquiry, medical innovation and personalised, patient-focused technology.

At the MMA, pharmaceutical entrepreneurship is considered beyond the invocation of business aptitudes and successes but rather as a product of creative thinking, the taking of calculated risk and evidence-based decision making leading to the progression of innovative advancements in the pharmaceutical field.

Legal Matters

During the year under review, the Legal Unit was requested to give advice on about thirty (30) different matters, assisting each Directorate in all legal matters in a timely and efficient manner. The Unit also dealt with external queries such as the licensing and authorisations of medicinal products and pharmacy licences amongst other inquiries.

Various legislation both under the Medicines Act and other laws, were either reviewed or drafted, including the transposition of Directive (EU) 2022/642 of the European Parliament and of the Council of 12th April 2022 amending Directives 2001/20/EC and 2001/83/EC as regards derogations from certain obligations concerning certain medicinal products for human use made available in the United Kingdom in respect of Northern Ireland and in Cyprus, Ireland and Malta, which was transposed under five (5) Subsidiary Legislations under the Principal Act, Chapter 458 of the Laws of Malta. There were five (5) legislative amendments during the year in review.

The Unit's remit extended to judicial processes, whereby it represented the legal interest of the Authority in the Maltese law courts and tribunals. It also assisted internally and with law enforcement in investigations concerning medicinal products. The Legal Unit was involved in thirteen (13) contentious matters.

The Unit was also broadly engaged in the drafting of legal letters, contracts, Memorandum of Understandings (MoU) and other agreements, and provided general legal assistance, including legal advice and the interpretation of laws when the need arose.

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