MALTA
MEDICINES
AUTHORITY

annual report 23

2023 STATISTICS AT A GLANCE

NUMBER OF EMPLOYEES

SCIENTIFIC

75

ADMINISTRATIVE

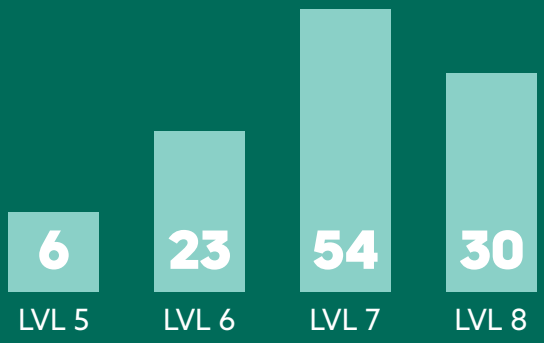
21

AGE AVERAGE

>40

ACADEMIC QUALIFICATIONS OF MMA EMPLOYEES

MQF LEVELS



IFP STUDENTS

104

RESEARCH PUBLICATIONS

19

QMS INTERNAL DOCUMENTS

107

INTERNAL AUDITS PERFORMED

11

FINALISED MRP/DCP PROCEDURES WITH MT ACTING AS RMS

50

LEGISLATIVE INTERVENTIONS

7

FORMULATION OF APPROVED CANNABIS-BASED PRODUCTS

OIL	DRIED FLOWERS	PURIFIED EXTRACT
16	15	3

SCIENTIFIC ADVICE
EMA SAWP PROCEDURES

19

ICSRS REGISTERED

120

REPORTS OF SUSPECTED ADRs

337

EU-GMP INSPECTIONS

LOCAL	3RD COUNTRY
17	24

EU-GDP INSPECTIONS

46

QP APPROVED

19

FREE SALE CERTIFICATES FOR MDs

39

MD REGISTRATIONS RECEIVED

86

APPROVED CANNABIS-BASED PRODUCTS

34

ARTICLE 20 EXEMPTION APPLICATIONS APPROVED

983

ACRONYMS

µ	Micro
AA	Authorisation according to Article 126(a)
ADR	Adverse Drug Reaction
AE	Adverse Event
AI	Artificial Intelligence
ANSM	Agence Nationale de Sécurité du Médicament et des produits de santé
API	Active Pharmaceutical Ingredient
ASID	Advanced Scientific Initiatives Directorate
BCC	Borderline Classification Committee
BE	Belgium
BEMA	Benchmarking of European Medicines Agencies
BG	Bulgaria
CAB	Conformity Assessment Bodies
CAPA	Corrective and Preventive Action
CBD	Cannabidiol
CEO	Chief Executive Officer
CH	Switzerland
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
CPCA	Carcinogenic Potency Categorisation Approach
CPPs	Certification of Pharmaceutical Products
CPSU	Central Procurement Supplies Unit
CTIS	Clinical Trials Information System
CTR	Clinical Trial Regulation
CY	Cyprus
CZ	Czech Republic
DC	Decentralised
DCP	Decentralised Procedure
DE	Germany
DHPCs	Direct Healthcare Professional Communications
DK	Denmark
DPU	Data Protection Unit
DSUR	Development Safety Update Report
EAHP	European Association of Hospital Pharmacists
EAFP	European Association of the Faculties of Pharmacy
EAT	Enhanced Ames Test
EC	European Commission
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
EU-IN	EU Innovation Network
EUCD	EU Coordination Department
EU-GDP	European Union-Good Distribution Practice
EU-GMP	European Union-Good Manufacturing Practice
EU-NTC	European Union-Network Training Centre
EURD	European Union Reference Dates
EVDAS	EudraVigilance Data Analysis System
FEBS	Fellowship of the European Board of Surgery
FCS	Finance and Corporate Services Unit
FI	Finland
FIP	International Pharmaceutical Federation
FMD	Falsified Medicines Directive
FOI	Freedom of Information
FOICU	FOI Coordination Unit
FR	France
FSCA	Field Safety Corrective Actions
FSN	Field Safety Notices
GACP	Good Agricultural and Collection Practices
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
GPI	Good Practice Initiative
HCPs	Healthcare Professionals
HMA	Heads of Medicines Agencies
HR	Croatia
HU	Hungary
ICO	Inspection Coordination Office
ICSRs	Individual Case Summary Reports
ICT	Information and Communications Technology
IE	Ireland
IED	Inspectorate and Enforcement Directorate
IFP	International Fellowship Programme
IPAS+	Internationalisation Partnership Awards Scheme Plus
IQA	Internal Quality Assurance
IRG	Inspections Review Group
IS	Iceland
ISO	International Organization for Standardization
IT	Italy
IVD	In-Vitro Diagnostics
JAP	Joint Audit Programme
JAT CAPA	EU Joint Action Team Corrective and Preventive Action
LA	Licensing Authority
LD	Licensing Directorate
LT	Lithuania
LU	Luxembourg
LV	Latvia
Lvl	Level
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder

MCCAA	Malta Competition and Consumer Affairs Authority
MCST	Malta Council for Science and Technology
MD	Medical Devices
MDH	Mater Dei Hospital
MDITF	Medical Devices Inspector Task Force
MDMS	Medical Device Management System
MDPCD	Medical Devices and Pharmaceutical Collaboration Directorate
MDR	Medical Device Regulation
MDRP	Medical Device Registered Person
ME	Malta Enterprise
MFHEA	Malta Further and Higher Education Authority
mg	Milligrams
MHRA	Medicines and Health Regulatory Agency
MIAU	Medicines Intelligence and Access
ml	Milligrams
MMA	Malta Medicines Authority
MNAT	Multinational Team
MoUs	Memorandum of Understandings
MQF	Malta Qualifications Framework
MR	Mutual Recognition
MRA	Mutual Recognition Agreement
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
NcWP	Nonclinical Working Party
NHS	National Health Service
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
PhV	Pharmacovigilance
PI	Parallel Import
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PL	Poland
PLD	Post-licensing Directorate
PPE	Pharmaceutical Products Entrepreneurship
PPPs	Pregnancy Prevention Programmes
PSURs	Periodic Safety Update Reports

PSUSAs	Periodic Safety Update Report Single Assessments
PSWG	Prescription Status Working Group
PT	Portugal
Q&A	Question and Answer
QIs	Quality Improvements
QM	Quality Management
QMS	Quality Management System
QP	Qualified Person
QRD	Quality Review of Documents
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
S.A.F.E.	Skills for Addiction Free Employees
SAWP	Scientific Advice Working Party
SCSA	Social Care and Standards Authority
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	Superintendence 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
VAT	Value Added Tax
VPN	Virtual Private Networks
w/w	Weight in weight
WHO	World Health Organisation
WP	Working Party
YoY	Year on Year

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FOREWORD FROM THE MINISTER

It is with pleasure that I address you in this annual report, reflecting on the accomplishments and milestones achieved by the Malta Medicines Authority. In navigating the dynamic pharmaceutical landscape, characterised by unprecedented challenges and prospects, acknowledging the crucial role of core values such as cooperation, good governance, compliance, collaboration, quality assurance, and digitalisation in advancing the MMA's objectives is imperative.

The Authority's commitment to collaboration and partnership with a diverse range of entities, namely government agencies, non-profit organisations, and private sector stakeholders in a sustainable manner is paramount. Through strategic alliances and synergistic efforts, the Authority can leverage collective expertise, resources, and networks to address complex issues, drive innovation, and deliver impactful outcomes for the benefit of society.

At the heart of the operations of the MMA lies a commitment to upholding the highest standards of

"...I must admit that the Authority's academic and research endeavours are very close to my heart..."

governance, transparency, and integrity. Whilst persistently adhering to ethical principles, regulatory requirements, and best practices, the Authority fosters trust and confidence among all stakeholders. The Authority ensures accountability, mitigates risk, and safeguards the interests of all stakeholders, through robust governance structures and processes.

Commitment to public health and safety remains unwavering, particularly when collaborating with other entities such as the Superintendent of Public Health. By aligning the Authority's proactive contribution to the promotion of health and well-being within the communities, various entities striving to work synergistically succeed in addressing emerging health challenges, enhancing healthcare infrastructure, and promoting equitable access to quality healthcare services for all citizens.

Quality serves as the cornerstone of the Authority's operations, permeating every facet of the work. The Malta Medicines Authority remains steadfast in its commitment to ensure that Malta has pharmaceutical products, medical devices, and services of the highest quality, meeting the expectations of all stakeholders. Through continuous improvement initiatives, rigorous quality assurance processes, and adherence to international standards, the Authority ensures excellence in all endeavours, thereby earning the trust and confidence of patients and stakeholders.

In a patient-centric era characterised by rapid technological advancement and digital transformation, the MMA continues to lead the charge in innovation, encompassing valuable changes. Recognising the transformative potential of digitalisation in enhancing efficiency, productivity, and service delivery, the Authority embraces digital technologies, data-driven decision-making, and agile methodologies to adapt to evolving needs and empower the workforce to thrive in the digital age.

I am proud to acknowledge the expansion of the workforce and the increasing number of personnel attaining advanced qualifications. This achievement underscores the Authority's commitment to academic excellence and professional development. The expertise and insights garnered enrich a collective knowledge base and contribute significantly to the organisation's continued success.

The Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences within the Authority serves as a pivotal platform for educational planning and academic development, facilitating tailored training programs to meet the evolving needs of stakeholders. I commend the diverse range of courses offered at various educational levels, and the framework established to yield mutual benefits for regulators, policymakers, industry professionals and society at large. The International Fellowship Programme provides invaluable opportunities for mentorship, collaboration, and career advancement. This programme fosters stronger ties with academia, such as the Faculty of Medicine and Surgery at the University of Malta (UoM).

I extend my heartfelt appreciation to every member of the Malta Medicines Authority for their dedication, passion, and hard work. Together, we have achieved remarkable milestones and surmounted formidable challenges. As we look ahead to the future, let us continue to innovate, collaborate, and lead with integrity, making a meaningful difference in the lives of those we serve – the patients and healthcare systems

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

MESSAGE FROM THE CHIEF EXECUTIVE OFFICER

The Malta Medicines Authority (MMA) has persistently, purposefully, vigorously, and meticulously sustained its core Directorates sustainably: Licensing (LD), Post-Licensing (PLD), and Inspectorate and Enforcement (IED). The MMA has expanded its horizon to safe, effective, and quality medicinal products and medical devices (MD), through the establishment of three (3) other Directorates: Regulatory, Operations, Medicines Intelligence and Access (ROMAD), Advanced Scientific Initiatives (ASID), and Medical Devices and Pharmaceutical Collaboration (MDPCD), also focusing on two additional pillars for regulatory sciences, namely accessibility and the environment. Concerted efforts have established a culture conducive to innovation and adaptability. A visionary approach has positioned the MMA at the forefront of the healthcare system, making it a reliable and reputable decision-making pharmaceutical regulator. The guiding principle remains unwaveringly centred on prioritising patient well-being. The diligent scrutiny of medicinal products and medical devices seizes the Authority's commitment to thoroughness, emphasising robust attention to detail while avoiding unnecessary bureaucratic impediments within the regulatory process.

The MMA takes great pride in being an integral part of the system within the European Union (EU) responsible for the authorisation and supervision of medicinal products and medical devices. Aligned with the Head of Medicines Agencies (HMA) and the European Medicines Agency (EMA), the MMA experiences a communicative nexus with other regulatory authorities. This collaboration is notably demonstrated through the Authority's thoughtful contributions, particularly in enhancing access to medicines, primarily through the Medicines Intelligence and Access Unit (MIAU).

The MMA's collaborative and teamwork philosophy extends beyond international engagements to local enterprises with various stakeholders, including governmental institutions, patient organisations, pharmaceutical industries, and workforce representatives. This synergistic spirit is instrumental in achieving notable milestones, underscoring the effectiveness of collective efforts. Proactivity is a defining characteristic of the MMA, serving as a cornerstone in associations that facilitate expeditious decision-making across various processes. The MMA's proactive stance, exemplified by initiatives such as the judicious use of Article 20 of the Medicines Act, signals a commitment towards providing impetus for the benefit of society.

"May the dedication to excellence inspire us all as we collectively strive to enhance the quality of healthcare for the benefit of humanity."

Looking forward, the MMA envisions a bright future with a strategic focus on digitalisation as a catalyst for change and innovation, leveraging tools such as big data for enhanced drug safety measures. Emphasis will persist on the importance of collaboration and cooperation, recognising regulatory expertise as a fundamental aspect of the Authority's functions. The success of the Licensing Directorate underscores the importance of continued teamwork in streamlining the licensing process, tailored to the unique characteristics of Malta as a small island state.

The MMA remains committed to accentuating the significance of academic and clinical expertise, exemplified by initiatives undertaken by the Academy for Excellence and Innovation in Patient-Centred Regulatory Sciences. Acknowledging the importance of sustaining connections with academic institutions, the MMA has implemented an International Fellowship Programme. This programme enhances ties with academia namely the University of Malta (UoM), ensuring that a highly skilled workforce remains at the forefront of the MMA, committed in its pursuit of its core values.

The cornerstone of these advancements lies in the Authority's unwavering dedication to ensuring a patient-centred approach to surveillance. In an era where the intricacies of medicinal products and medical devices necessitate continual scrutiny, the Post-Licensing Directorate and the Medical Devices and Pharmaceutical Collaboration Directorate are strategically positioned at the forefront, championing vigilant practices prioritising patient well-being. This approach transcends mere compliance, aiming for a holistic understanding of the impact of medical interventions on the lives of those we serve.

I want to shed light on the remarkable strides made by the Medical Devices and Pharmaceutical Collaboration Directorate in pursuing excellence and innovation. The Directorate's commitment to advancing healthcare was manifested through various initiatives, with a particular focus on sustained response to the application of the establishment of Notified Bodies (NBs) in Malta. The principle of leadership is illustrated within the framework of the Joint Action on Market Surveillance 2.0 Work Package 5, specifically focusing on signal detection in the domain of medical device vigilance.

These collaborative efforts underscore the Authority's commitment to holding the highest standards of quality and safety of medicinal products and medical devices. By engaging in inspections, the Authority not only ensures regulatory compliance but also strives to foster an environment where innovation coexists harmoniously with stringent oversight. This year, the Inspectorate

and Enforcement Directorate has carried out a record number of third-country inspections that benefit the local pharmaceutical industry and improve accessibility to medicines within the EU.

I am pleased to report the positive outcomes of both audits, reflecting the Authority's commitment to excellence in pharmaceutical regulatory practices.

As we stand on the threshold of transformative developments in healthcare, it is heartening to witness the diligence and foresight demonstrated by all the Directorates and Units within the MMA. The endeavours in sustained response, signal detection, inspections, and engagement with educational institutions are building the foundation for a safer, more efficient, and patient-centric healthcare ecosystem.

In conclusion, let us acknowledge and commemorate the achievements of the MMA. The MMA takes pride in its sustainability, attributed to its highly qualified and competent staff, enabling the Authority to engage in innovative activities beyond its core functions. The Authority looks forward to continued collaboration, growth, and contributions to the advancement of medicinal products within the EU framework.

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

REMARKS FROM THE DIRECTORS

Dr Annalise Attard
Officer in Grade 2,
Office of the CEO

During 2023, the Office of the Chief Executive Officer (CEO) worked towards commitment to operational excellence, transparency, and accountability in fulfilling the MMA's regulatory mandate. Through such commitment, we have strengthened collaboration with stakeholders, fostering greater communication and alignment in our regulatory efforts, while actively participating in EU and international meetings, contributing our expertise and insights to global discussions on pharmaceutical regulation and public health.

The Authority's dedication towards regulatory compliance is reflected in our five (5)-year audit strategy launched in 2023 to enhance transparency and maintain the highest standards of integrity and accountability in our regulatory processes. Furthermore, the Authority's commitment to benchmarking regulatory practices against international standards was reaffirmed by the BEMA assessment, ensuring alignment with best practices and continuous improvement.

In 2023, we have played a pivotal role in advancing collaborative efforts to enhance regulatory capacity and efficiency across borders as lead participants in the IncreaseNet EU project. In addition, the successful organisation of the second Med-In Pharma Conference attests to our efforts in collaborating with key stakeholders in the pharmaceutical sector, whereby we provided a platform for knowledge exchange and networking.

Legal amendments in the sector of cannabis for medicinal and research purposes reflect our commitment to supporting industry growth, fostering research activities, and improving patient accessibility to cannabis-based treatments. We are also pleased to announce the granting of the first cannabis research license marking a significant milestone in promoting scientific inquiry and innovation in this field.

The progress made by the Authority in fiscal responsibility and resource optimisation in 2023 is remarkable. The Authority started a proactive approach to debt monitoring and recovery highlighting our commitment to ensuring the sustainability of our operations. Moreover, the opening of a new bank account enhances risk management and provides better access to stakeholders, streamlining financial transactions and improving operational efficiency.

We look forward to another year of dedication to continuous improvement as we strive to optimise regulatory processes, enhance stakeholder engagement, and adapt to evolving challenges and opportunities in the pharmaceutical landscape.

Dr John Joseph Borg
Director, Post-licensing

Pharmacovigilance (PhV) is the science of monitoring the safety of medicines and taking action to reduce the risks and maximise the benefits of medicines. Pharmacovigilance is instrumental in helping to ensure patient safety throughout the lifecycle of both newly authorised medicinal products and those that are well established in health care practice. Since side effects can influence the quality of life of patients, patient safety is Key for the MMA. The EU pharmacovigilance system is one of the most advanced and comprehensive in the world and the MMA both contributes to and leverages this robust network to ensure the safe use of medicinal products on the local market and throughout the EU.

Challenges in the coming years will include harnessing technology advancements, rationalising the increasing volumes of data available to regulators and companies, and increasing the engagement of patients in healthcare decision-making.

Ms Helen Vella
Director, Licensing

The Licensing Directorate's main responsibilities are the registration and life-cycle management of medicinal products, through national and European procedures. Registration of medicinal products in accordance with established European legislation, guidelines and standards enables the supply of high-quality, safe, and effective medicines. This applies to all medicinal products, both originators and generics, since the same standards are applicable, which is imperative for public health and safety. The Directorate continues to efficiently participate as a Reference Member State (RMS) in the Decentralised Procedure (DCP) and contributes to the authorisation of medicines not only in Malta but in other EU countries. A multi-disciplinary team composed of regulatory and scientific experts' reviews and assesses each application for marketing authorisation (MA). At the end of this process, a product is authorised to be placed on the market based on the approved indications. Information on each authorised product is published on the MMA website. This information is continuously kept updated when changes to the product are approved. These changes follow standard procedures designated by variations to the terms of MA. This ensures that patients and healthcare professionals have available the most updated information about the product.

The LD supports the availability of medicinal products for the Maltese market by granting other authorisations on the grounds of public health needs. This ensures continuity of supply of products whilst ensuring the same standards are being met. This is achieved by working together with other national competent authorities in the EU.

It is becoming a challenge for the Directorate to accommodate the increasing number of requests for Malta to be a RMS. Whilst there is a continued effort to increase the staff complement to service these requests, increasing the capacity for carrying out more procedures and taking on more challenging ones is the main priority for the coming years.

Dr Mark Cilia
Director, Inspectorate and Enforcement

During 2023, the Inspectorate and Enforcement Directorate also achieved another important and significant milestone and target as it successfully passed through its second JAP assessment thus renewing the mutual recognition (MR) of all its work by all the Member States (MS) within the EU, and by countries having a Mutual Recognition Agreement (MRA) with the EU for Good Manufacturing Practice (GMP) certification of companies. This is an important achievement not only for the Directorate but also for the pharmaceutical industry in Malta whose survival depends on their capability to be able to export their products unhindered to other highly regulated markets.

I would like to conclude this short remark note with the following thought: As we look towards the future beyond the post-pandemic phase, much of the focus of our discussions both within and with other member state countries is how we can help together create a more resilient yet flexible regulatory framework of medicinal products for the future to better cater for the industry needs whilst protecting public health. I hope that in the upcoming year and beyond, together with our stakeholders, we will gain more insights on how we can continue to achieve this goal.

Dr Luana Mifsud Buhagiar
Director, Advanced Scientific Initiatives

Implementing policy mandates, overseeing compliance, and taking enforcement actions are only parts of the regulation spectrum. Innovations in technologies, products, research, services and business models make it complex for regulators to navigate today's and tomorrow's challenges. Industry-led disruption can serve as an opportunity for competent authorities to rethink outreach because with an us-versus-them approach, patients get confined in the split. Consultations and focus groups work, as do guidance and engagement exercises – people development, however, is key.

The MMA, through its established Academy, is primed to deliver educational programmes that translate regulatory standards into day-to-day excellence. Collaborative efforts foster a win-win scenario where procedures can be streamlined, and gaps addressed. Whilst some hesitancy about leveraging the regulator-industry interdependence persists, building a synergistic culture where the patient comes first drives all towards one mutual interest and with necessary safeguards in place, there shall be no conflict in the sharing of knowledge and best practices.

Dr Caroline Muscat
Director, Regulatory Operations, Medicines Intelligence and Access

In the rapidly evolving landscape of medical products, competent authorities are continuously navigating challenges related to regulatory compliance and patient safety without impeding the timely availability of medical products. Within the Regulatory Operations, Medicines Intelligence and Access Directorate, we spearhead patient-centred regulatory operations and best practices to enhance access to medicines.

The Operations and Pharmacy Practice Unit continuously monitors and optimises performance by evaluating key performance indicators in line with the vision, mission, values, and strategic goals of the Authority. In addition to conducting community pharmacy inspections, coordinating communication initiatives, EU and international regulatory affairs, public relations, and stakeholder engagement fall within the responsibilities of the Directorate.

A proactive, patient-centred approach is sustained by the MIAU to bridge the gap between the Authority as a regulator and patient needs by compiling medicines intelligence, providing targeted recommendations, and supporting stakeholders to ensure the continuous provision of medicines in the local public and private market.

Embracing innovation and flexibility in our operations is key for effective organisational change management and adaption of regulatory requirements to shape the trajectory of pharmaceutical advancements. Having the right people is the greatest resource for the Authority to advance. The People Management team upholds a positive organisational culture that promotes people development, innovation, integrity, equal opportunities, and optimised capacity to support the overall strategic functions of the Authority.

Dr Louise Grech
Director, Medical Devices and Pharmaceutical Collaboration

At the heart of healthcare, medical devices play a pivotal role across the continuum of care, from prevention to diagnosis, treatment, monitoring, rehabilitation, and palliative care. The Medical Devices and Pharmaceutical Collaboration Directorate is unwavering in its commitment to a patient-centred approach, actively engaging with stakeholders at both national and international levels to ensure the availability of safe, effective, and high-quality medical devices on the market, aligning with the overarching goal of enhancing patient outcomes.

The remarkable progress made by the Directorate is evident in key accomplishments, including the strengthening of the medical device and pharmaceutical collaboration to ensure a robust infrastructure capable of addressing the dynamic needs of the healthcare landscape, a sustained and responsive approach to notified bodies, and the establishment of a robust clinical investigations and inspections framework. In an era of rapid technological advancement and evolving healthcare landscapes, collaboration is a linchpin for success. I am particularly pleased to witness the flourishing patient-centred partnerships between the pharmaceutical collaboration arm of the Directorate and various entities, fostering innovative ideas for the mutual benefit of the MMA and society at large.

As we look ahead, the Directorate remains poised for the forthcoming opportunities and challenges. With a steadfast commitment to excellence, we will continue to push the boundaries, ensuring the highest standards in medical device and pharmaceutical regulation. The journey ahead is exciting, and we embrace it with enthusiasm, confident in our ability to navigate the complexities of a rapidly evolving medical device landscape.

THE MALTA MEDICINES AUTHORITY - BACKGROUND

The MMA was established by 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 providing high-quality licensing, pharmacovigilance, pharmaceutical inspections, and enforcement services to its stakeholders for the ultimate benefit of the public.

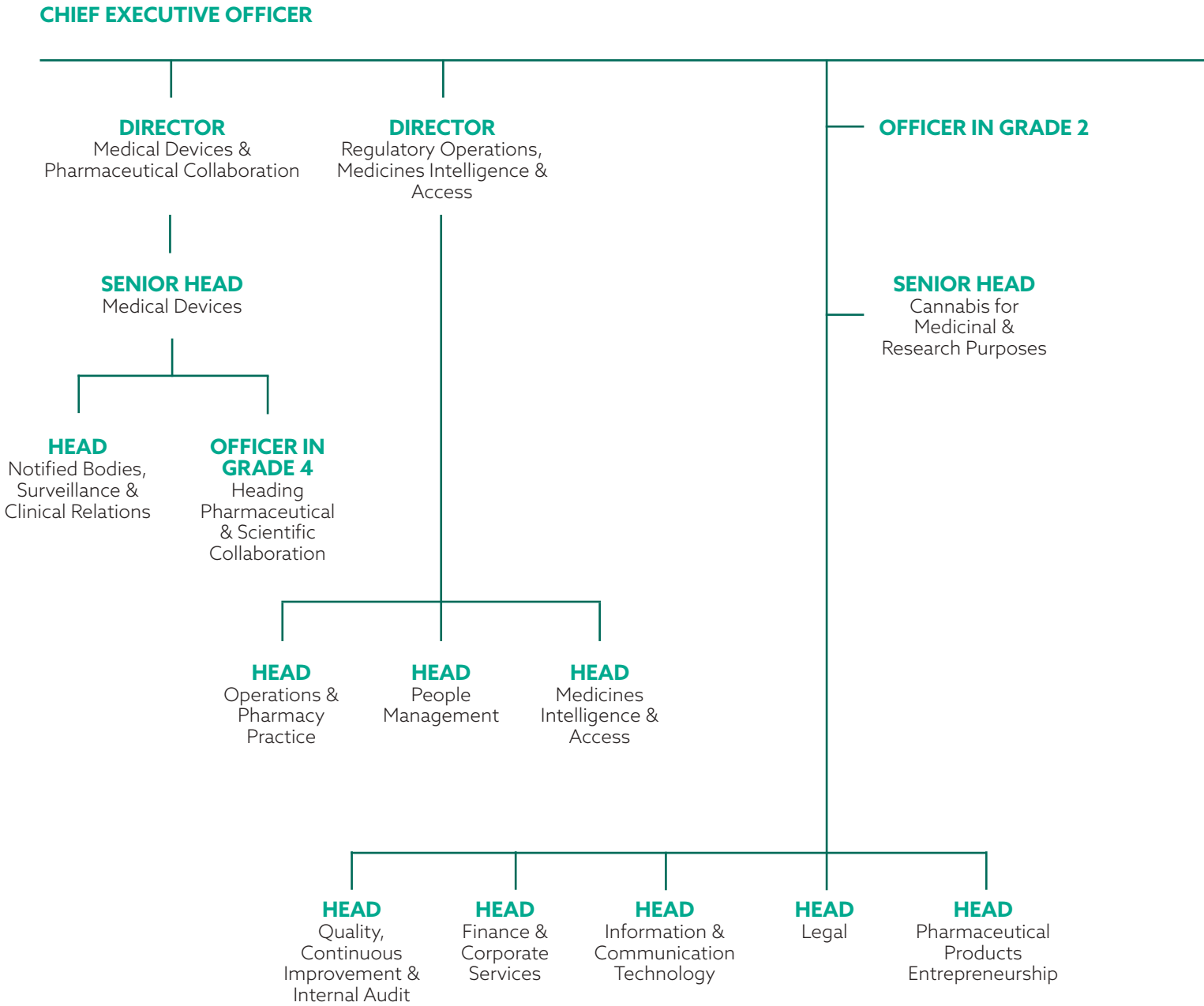
The MMA is established by six (6) Directorates under the guidance of the Chief Executive Officer. These are the Licensing Directorate, the Post-licensing Directorate, the Inspectorate and Enforcement Directorate, the Advanced Scientific Initiatives Directorate, the Regulatory Operations, Medicines Intelligence and Access Directorate and the Medical Devices and Pharmaceutical Collaboration Directorate.

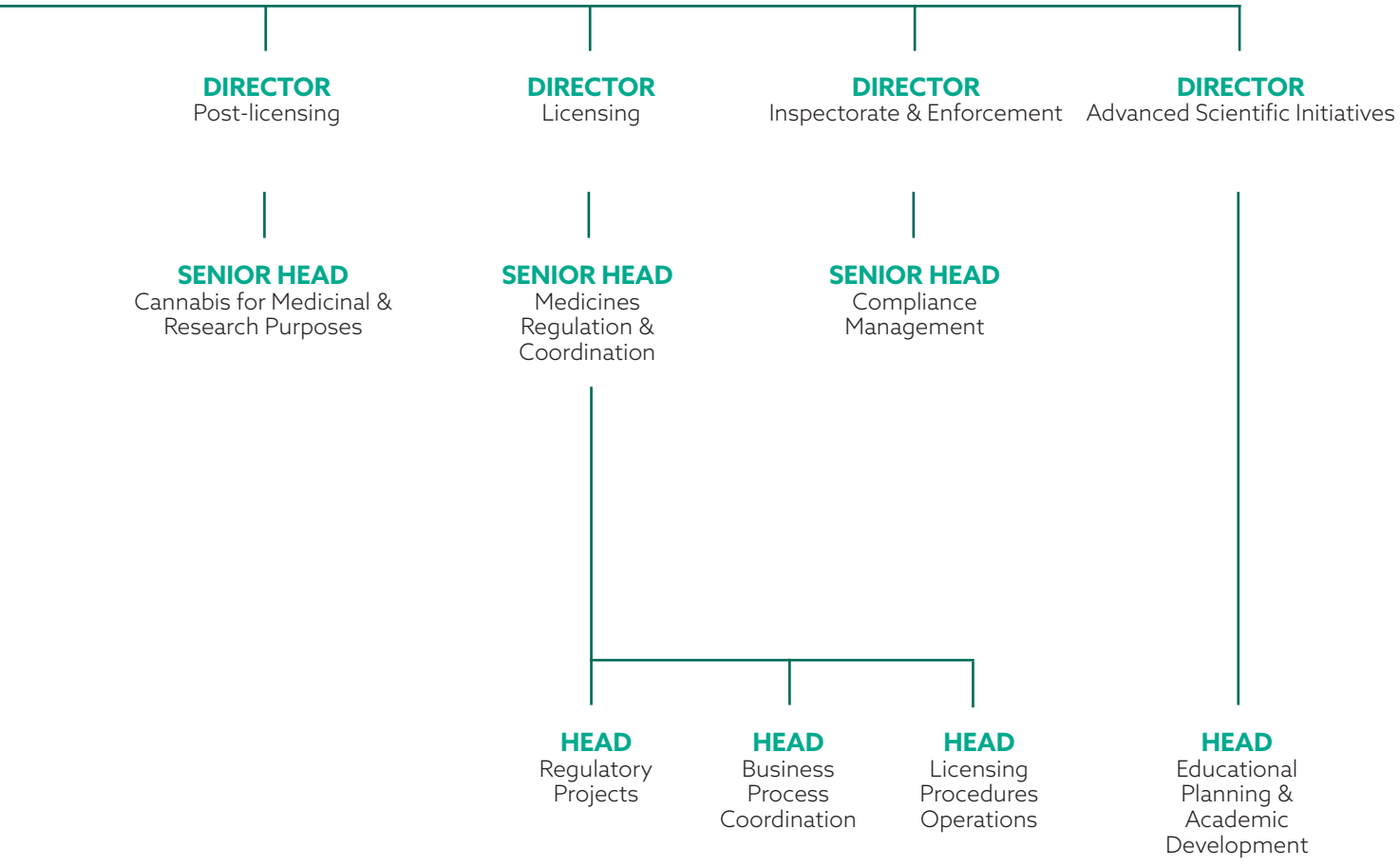
Their core work is supported by five (5) Senior Heads, namely the Medicine Regulation and Coordination, the Pharmacovigilance, Medicines Safety and Regulatory Response, the Compliance Management, and the Medical Devices, eight (8) Units within Directorates, namely the Educational Planning and Academic Development (EPAD), the Medicines Intelligence and Access, the People Management, the Operations and Pharmacy Practice, the Notified Bodies, Surveillance and Clinical Relations, the Regulatory Projects, the Business Process Coordination, and the Licensing Procedures Operations.

The Authority is also supported by the continuous collaboration of six (6) Units that fall within the Office of the Chief Executive Officer (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).

Given 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 invest in manpower sustainably.

ORGANOGRAM


CHIEF EXECUTIVE OFFICER
DIRECTOR
Medical Devices & Pharmaceutical Collaboration
DIRECTOR
Regulatory Operations, Medicines Intelligence & Access
OFFICER IN GRADE 2
SENIOR HEAD
Medical Devices
SENIOR HEAD
Cannabis for Medicinal & Research Purposes
HEAD
Notified Bodies, Surveillance & Clinical Relations
OFFICER IN GRADE 4
Heading Pharmaceutical & Scientific Collaboration
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


DIRECTOR
Post-licensing
DIRECTOR
Licensing
DIRECTOR
Inspectorate & Enforcement
DIRECTOR
Advanced Scientific Initiatives
SENIOR HEAD
Cannabis for Medicinal & Research Purposes
SENIOR HEAD
Medicines Regulation & Coordination
SENIOR HEAD
Compliance Management
HEAD
Regulatory Projects
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Educational Planning & Academic Development

THE MALTA MEDICINES AUTHORITY'S 20TH ANNIVERSARY

The year 2023 marked the 20th anniversary of the establishment of the MMA as the Maltese National Competent Authority with a specific and unique mission to safeguard public health. The advancement of the Authority has been reflected throughout these two (2) decades, by working actively at the forefront to contribute towards the achievement of this mission. The MMA was able to reach a milieu of milestones despite numerous challenges being encountered along the way. The latest challenge which the MMA had to cope with was the COVID-19 pandemic. The year 2023 can be considered as the post-pandemic year where the Authority had to adapt all its work with full energy and address any pending issues that arose during the pandemic.

TIMELINE

The MMA has evolved its mission to cater for the regulation of medical products, including medical devices and cannabis for medicinal and research purposes. The below timeline showcases the main organisational achievements and exhibits the capability of the organisation to promptly adjust and respond to current challenges by implementing regulatory flexibility.

2003

The Medicines Act, 2003 Chapter 458 of the Laws of Malta came into force and established the Malta Medicines Authority.

2004

The following Directorates/Units were established:

- Licensing Directorate
- Post-licensing Directorate
- Inspectorate and Enforcement Directorate
- Information and Communication Technology Unit

2014

The Strategic Operations and Regulatory Affairs Directorate was officially established.

2016

The following Units were established:

- Finance and Corporate Services Unit
- Medicines Intelligence and Access Unit

2017

The Research, Scientific Affairs and Innovation Unit was officially established

Food and Drug Administration recognition for GMP inspections

2018

The following Directorates/ Units were established:

- Advanced Scientific Initiatives Directorate
- Quality, Continuous Improvement and Internal Audits Unit
- Regulatory Project Leader Unit
- Research, Scientific Affairs and Innovation Unit

2019

The following Units were established:

- Operations and Pharmacy Practice Unit
- Educational Planning and Academic Development Unit

2021

The following Directorates/ Units were established:

- Legal Unit
- People Management Unit
- Medical Devices and Pharmaceutical Collaboration Directorate
- Establishment and recognition of Academy by Malta Further and Higher Education Authority

2022

The following Units were established:

- Notified Bodies, Surveillance and Clinical Relations Unit
- Pharmaceutical Products Entrepreneurship Unit
- Cannabis for Medicinal and Research Purposes Unit

2023

The following Units were established:

- Business Process Coordination Unit
- Licensing Procedures Operations Unit

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 Malt and the 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 economic operators and the performance of notified bodies 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 that 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 Scientific Measurable Attainable Relevant Time-bound (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 in European fora of the 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."

INTEGRITY

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

QUALITY

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

INNOVATION

In an ever-changing 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.

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.

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 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 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 of the MMA and the appropriate use of medicines.

PROMINENT INITIATIVES

Over the last year, the Quality, Continuous Improvement and Internal Audit Unit, in collaboration with the Regulatory Operations, Medicines Intelligence and Access Directorate hosted a team of assessors as part of the BEMA programme. The assessment highlighted the robust, stable quality system and regulatory operations the MMA embraces. The Quality, Continuous Improvement and Internal Audit Unit assisted the Inspectorate and Enforcement Directorate during the JAP audit.

The Inspectorate and Enforcement Directorate effectively met the standards required for the JAP audit. The successful results achieved will reflect in the local pharmaceutical sector's capability to export medicinal products to highly regulated markets.

The MMA is contributing to the EU4Health Programme by participating and leading working packages of the Joint Action on:

- Increasing capacity building of the EU Medicines Regulatory Network (EMRN) which encourages the sharing of best practices and development of training opportunities, aims to build capacity, build competence, promote work-sharing, and increase network collaborations. The joint action will encourage efficient use of resources, avoiding duplication of work and optimising regulatory processes, thereby fostering a long-lasting opportunity for cooperation; and

- Reinforced market surveillance of medical devices and in vitro medical devices (JAMS 2.0) which aims to enhance the safety of medical devices, thereby effectively contributing to public health protection by ensuring market availability of safe, effective, and good quality devices compliant with regulations. This Joint Action will also facilitate sharing of best practices and development of training modules for medical devices and in vitro medical devices market surveillance.

In 2024, the Advanced Scientific Initiatives Directorate shall be organising a collaborative initiative on *The Silent Threat – Antimicrobial Resistance Uncovered*, a project granted funding under the Internationalisation Partnership Awards Scheme Plus (IPAS+) 2023 of the Malta Council for Science and Technology (MCST).

The MMA Academy intends to continue optimising the interface with all stakeholders, reflecting on commended feedback and market demand analysis for the delivery of repeat and newly accredited programmes. Several courses, including cannabis for medicinal and research purposes as well as medication management are under development, whilst considering investment for hybrid/digital provision, alongside prospective integration of innovative tools such as Artificial Intelligence (AI).

ORGANISATIONAL DEVELOPMENT, A POSITIVE WORKING ENVIRONMENT, A PATIENT-CENTRED ETHOS, AND A PROACTIVE APPROACH

Throughout 2023, 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 that 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 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.

QUALITY MANAGEMENT, SIMPLIFICATION MEASURES AND GOOD GOVERNANCE

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

2023

61 **SOPs**

27 **Policies**

19 **Guidelines**

Figure 2.1: SOPs, Policies and Guidelines of the MMA that were revised or introduced in 2023.

By the end of 2023, the foundation of the Quality Management System at the Authority, which ensures uniform and high-quality operations, consisted of forty-three (43) policies, one hundred and twenty-eight (128) Standard Operating Procedures (SOPs) and forty (40) guidelines. In 2023, twenty-seven (27) policies, sixty-one (61) SOPs, and nineteen (19) 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 QMS *(Figure 2.1)*.

The MMA implemented even (11) internal audits throughout 2023, in line with the five (5)-year audit strategy. Overall, a total of one hundred and thirty-three (133) 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's direction to simplify the Public Sector system and processes, the MMA identified one (1) simplification measure. A Standard Operating Procedure and guidelines are developed to formalise the application process and evaluation of clinical trials in accordance with the new EU Clinical Trial Regulation for medicinal products for human use. This measure enhances the transparency of information on clinical trials and fosters innovation and research in Malta and in the EU. These SOP and guidelines aim at strengthening and harmonising the decision-making process to safeguard the safety and well-being of all the individuals taking part in clinical trials.

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 an additional measure abridging the gap between the Authority and its stakeholders by delivering a strong and comprehensive foundation in basic aspects of regulatory sciences. This measure is oriented to reinforcing an innovative and active scenario for learning, strengthening the Authority's sustainability while encouraging the progress of the pharmaceutical and life sciences sector in our country.

The MMA is responsible to conduct four (4) Electoral Manifesto Proposals by 2026:

i. Electoral Manifesto Proposal 82 - Reinforce the functions of the Medicines Authority in safeguarding public health through the regulation of medical products and pharmaceutical activities by performing inspections and certifying pharmaceutical manufacturing facilities in the EU and third countries according to Good Manufacturing Practice (GMP) standards. Through this measure, the MMA is increasing the number of inspections carried out overseas and extending its remit to certify manufacturing facilities that produce advanced medicinal products such as biosimilars by strengthening the skills and competences of the inspectors.

ii. Electoral Manifesto Proposal 83 - Establish Notified Bodies in Malta - The MMA is proactively addressing the international challenge of shortages in Notified Bodies in the area of medical devices and in-vitro diagnostics by EU regulations through its commitment to designate and subsequently continuously monitor the performance of Notified Bodies registered in Malta. Two (2) conformity assessment bodies have ongoing applications in Malta for designation as a Notified Body.

iii. Electoral Manifesto Proposal 84 - Extend the International Fellowship Programme of the Medicines Authority at Post-Doctoral level to address the need of high-level technical experts in the pharmaceutical industry to meet the demands of local companies and new foreign direct investment projects in life sciences. The success of the Medicines Authority's International Fellowship Program up to doctoral level will be extended to include postdoctoral course opportunities.

iv. Electoral Manifesto Proposal 490 – Availability of medicines at affordable prices – The MMA is in continuous dialogue with local and international pharmaceutical stakeholders to ensure that consumers continue to have access to a wide choice of medicines at fair prices that conform to the established European standards of quality, safety and efficacy.

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 are published on the Authority's official website. Privacy by design is a concept brought about by the Data Protection Regulation that is fully embedded within the Authority's operational framework for processes handling personal data. Throughout 2023, the MMA continued to process FOI requests and promptly provide support with regards to data protection access requests and queries promptly, 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 to data.medicinesauthority@gov.mt.

OUR PEOPLE

The People Management team delivered several operational and strategic areas throughout 2023. Our primary focus was to continue managing appropriately the allocation of human resources, including recruitment of employees in Directorates and Units and to equip the Authority for successfully implementing its mission.

EMPLOYEE ENGAGEMENT

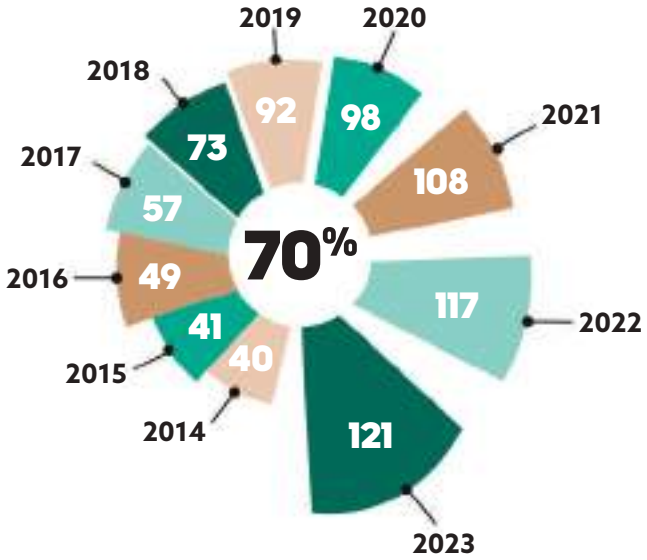


Figure 2.2: Number of employees at the MMA (2014-2023).

Employee engagement is an ongoing priority for the MMA. In 2023, employee engagement and appointments were maintained in line with the approved capacity building, availability of funds and the MMAs operational requirements. A total of nine (9) employees were recruited.

Figure 2.2 represents the total number of employees engaged in full-time (n=119) or part-time (n=2) Contracts of Service with an increase of 70% between 2013 and 2023. On-loan (n=2) and unpaid leave (n=2) employees are included.

EMPLOYEE WELLBEING

The MMA recognises that employee motivation is crucial in fulfilling its objectives and ensuring overall productivity. Thus, the Authority remains committed to maintaining an environment that brings out the best in each employee.

In 2023, the People Management team organised team building events and offered courses to support employees' physical health, safety, and mental health. Three (3) main teambuilding events were held in 2023.

3

A Sports Day which had both physical and mindful activities

A Staff meeting was held in June in Gozo

A Staff meeting was held in November at Esplora

"...These activities provide the opportunity to foster unity and strengthen collaboration..."

During February and September, the MMA offered a Mindfulness course to all its employees. The outcome of this course was to teach how to alleviate stress at the workplace and empower them with the right tools they need to succeed better at tackling responsibilities and communicating effectively with one another.

In the first and second quarter of 2023, the People Management team in collaboration with the Foundation for Social Welfare Services introduced the S.A.F.E. programme amongst its employees. In September, the MMA received an award as a tribute for investing in the well-being of its employees.

THE MMA'S INTERNATIONAL FELLOWSHIP PROGRAMME

The MMA's International Fellowship Programme (IFP) is offered to prospective and current individuals to pursue further levels of academic research. The objectives of the Programme are to strengthen skills in the pharmaceutical and life sciences sector, to increase competence on topics relevant to innovative therapies and technologies and to expand the capacity and level of research and development activity.

Figure 2.3 illustrates the number of new fellows who enrolled for Malta Qualifications Framework (MQF) Level 6, MQF Level 7 and MQF Level 8 degrees between 2014 and 2023.

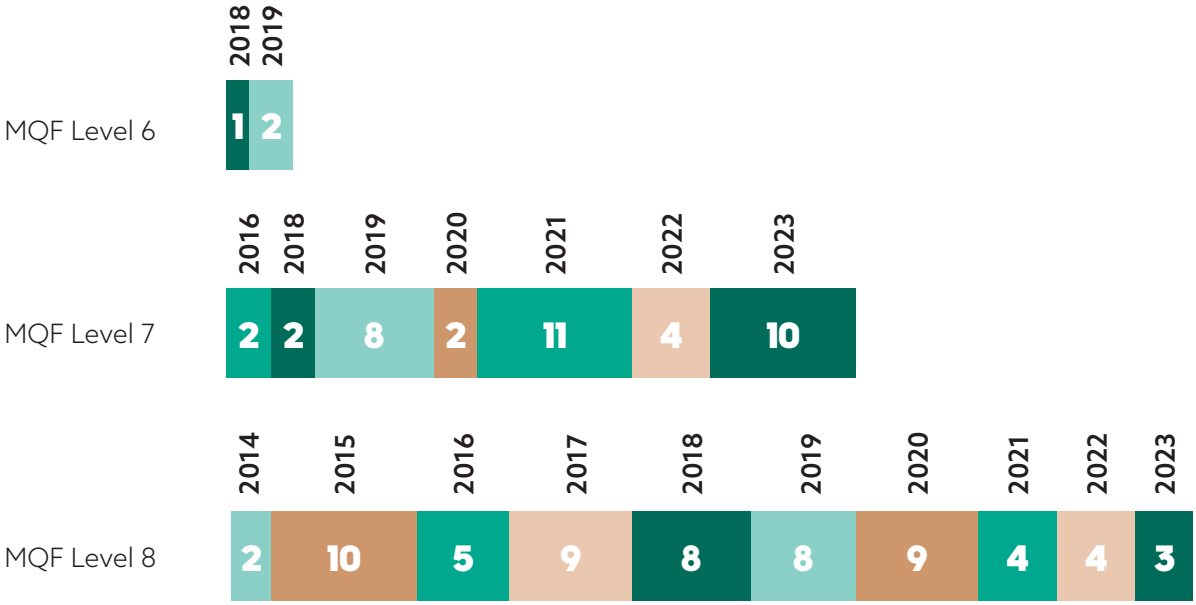


Figure 2.3: New fellow students subdivided per year and MQF level (N= 106).

EDUCATION AND PROFESSIONAL DEVELOPMENT

The MMA acknowledge that education and professional development allow employees to learn and apply new knowledge and skills that can help them perform better at work.

In terms of self-development, in 2023, its employees successfully attained two hundred and seventy-nine (279) certificates related to training initiatives that were offered internally and externally

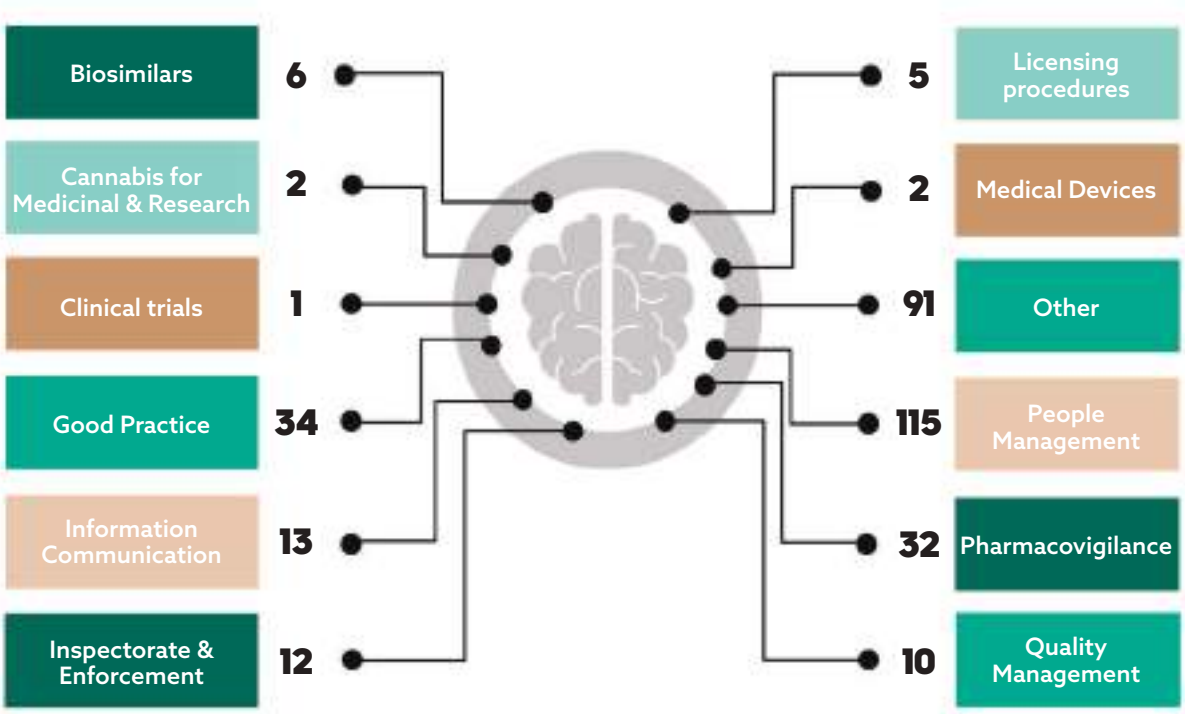


Figure 2.4: Number of training certificates attained by employees at the MMA (N=279).

A EUROPEAN AND GLOBAL PLAYER

During the year under review, the MMA underwent the assessment as part of the BEMA, obtaining a final score of 4.2 out of 5. Through this assessment, the systems and processes of individual agencies are evaluated, and best practices are identified in the areas related to strategic operations, quality management systems, Marketing Authorisation applications, pharmacovigilance, and inspectorate activities. BEMA is an opportunity for European National Competent Authorities to identify and share best practices within the network towards the development of a world-class medicines regulatory system.

Following appropriate training, four (4) members of the MMA have contributed as assessors in the BEMA assessments of five (5) Medicines Agencies. These assessments emphasise the contribution of the MMA in the strengthening of the European network of medicines agencies while constituting an enriching opportunity for the MMA BEMA assessors.

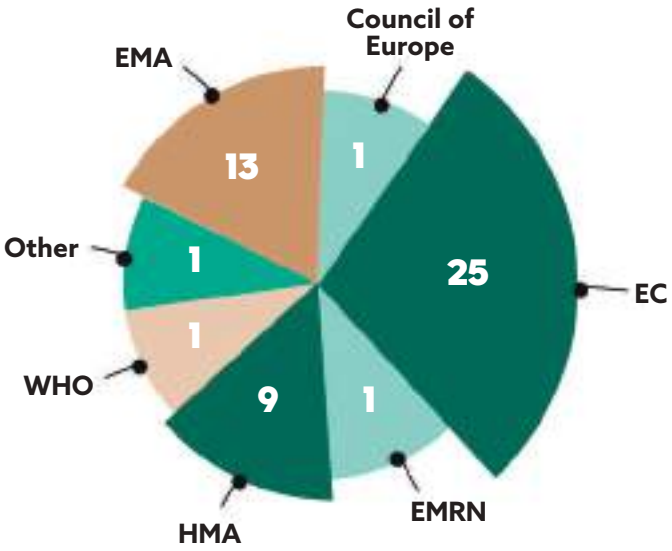


Figure 2.5: Representation by the MMA in European institutions and professional bodies (N=51).

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 2023, the extent of the Authority's representation in professional bodies was sustained and surpassed the Authority's engagement of 2022. By the end of the year, MMA delegates were involved in a total of fifty-one (51) strategic and scientific expert groups, committees, and boards (Figure 2.5).

The MMA was consulted on two hundred fifty-four (254) established and proposed EU legislative files and any relevant outputs from the EU institutions, which mostly concern the regulation of medicines, medical devices, 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 2.6), keeping the interest and safety of patients and consumers at the core of all positions put forward.

Proposal for a Regulation of the European Parliament and of the Council on fees and charges payable to the EMA, amending Regulation (EU) 2017/745 of the European Parliament and of the Council and repealing Council Regulation (EC) No 297/95 and Regulation (EU) 658/2014 of the European Parliament and of the Council

Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC

Proposal for Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the EMA, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

Proposal for a Regulation of the European Parliament and of the Council on compulsory licensing for crisis management and amending Regulation (EC) 816/2006

Proposal for a Regulation of the European Parliament of the Council amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices

Proposal for a Regulation of the European Parliament and of the Council on specific rules relating to medicinal products for human use intended to be placed on the market of Northern Ireland

Proposal for a Regulation of the European Parliament and of the Council on the supplementary protection certificate for medicinal products

Proposal for a Regulation of the European Parliament and of the Council on the unitary supplementary certificate for medicinal products, and amending Regulation (EU) 2017/1001, Regulation (EC) No 1901/2006 as well as Regulation (EU) No 608/2013

Proposal for a Directive of the European Parliament and of the Council concerning urban wastewater treatment

Figure 2.6: EU legislative files and any relevant outputs from the EU institutions on which the MMA was consulted in 2023.

Through the tenets of knowledge dissemination and training in advanced pharmaceutical research, the MMA reaches out to its counterparts in third-country states intending to consolidate the quality of medicines and medical devices imported into the EU and spur the accessibility of medical products in the Maltese islands. The Authority has sustained the impetus in international affairs through several networking initiatives that consolidate the role of Malta as a global player. The MMA was consulted on several bilateral collaborations including with Qatar, Libya, Saudi Arabia, Ghana, India, Kyrgyzstan, and Algeria. In 2023, the MMA initiated a collaboration with Montenegro which was established by the endorsement of a Memorandum of Understanding (MoU) agreement providing support in the alignment process to European standards with relevance to medicinal products, medical devices, and pharmaceutical activities. The year 2023 saw the incipit for the strengthening of a collaborative relationship between the MMA and the French Agence Nationale de Sécurité du Médicament et des produits de santé (ANSM). A MoU between the entities is being drafted to foster cooperation in multinational teams (MNAT) in the context of applications assessed through the centralised procedure and optimising use of expertise to assessments and inspections on medicinal products' manufacturing and clinical trials, cannabis for medicinal and research purposes and medical devices. 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 concerning pharmaceutical product registration, pharmaceutical quality control, and pharmacovigilance.

Members of the Authority have also contributed to other related platforms, including the EU Executive Steering Group on Shortages of Medicines and Medical Devices (MSSG) 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 medical devices and increasing capacity building of the EU Medicines Regulatory Network (EMRN).

COMMUNICATION AND STAKEHOLDERS SYNERGY AT AN ENTREPRENEURSHIP LEVEL

Pharmaceutical Entrepreneurship

The Pharmaceutical Products Entrepreneurship Unit:

- Coordinates synergy in pharmaceutical entrepreneurship processes, spearheads projects of relevance to regulatory sciences;
- Ensures the effective and efficient management of entrepreneurship processes related to pharmaceutical products, and
- Addresses pharmaceutical queries in an entrepreneurship manner and supports financial planning and management within the Authority, including the identification of opportunities for EU funding.

The Unit collaborates with private enterprises, entities, and public figures on relevant projects. To this end, in 2023 the Unit engaged with thirty-six (36) stakeholders to discuss pharmaceutical entrepreneurship initiatives on key projects, including services in support of special groups of patients, research and advanced therapies.

The Authority undertook an entrepreneurial initiative by collaborating with stakeholders in the organisation of a conference held locally which aimed to attract enterprises to Malta and offered the opportunity for networking and discussions on policy making and regulation, medical innovation, and personalised, patient-focused technology. Topics discussed at the conference included interventional and technological innovation, digital health, and medical devices.

The Authority is actively participating in an EU joint action within the EU4Health Programme which is working towards increasing the capacity building of the EMRN by leading a work package within the joint action. The overall objectives of the joint action are to improve the accessibility, availability and affordability of medicinal products, medical devices and products required in a crisis within the EU, to encourage innovation concerning medical products by increasing the necessary regulatory expertise and competencies within the EMRN, and to establish further capacities to enable the facing of challenges related to upcoming scientific advancements. The establishment and exchange of knowledge and capacity to facilitate improved collaboration among members of the EMRN, including the sharing of best practices and development of training opportunities, aims to build capacity, build competence, promote work-sharing, and increase network collaborations. The joint action will encourage efficient use of resources, avoiding duplication of work and optimising regulatory processes, thereby fostering a long-lasting opportunity for cooperation.


VIRUS

QUALITY, SAFETY, EFFICACY: THE 3 PILLARS OF AN EFFECTIVE MEDICINES REGULATOR

ASSESSMENT OF MARKETING AUTHORISATION APPLICATIONS

One of the main priorities of the MMA is to ensure 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 Authorisations

The number of procedures positively finalised with a grant of MAs in 2023 is shown in Figure 3.1. These submissions include applications for National MAs as a result of:

- Purely national procedures (n=2);
- MAs 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=501), and
- Parallel Import (PI) licenses (n=79).

A total of eight hundred and forty-eight (848) new products were authorised in 2023.

New authorised products according to the route of registration	Number of authorisations issued
DCP/MRP Malta RMS	72
DCP/MRP Malta CMS	194
AA	501*
National Applications	2
PI	79*

*Some procedures are still ongoing given pending information from applicants

Table 3.1: Total number of product applications and resulting product authorisations through all routes in 2023 (N=848)

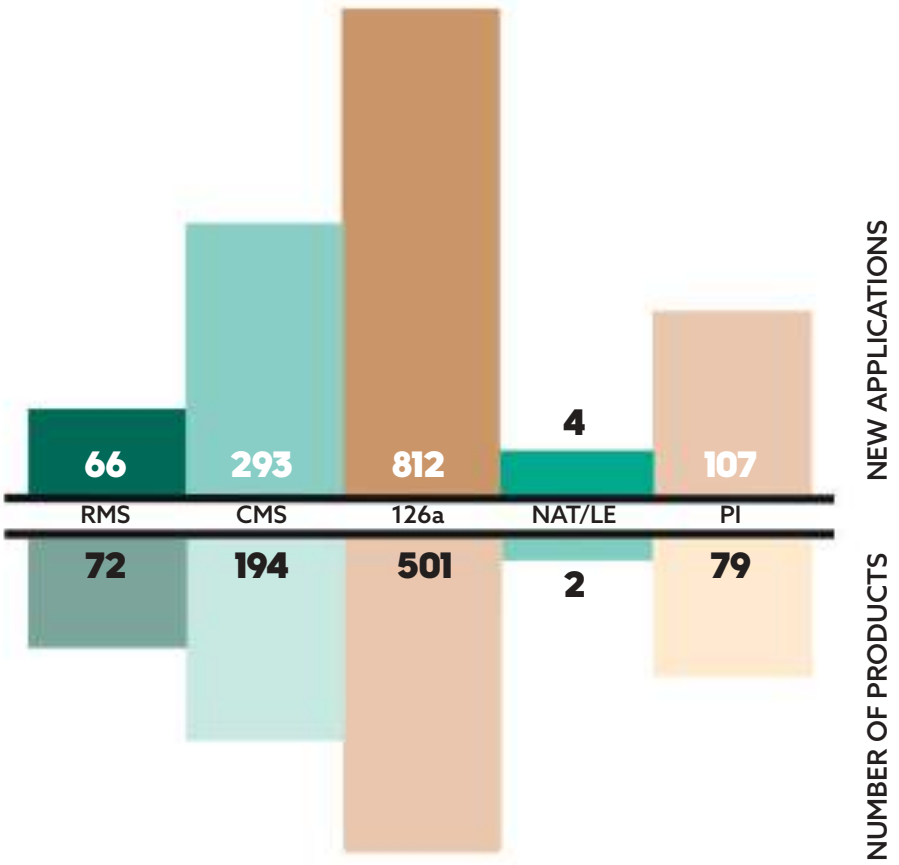


Figure 3.1: Total number of product applications (N=1282) and resulting product authorisations through all routes in 2023 (N=848).

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

The cumulative number of authorisations in accordance with Article 126(a) of Directive 2001/83/EC standing at the end of 2023 was two thousand three hundred and seventeen (2,317), whilst eight hundred and twelve (812) applications were received. There was a 123% increase in the number of applications received when compared to the previous year. As a result of Brexit, a shift in source countries in 2023 continues to be observed, with most products now originating from Ireland (IE), followed by Germany (DE). The Licensing Directorate continued to support companies to apply for MAs through the MRP. One-to-one meetings with companies are held to encourage the use of the Zero-day MR Procedure over applications in accordance with Article 126(a). As a result of the use of the MR procedure, several authorisations in accordance with Article 126(a) were subsequently revoked (n=23). Out of these twenty-three (23) authorisations, nine (9) have been authorised specifically through the Zero-day procedure and fourteen (14) products have been included in procedures where Malta was a CMS.

Companies are always supported to make use of the established European procedures, through sound regulatory advice, reduction of bureaucracy and enabling communication channels with other competent authorities for this route to be made more feasible. A European guideline regarding this procedure is being drafted.

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 is primarily achieved through its role as a Reference Member State via the European DCP and the MRP, and by acting as co-/rapporteur for the authorisation of medicinal products through the Centralised procedure.

The MMA is steadily increasing its portfolio and embarking on the assessment of more complex products. The MMA continues to receive numerous requests to act as RMS in the DCPs. In 2023, the requests in this regard reflect the current European trends experienced by all Member states, cementing Malta as an attractive option for industry to select as an assessing country for medicine quality, safety, and efficacy. Meetings with industry stakeholders are held regularly to plan for their proposed portfolio to submit to Malta as a Reference Member State. Efforts to service the industry, recruitment, and training of staff to be able to handle more procedures continue to be a priority.

During 2023 a reorganisation of existing resources was carried out within the Licensing Directorate, with the intent of rationalising and making better use of the current resources. The management team of the Directorate has been strengthened to be able to handle the increasing workload and personnel.

The number of authorisation procedures led by Malta as RMS in the DCP received in 2023 was fifty-two (52) procedures with a resulting of one hundred and two (102) MAs 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 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 2023, Malta ranked eleventh (11th) as a Reference Member State for the number of started MR and DC procedures and tenth (10th) (Figures 3.2 and Figure 3.3) in the number of finalised procedures with Malta as RMS.

In 2023, Malta was rapporteur for one (1) application 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-four (44). This sets 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 where expertise is available to contribute, through internal staff and external international experts engaged

with the MMA. This enhances collaboration with other European countries and allows for these internal and external experts in the organisation to work with counterparts in other agencies.

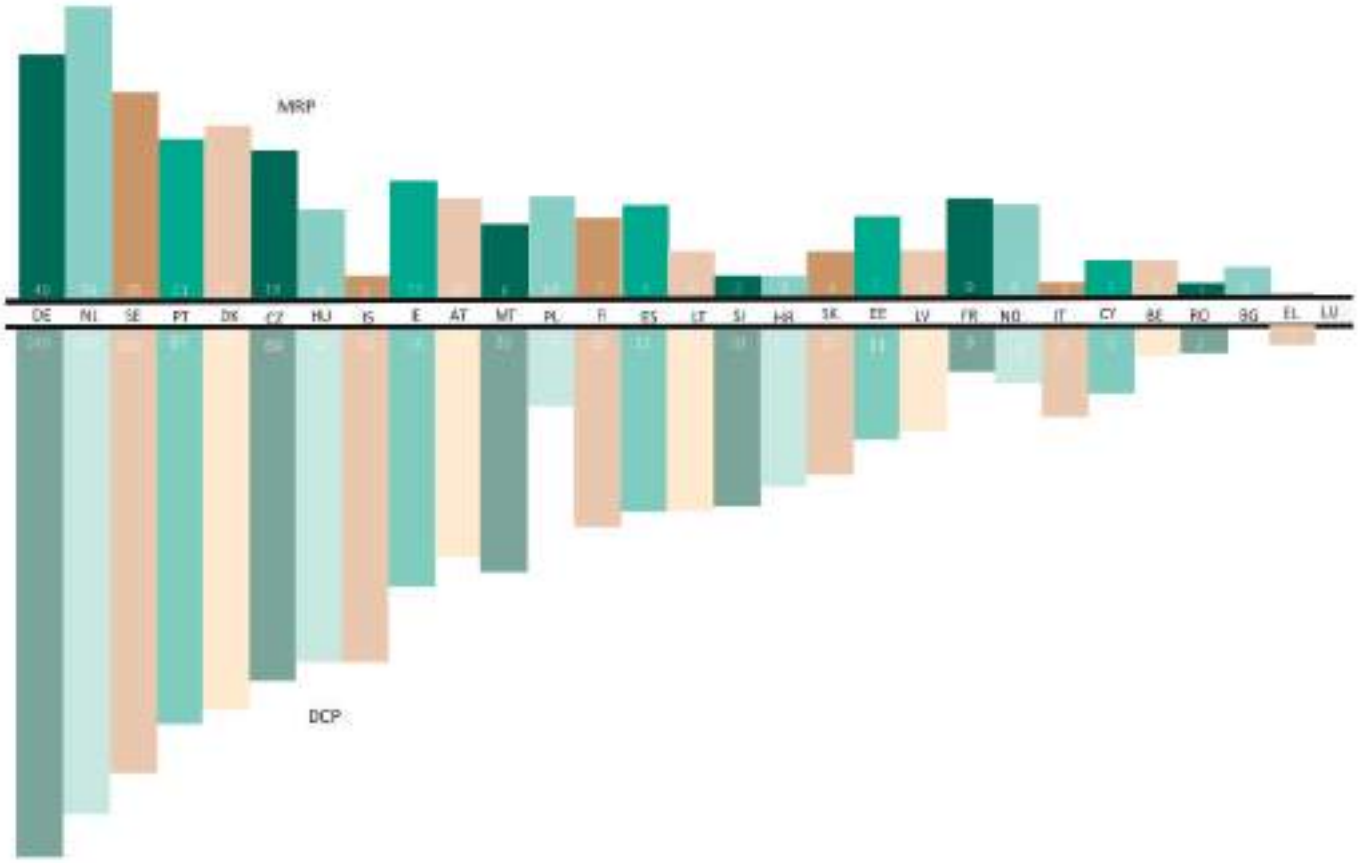


Figure 3.2: 2023 started MR/DC procedures by RMS.
Total: 314 MRP and 1215 DCP (regarding 549 and 2446 products respectively) (source CMDh).

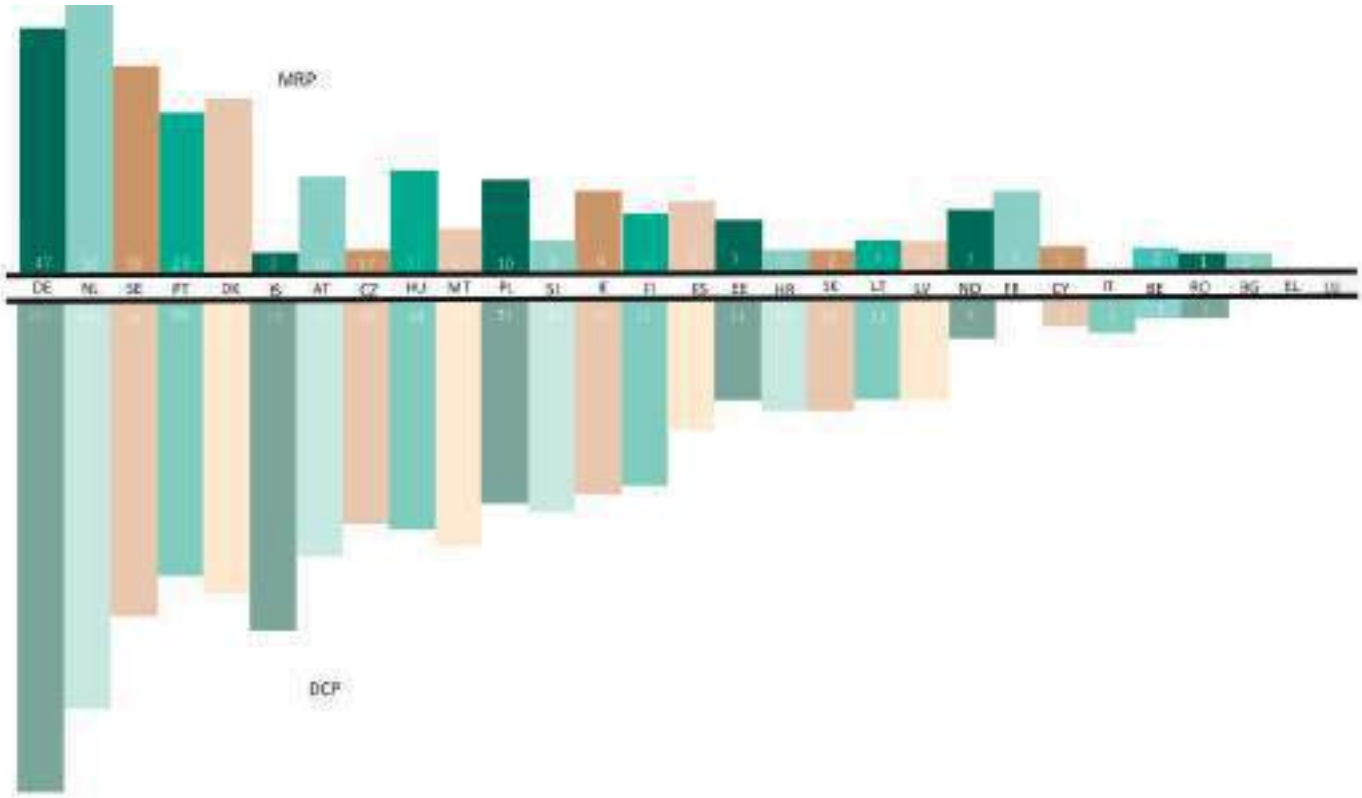


Figure 3.3: 2023 Finalised DC/MR procedures by RMS.
Total: 293 MRP and 953 DCP (regarding 531 and 1864 products respectively) (source CMDh).

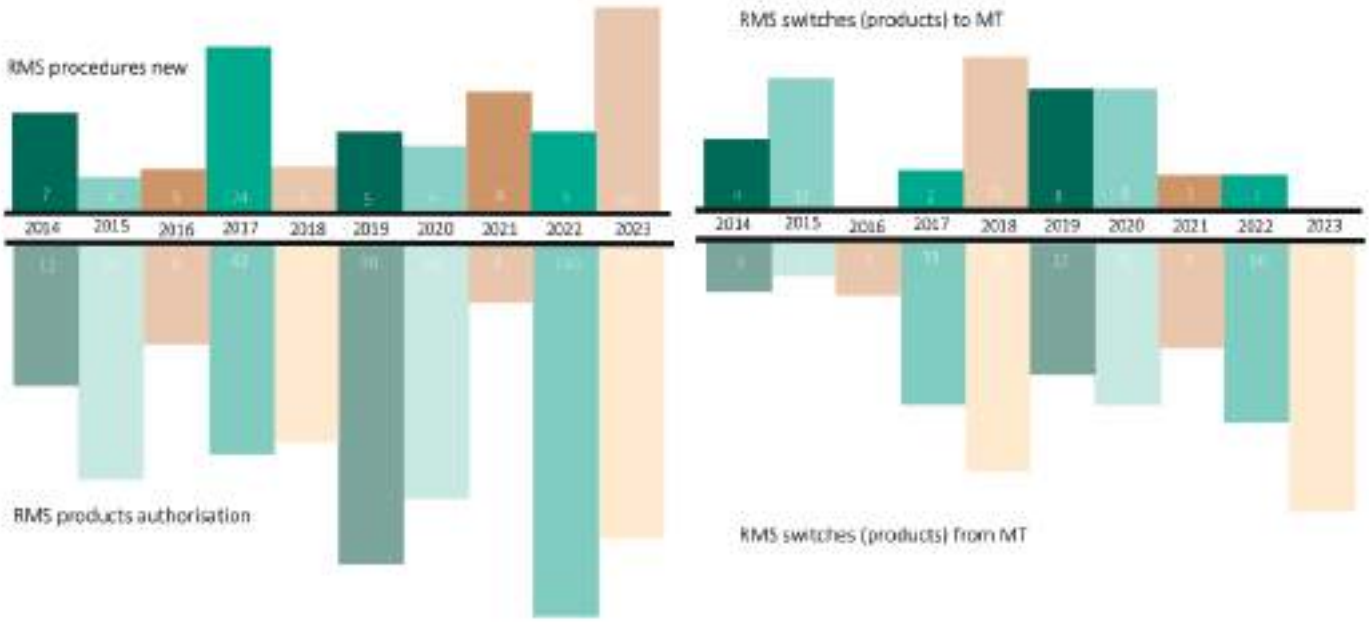


Figure 3.4 and Figure 3.5: Non-cumulative overview of applications as the number of procedures (and resulting product authorisations) with MT as RMS, inclusive of RMS switches (2014-2023)

Figure 3.4 and Figure 3.5 give a year-on-year (YoY) overview of the number of procedures handled by the MMA over the period 2014-2023. In 2021 a record number of duplicate procedures were received, and this explains the very high number of procedures during that year. In 2022, the number of duplicates stabilised to previous numbers but there was an overall increase of procedures received over the previous years. This level of duplicates was maintained in 2023, and the increase in new applications were for different active moieties.

Malta as a Contributor in European Procedures

The number of MA applications received in 2023 in the MRP and DCP with Malta as CMS were two hundred and ninety-three (293), whilst one hundred and ninety-four (194) new 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 to which smaller Member States are included as CMS in European procedures by pharmaceutical companies.

However, during the last year, Malta has continued to see an increase in the number of European Marketing Authorisations applications received through this route, also resulting from the increasing use of the Zero-day MR Procedure 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, where the products are required.

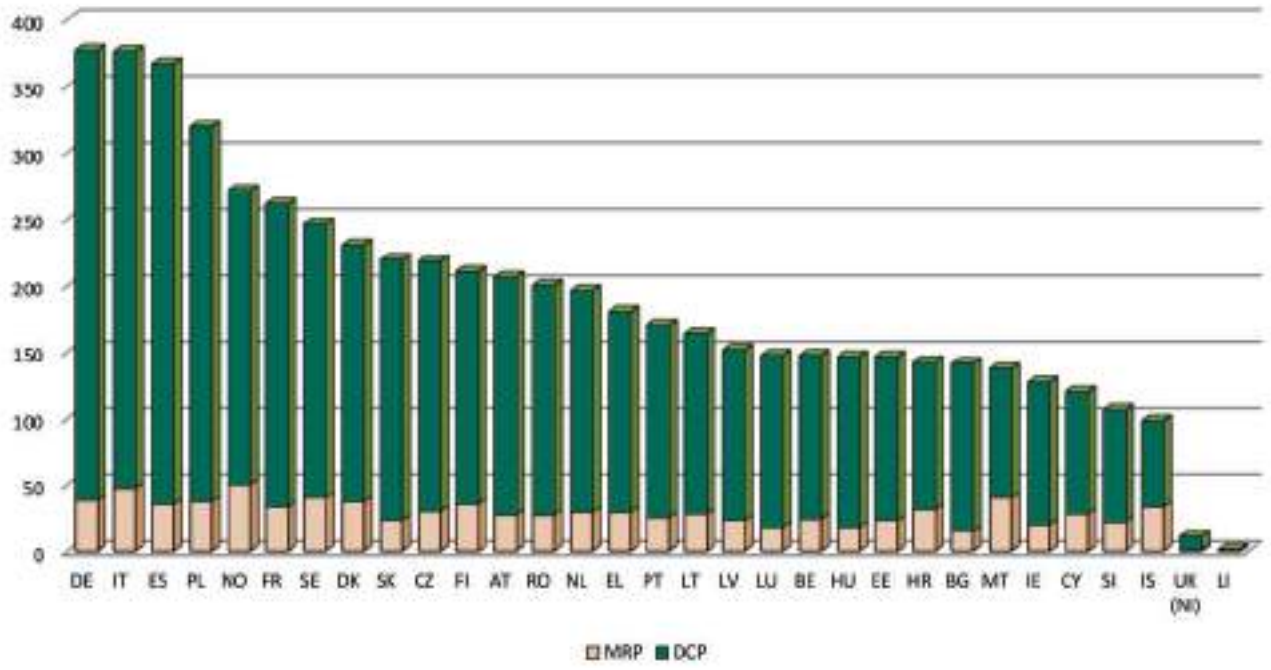


Figure 3.6: Number of MRPs and DCPs started in 2023 by CMSs.
Total: 314 MRP and 1215 DCP (regarding 549 and 2446 products respectively) (source CMDh).

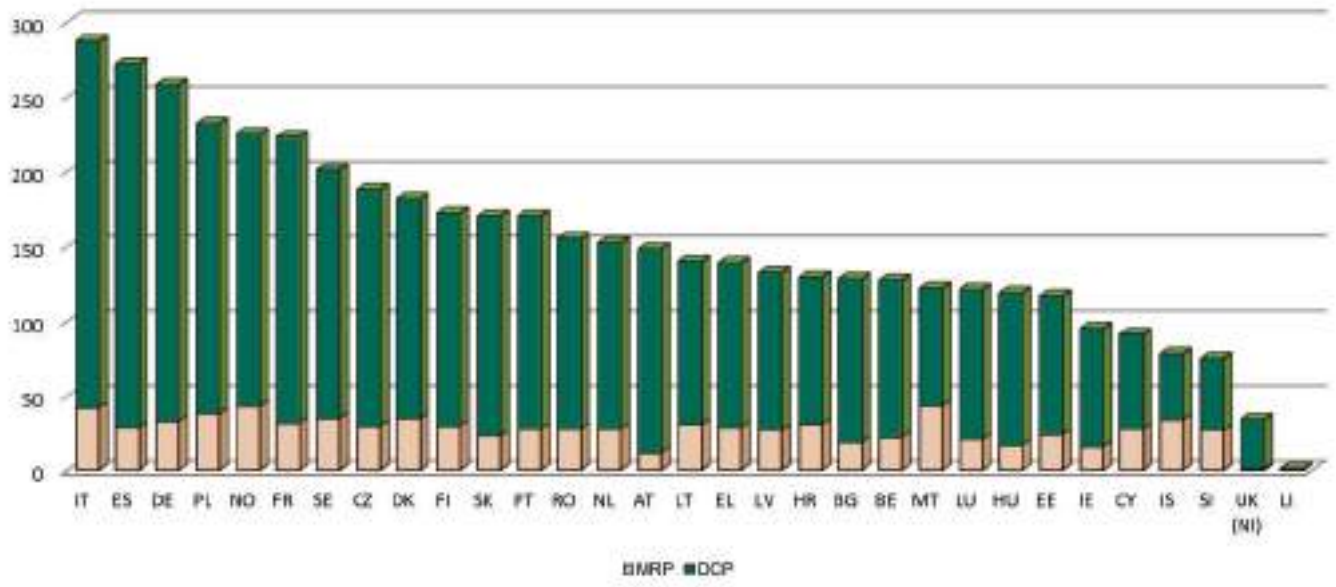


Figure 3.7: The number of MRPs and DCPs finalised in 2023 by CMSs.
Total: 293 MRP and 953 DCP (regarding 531 and 1864 products respectively (source CMDh).

Figure 3.8 gives an overview of the registration of medicinal products over the period 2014 - 2023 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 2020. Therefore, despite the loss of medicinal products that were withdrawn because (mainly) of Brexit, the number of authorised products remained constant. The years 2019 and 2020 were exceptional for the number of applications for authorisations in accordance with Article 126(a) from the UK. 2023 saw another increase in the number of applications via Article 126(c) of Directive 2001/83/EC as amended by Directive 642/2022, reaching the 2019 trend. This has helped to maintain several authorisations in place until alternatives from other European Member States are being identified by companies, for the supply of medicinal products for the national health service. The products can continue to be made available based on the derogations granted by the European Commission (EC) until the end of 2026, in case of no availability of alternatives from the EU.

Figure 3.8: A 10-year overview of non-cumulative products registered yearly in MT by route of registration.

NITROSAMINES REFERRAL

All Market Authorisation Holders (MAHs) were requested to review their manufacturing processes for all products containing chemically synthesised or biological active substances to identify and, if necessary, mitigate the risk of the presence of nitrosamine impurities. By March 2021 (chemical medicines) and July 2021 (biological medicines) a risk evaluation, known as the Step 1 Risk Evaluation, was requested from all MAHs. If a risk for nitrosamine formation was identified in Step 1, MAHs were requested to proceed with Step 2 confirmatory testing of the finished product by September 2022.

All Step 2 responses were reviewed by a team of two (2) members from the Licensing Directorate and tabulated. In cases whereby a scenario A or D was declared by the applicant, the communication was forwarded to the lead Member State for the preparation of the AR as per CMDh's internal guidance. For scenarios B and C, the data was tabulated and saved in the respective product folders.

All incoming variations including the nitrosamine specifications are being individually assessed by the quality assessors as per usual variations timelines. In 2023, MT volunteered to be the lead Member State for one (1) Active Pharmaceutical Ingredient (API) for which a nitrosamine was detected during a DCP procedure. To date, there have been no requests for assessments on Scenario A cases from other Member States.

In July 2023, the nitrosamines Q&A amended Question 10 to include the Carcinogenic Potency Categorization Approach (CPCA) and the Enhanced Ames Test (EAT) for establishing AIs for N-nitrosamines. In addition, Appendix 1 listing the nitrosamines for which AI have been established by the Nonclinical Working Party (NcWP), including new AIs for N-nitrosamines determined using the CPCA was published. This has led to the widening of a large number of impurity limits which in turn increased the number of variations submitted by MAHs.

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 concerning quality, safety and efficacy of all products is always available to the Authority, Healthcare Professionals and patients and published on the MMA website product database.

Post-authorisation activities, especially for procedures where Malta is an RMS, maintained an increased average, 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 3.10). As the RMS portfolio increases, this results in a consistent increasing trend in the number of post-authorisation procedures. The MMA received four hundred thirty-nine (439) variation applications in this category with resulting updates to nine hundred and seventy-

six (976) products in procedures where Malta is the RMS (Figure 3.9). It has been noticed that companies in their recuperation phase have refocused on implementing quality and manufacturing site changes to ensure continued stock supply.

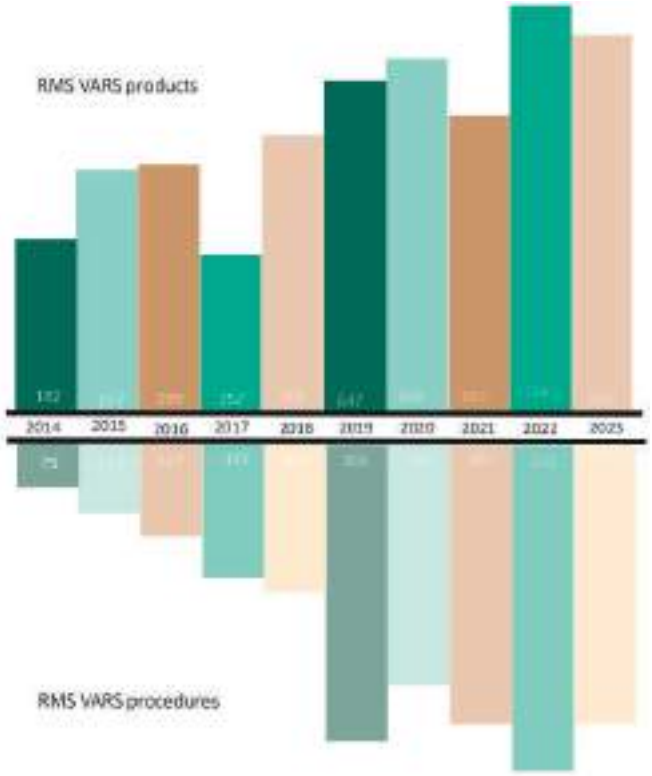


Figure 3.9: Overview of the number of VARS applications (with resulting product information changes) received for procedures with MT as RMS.

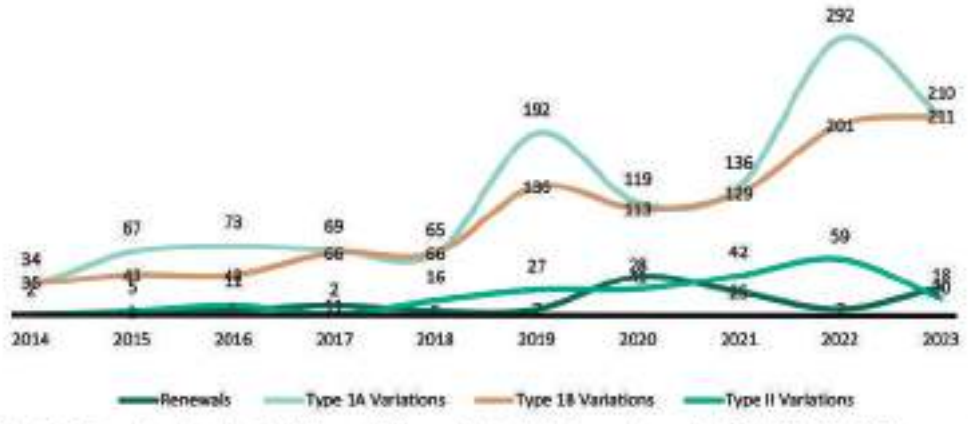


Figure 3.10: Number of post-authorisation applications received by MMA for procedures where MT is RMS (2014-2023).

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. Forty-one (41) post-authorisation activities for Centralised procedures where Malta is rapporteur were reported for 2023. Thirty-eight (38) were variations, including Type 1B and Type II variations, while three (3) were renewal of MAs (Figure 3.11).

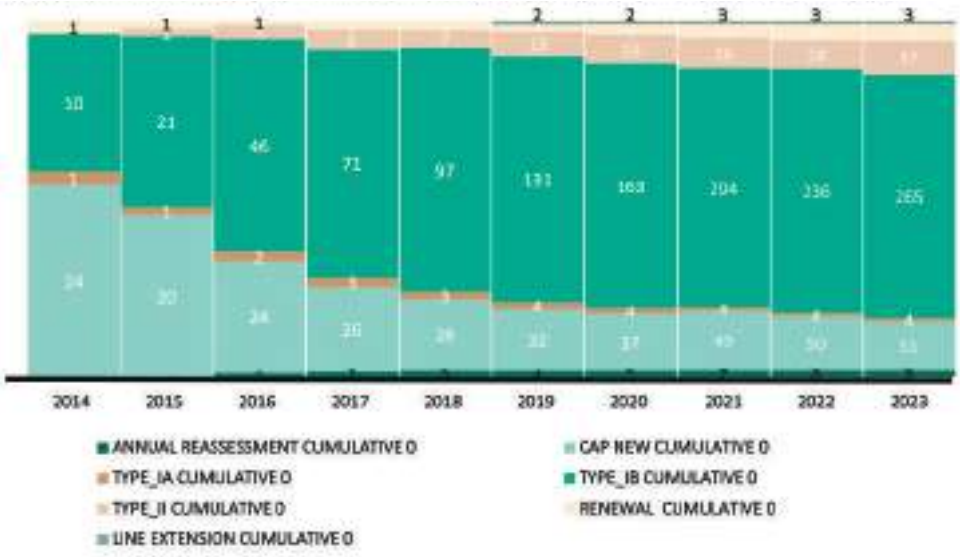


Figure 3.11: Cumulative number of post-authorisation procedures with MT as co/rapporteur in the centralised procedure (2014-2023).

In 2023, the MMA received:

- One thousand four hundred and fifty-seven (1457) procedural variation applications, and
- Other post-authorisation procedures including twenty-nine procedural (29) renewals and forty-nine (49) 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 2023.

Figures 3.13, Figure 3.14, and Figure 3.15 show the number of national post-authorisation procedures, including renewals, variations, MAH transfers and notifications in accordance with Article 61(3) of Directive 2001/83/EC.

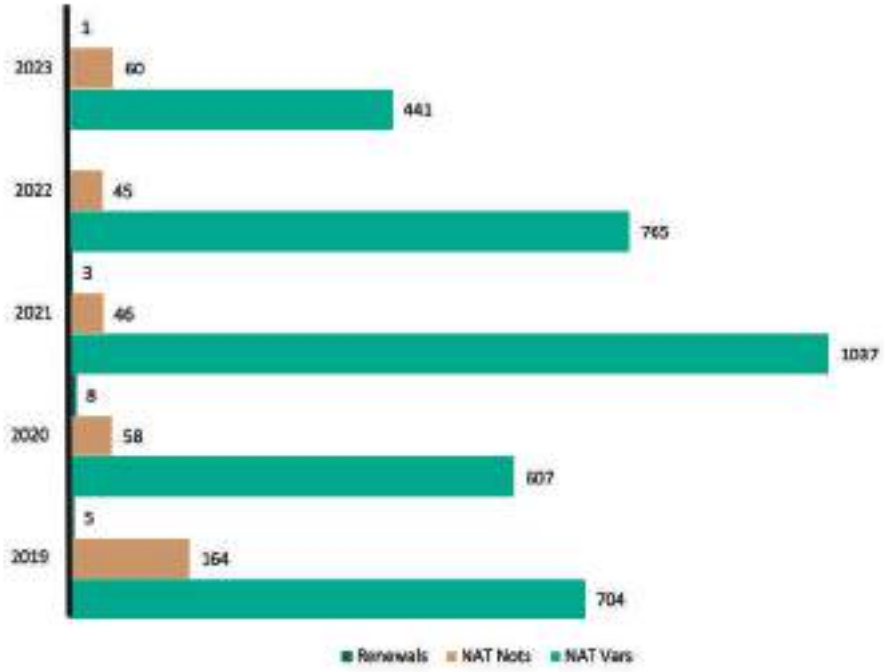


Figure 3.13: Number of post-authorisation procedures for NAT MAs received in 2023 (N=502).

Over the previous year, the number of post-authorisation procedures decreased for these products because of the reduction in several 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 3.14 and Figure 3.15 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. Product information must be 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.

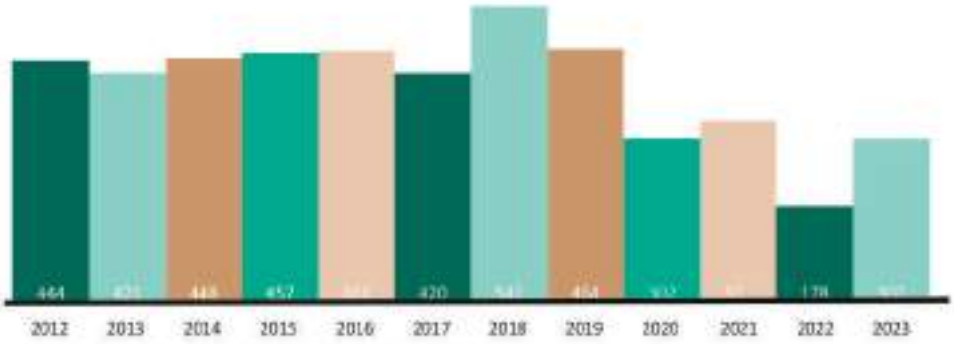


Figure 3.14: Number of post-authorisation procedures received.
For authorisations in accordance with AA of Directive 2001/83/EC in 2023 (N=302)

Figure 3.15 gives a breakdown of variation applications received by type and applications for the renewal of MAs

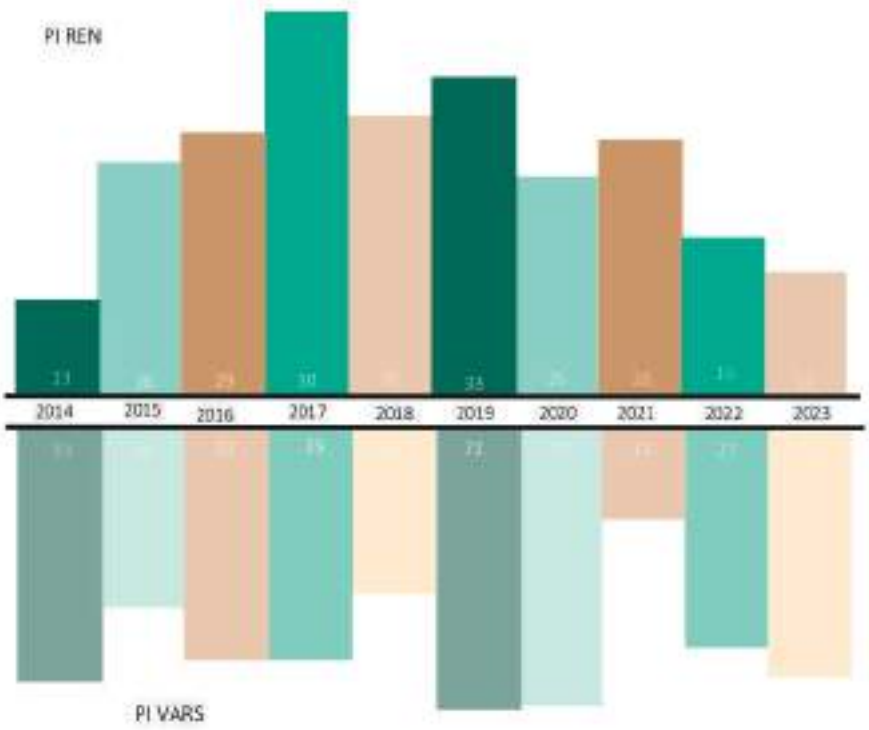


Figure 3.15: Number of post-authorisation procedures received for PI licences in 2023 (N=45).

PHARMACOVIGILANCE ACTIVITIES

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 includes the evaluation, monitoring and communication of safety-related data and, where

appropriate, implementation of regulatory action to maximise benefits and minimise risks associated with medicinal products.

The collection, investigation, and transmission of Adverse Drug Reaction (ADR) reports to EudraVigilance comprises a major Pharmacovigilance activity carried out. In 2023, 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 2023, included participation in two (2) face-to-face seminars targeting patients and professionals and participation in the annual ADR awareness week social media campaign (#MedSafetyWeek). During the seminars, MMA staff instructed participants on how to report ADRs and explained how ADR reporting translates into improving the safety of medicines. In 2023, #MedSafetyWeek was held between the 6th to 12th of November 2023 and aimed to increase awareness of the importance of monitoring 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 the EudraVigilance Data Analysis System (EVDAS) allow for detailed analysis of ADR data.

A total of one hundred and twenty (120) Individual Case Summary Reports (ICSRs) were registered in 2023. These cases detailed at least one (1) ADR to the medicinal product concerned and together these one hundred and twenty (120) ICSRs resulted in three hundred and thirty-seven (337) suspected Adverse Events (AE). Figure 3.16 gives a breakdown of these ADRs according to System Organ Class (SOC) classification.

Figure 3.16: Distribution of ADRs according to SOC in 2023 (N=337).

Each case report received at the MMA was assessed and reported electronically to the EMA and the WHO as the central ADR repositories. Figures 3.17 and Figure 3.18 further classify the adverse ICSRs (as received over 2023) 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 3.17 and Figure 3.18 further classify the adverse ICSRs (as received over 2022) according to the 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 3.17: Frequency of ICSRs according to seriousness in 2023 (N=120).

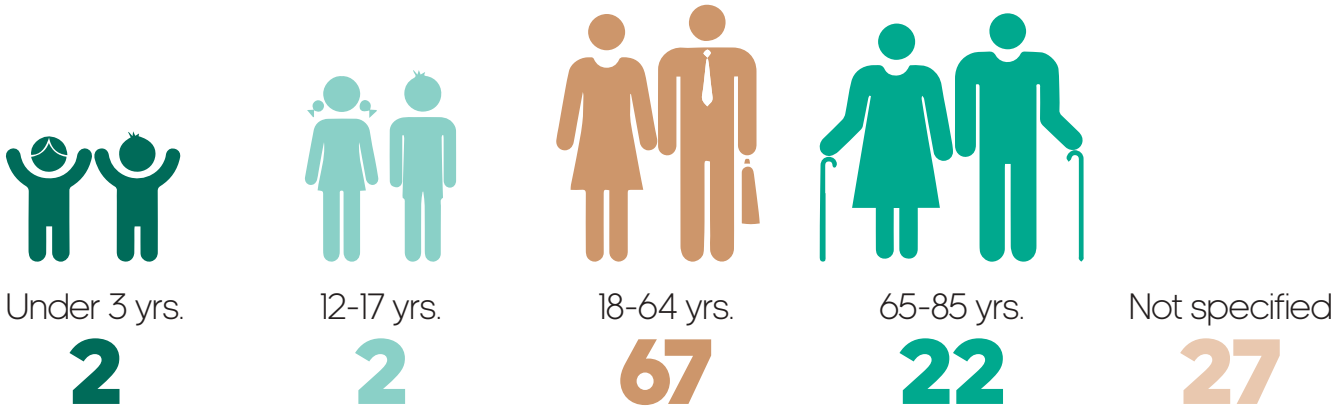


Figure 3.18: Distribution of ICSRs according to patient age in 2023 (N=120).

In addition to the management of ADRs and routine safety signal management as relevant, several other activities were undertaken nationally by the Authority in 2023 to attain 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, and product recalls which, where necessary, can lead to immediate product suspension and/or recall,
- Approval and monitoring of Risk Minimisation Measures (RMMs) and educational material relating to high-risk medicinal products as well as approving Pregnancy Prevention Programmes (PPPs) as proposed to potentially teratogenic medicinal products,
- Issue of safety circulars and media statements addressed to healthcare professionals and the public respectively. Safety Circulars give recommendations on medicinal product use and applicable cautionary and precautionary measures. Throughout 2023 the Authority continued implementing the SMS notification service that allows subscribed medical and healthcare professionals 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 combinations not included in the list of European Union reference dates (EURD list) and Periodic Safety Update Report Single Assessments (PSUSAs) work-sharing at an EU level,

- Assessment of risk management plans during national and centralised procedures.

Table 3.2 gives the distribution of safety communications and Risk Minimisation Measures (RMMs) approvals which the MMA handled over 2023:

Activity	Number of safety communications and RMM approvals
DHCPs	5
Joint DHPCs	6
Safety Circulars	8
RMMs	95

Table 3.2: Safety Communications and RMMs approvals in 2023 (N= 114)

An additional stakeholder service performed by the MMA is that of responding to any queries related to Pharmacovigilance activities promptly. In 2023, queries received were mostly related to:

- National pharmacovigilance legislation and requirements locally, and

- Clinical trial pharmacovigilance requirements Suspected Unexpected Serious Adverse Reactions (SUSAR) and Development Safety Update Reports (DSURs) (Table 3.3).

Area Queries	Number (n)
National pharmacovigilance legislation and requirements locally	12
Clinical trial SUSARs and DSURs	8
Literature monitoring requirements	3
Qualified Person for pharmacovigilance/Local contact person for pharmacovigilance	2
ADR Reporting/ICSR transmission requirements	2
Submission requirements of PSURs	2
RMPs/RMMs/Educational Material	2
Post-Authorisation Efficacy Studies (PAES) and Post-Authorisation Safety Studies (PASS)	1
Total	**32**

Table 3.3: Pharmacovigilance-related queries in 2023 (N=32)

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 material 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 2023, two (2) advertising complaint procedures were registered.

CLINICAL TRIALS

The role of the MMA concerning clinical trials is to evaluate both the quality of the investigation and the patient safety of clinical trials provide recommendations to the licensing authority and provide authorisation based on the Authority's and the Health Ethics Committee's recommendations.

The new Clinical Trial Regulation (CTR), Regulation (EU) No 536/2014, came into application on 31 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. As of 31 January 2023, all initial clinical trial applications must be submitted through the new Clinical Trials Information System. For 2023, no clinical trial assessment procedures were registered.

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 MA 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 several 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 to produce cannabis for medicinal and research purposes. In close cooperation with relevant stakeholders, the Authority was central in coordinating the passing of a legal amendment to Subsidiary Legislation 578.01 of the Laws of Malta which aims at ensuring good governance and transparency, enhancing the sustainability of the local cannabis industry, improving patient accessibility to quality cannabis-based products, promoting research activities in the medicinal cannabis sector and safeguarding sufficient resources for the performance of regulatory activities.

The regulatory framework, as published in the respective MMA Guidelines, involves several 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.

The total number of approved cannabis-based products standing at the end of 2023 was thirty-four (34), where such products may have varied pack sizes and were commercialised through both wholesale and production routes; the charts in Figure 3.19A and Figure 3.19B respectively characterise their formulation and cannabinoid concentration. A similar 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 two-thirds of the products fall in the THC-dominant type category. The cannabinoid concentration for the approved oils and extracts ranges from 240mg/ml for most CBD-dominant products to a THC concentration of 8.7mg/10µl present in the purified extract. The most potent THC-approved flower product has a concentration of 25% w/w.

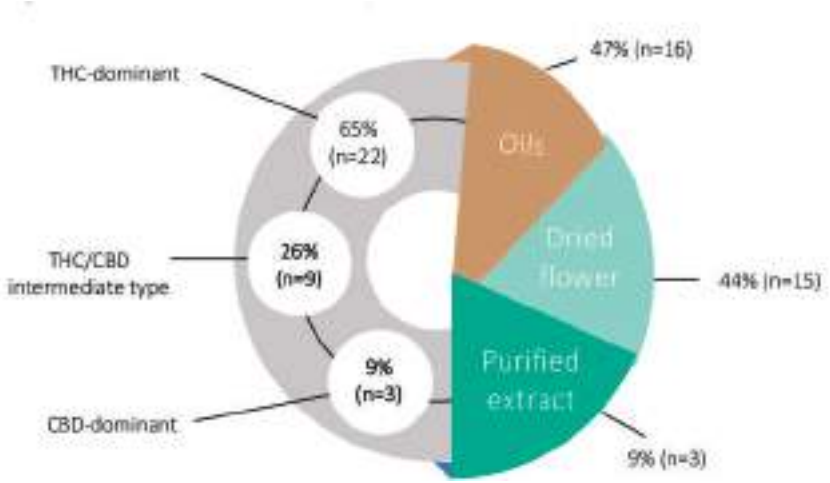


Figure 3.19A: Characterisation of the approved cannabis-based products according to their cannabinoid content (N=34).
Figure 3.19B: Characterisation of the approved cannabis-based products according to their formulation (N=34).

The Authority continuously upholds the integrity of transacted cannabis material by monitoring for reconciliation and traceability through periodic updates from its stakeholders. For 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 thirty-five thousand (35,000) serialisation codes were issued by the Authority to local operators throughout 2023 for product units intended to be marketed (Figure 3.20). 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 3.20: Units of cannabis-based products for medicinal use issued with a serialisation code, characterised by pharmaceutical activity, 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 an annual renewal, including a review of emerging data in updated studies.

- **WHOLESALE DISTRIBUTION**

Two (2) operators are approved for wholesale distribution activities, both of which source cannabis in its dried inflorescence form. A total of forty-four (44) new and sixteen (16) renewal applications for cannabis-based products were received and reviewed by December 2023. A notification of approval was issued for ten (10) dried flower products throughout 2023.

- **PRODUCTION AND RESEARCH**

The total number of companies issued with a positive recommendation for the grant of a licence to produce cannabis for medicinal and research purposes by the end of 2023 stood at six (6) from the seven (7) applications received. The first application for the renewal of a production licence was received in 2023, whilst the first company was granted a research licence in the same year. One (1) facility produces oils and purified extracts, another three produce flowers, with the remaining company manufacturing products in both inflorescence and oil formulations. A total of forty-three (43) applications for a variation to the production licence were received throughout 2023. This represents a spike of 153% in the total number of variation applications received throughout the year under review when compared to the preceding two (2) years combined. The variations which requested amendments to the conditions of the licence or proposed changes to relevant application documents are broadly categorised in Figure 3.22. Half of the variation applications received in 2023 were of variation type A3, relating to changes in product details.

Figure 3.21: Types of VARS applications received requesting changes/introductions to the production licences.

Through liaison with relevant bodies, seven (7) local inspections were coordinated in 2023, including five (5) for EU-GMP and two (2) for facility/physical security. The licensed operations include the production of five (5) products in dried flower form, sixteen (16) oils and three (3) purified extracts, seventeen (17) of which are intended for export in destination markets, three (3) for domestic consumption and four (4) can be commercialised both locally and abroad.

REGULATING MEDICAL DEVICES

Authorisation Activities

The Directorate is responsible for the processing of applications 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 in-vitro diagnostics in Malta are to register with the 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.

Certificates of Free Sales are issued by a European Competent Authority, in this case by the MMA, upon technical regulatory consideration following a request by a manufacturer or an authorised representative. By way of derogation from the Regulations, the Malta Medicines Authority may grant an exemption from the conformity assessment procedures set out in Regulation (EU) 2017/745 and Regulation (EU) 2017/746 (IVDR). An exemption may be granted after having evaluated following MDR article 59 or article 97; or IVDR article 54 or article 92. The device must not present an unacceptable risk to the health or safety of patients, users, or other persons, or to other aspects of the protection of public health.

Table 3.3 summarises the authorisation activities processed in 2023.

Application Type	Number Received
EUDAMED actor registration processed and approved by the Authority, on the European Databank	88
Medical Device Registration	86
Organisation registration	50
Certificate of free sale	39
Medical Device Registered Person Registration	33
Medical Device notification	35
Derogation related to MDR Article 97	10
COVID-19 designated premises	6
Derogation related to MDR Article 59	2
Request for Medical Device/In Vitro Diagnostic (IVD) advice	2
Request for Medical Device/IVD classification confirmation	1

Table 3.3: Applications processed to operations of stakeholders in the MD and IVD field (N= 352).

Notified Bodies, Surveillance and Clinical Relations

The Notified Bodies, Surveillance and Clinical Relations Unit is responsible for conducting assessments of conformity assessments bodies that apply for designation as a Notified Body in the field of medical devices and/or in vitro diagnostic medical devices, and for the re-assessments of Notified Bodies. The Unit proactively provides market surveillance of medical devices and in-vitro diagnostics and the economic operators. It promotes a patient-centred clinical relations approach by coordinating vigilance through the evaluation of reported incidents and complaints. The Unit 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 the safeguarding of 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 by EU regulations through its commitment to designate and subsequently continuously monitor the performance of Notified Bodies registered in Malta. Two (2) conformity assessment bodies have ongoing applications in Malta for designation as a Notified Body. Both processes have reached the post-on-site assessment activity phase, following the two (2) joint assessment audits undertaken, which were led by the Directorate, in collaboration with the Joint Assessment Team (JAT), composed of EC auditors and other European Member State experts. One (1) process is in the assessment phase of the Corrective and Preventive Action (CAPA) plan by the designating authority, while the other process has reached the phase, whereby, the designating authority is finalising its assessment of the CAPA plan and providing the Conformity Assessment Bodies (CAB) with feedback further to the receipt of the EU Joint Action Team Corrective and Preventive Action (JAT CAPA) review. The designation processes are continued procedures set to continue in 2024.

- **CLINICAL RELATIONS: VIGILANCE**

A robust incident reporting framework that allows for the visibility of incident reports and communication with economic operators and stakeholders is deemed a strategy that promotes medical device safety. The strategy bridges enhancement of safety requirements to EU legislation taking into consideration challenges encountered by end users when using medical devices that do not meet the intended purpose. During 2023, a total of two hundred and twenty-five (225) incident reports from healthcare professionals were processed in addition to forty-two (42) device complaints/incident reports received from the public. The incident reporting system adopts a patient-centred approach in collaboration with Mater Dei Hospital (MDH) and the Central Procurement Supplies Unit (CPSU) in the interest of patient safety. A total of two hundred and twenty-six (226) Field Safety Notices (FSN)/Field Safety Corrective Actions (FSCA) were received and processed in 2023, one hundred and fourteen (114) of which were initial reports, sixty-four (64) follow-ups and forty-eight (48) final reports.

- **CLINICAL RELATIONS: CLINICAL INVESTIGATIONS/PERFORMANCE STUDIES**

A quality management system was designed and validated to support the Directorate's procedures and communication with stakeholders with an interest in running clinical investigations and performance studies in Malta. A total of five (5) application forms and one (1) review form were developed. Four (4) application forms relate to processes of clinical investigations or performance studies and adverse events whereas one (1) application form is a pre-submission meeting request. A total of six (6) guidance documents were developed, one for each form assisting the stakeholders in completing the forms. A total of five (5) SOPs were developed namely:

- Processing pre-submission meetings,
- Processing of applications related to clinical investigations,
- Processing of applications related to performance studies,
- Processing of modifications to clinical investigations or performance studies, and
- Management of serious adverse events during clinical investigations or performance studies, was developed.

In liaison with Malta Enterprise, discussions have been held with international manufacturers interested in initiating clinical investigations in Malta, with the participation and input of clinicians, willing to be involved in these investigations.

During 2023, the Directorate gained the expertise of a senior inspector thus enabling further advancement in the area of market surveillance. A Quality Management System that has been designed and validated was adopted within the medicines sector and in accordance with the European Legislation covering medical devices. This QMS supports the Directorate's procedures concerning inspection strategy to ensure patient safety and compliance with EU regulations across our national stakeholders. The Directorate proactively participates in the Medical Devices Inspector Task Force (MDITF) and is committed to supporting other member states in carrying out joint inspections in the area of medical devices and in-vitro diagnostics.

MEDICAL DEVICE MANAGEMENT SYSTEM

The MMA is creating a Medical Device Management System (MDMS), including a national database for all medical devices and in-vitro diagnostics available on the national market, The scope of this project is to enhance transparency and traceability of all products. The MDMS will host the following modules namely: entity or organisation registration, device notification, vigilance, market surveillance, invoicing and payments, and reporting module.

PHARMACEUTICAL COLLABORATION

The Pharmaceutical Collaboration arm within the Directorate is committed to fostering synergy with various entities on existing and innovative ideas for the mutual benefit of the MMA and society. In 2023, a strategic partnership was established between the MMA and Saint Vincent de Paul Long Term Care Facility (SVP-LTCF) for the development and implementation of a scientific research pilot project on clinical pharmaceutical activities and services with a focus on geriatric medicine. It is intended to develop an innovative process where pharmaceutical care goes beyond the conventional provision of safe, effective, and quality medicines to the elderly but ensures that the treatment takes into consideration active ageing. The Unit actively collaborated with the Social Care and Standards Authority (SCSA), in an exercise to identify gaps within the medication management process of residential homes for persons with disabilities and the older persons sector were identified.

These collaborative efforts have paved the way for potential improvements in the identified areas. Collaborative endeavours with the Department of Pharmacy at the University of Malta were sustained to advance the sharing of expertise and further contribute to the enhancement of pharmaceutical practices and services. 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.

ENSURING PATIENT SAFETY THROUGH HIGH STANDARDS OF PHARMACEUTICAL ACTIVITIES

The Inspectorate and Enforcement Directorate is responsible for inspecting and recommending the issue of licences for manufacturers and wholesale dealers according to national legislation, EU-GMP and EU-Good Distribution Practice (EU-GDP) respectively. The IED also carries out Good Clinical Practice (GCP) inspections of clinical trials and Pharmacovigilance inspections on a risk-based approach.

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 following the principles and guidelines of the EU-GMP. The IED manages and currently maintains a portfolio of ninety-seven (97) licensed/certified entities, local and in third countries, involved in the manufacturing, importation or other GMP related activities of medicinal products for human use, which is an increase of eighteen (18) sites/entities from the previous year (2022).

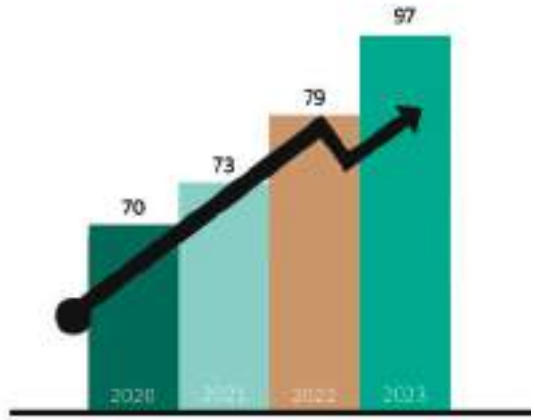


Figure 4.1: Manufacturing and importing entities supported by IED.

During 2023, the IED carried out seventeen (17) local GMP inspections for new, renewal, or variation of follow-up of GMP licences/certificates. These included:

- One (1) inspection for sterile dosage forms (aseptically prepared and terminally sterilised),
- Two (2) inspections for full-line non-sterile solid dosage forms manufacturer,
- One (1) inspection for an APIs manufacturer,
- Five (5) inspections for cannabis products for medical use manufacturers,
- One (1) inspection for a manufacturing authorisation of repackaging and re-labelling/partial manufacturing operations,
- Six (6) inspections for MAs of importation and/or batch release activities, and
- One (1) for-cause inspection.

A total of fifty-six (56) MA variation applications were processed in 2023, out of which fifty-three (53) were administrative variations, whilst the other three (3) application variations required an onsite GMP inspection.

There were three (3) Inspections Review Group (IRG) meetings held throughout 2023, during which three (3) cases were discussed and decided upon.

During 2023, the IED received five hundred and nineteen (519) rapid-alert and GMP non-compliance notifications, (a 46% increase over the previous three-year period – 2020/2022) which were investigated and out of which five (5) resulted in a recall of medical products from the local market.

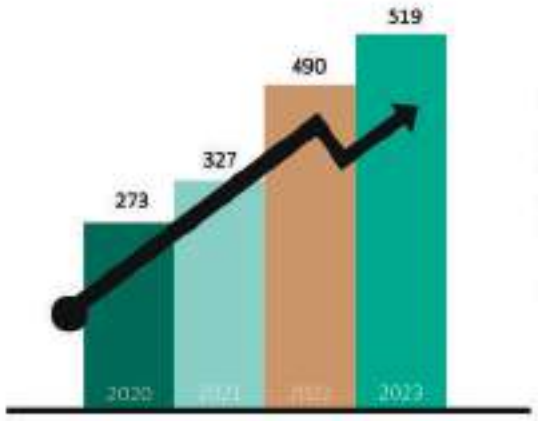


Figure 4.2: Rapid alerts trend.

During the year under review, the IED carried out twenty-four (24) GMP Inspections in countries outside the EU. 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 whilst supporting the local industry where products coming from third countries are imported and batch released by local companies. Additionally, these procedures attract new revenue to the MMA and provide exposure for the medicine inspectors of the MMA to different manufacturing facilities, thus increasing the collective corporate knowledge and experience.

Distribution

A distributor of medicinal products sources the products one distributes from within the EU/EEA. Distributors are required to follow good practice guidelines known as Good Distribution Practice (GDP) to ensure that the quality of the medicinal products is not compromised in the supply chain and to be able to carry out a recall of any defective product. The IED currently manages and maintains a portfolio of one hundred and nine (109) licensed/certified local entities involved in wholesale-dealing and brokering activities of medicinal products for human use, and of APIs distribution and importation, an increase of ten (10) sites/entities from the previous year (2022).

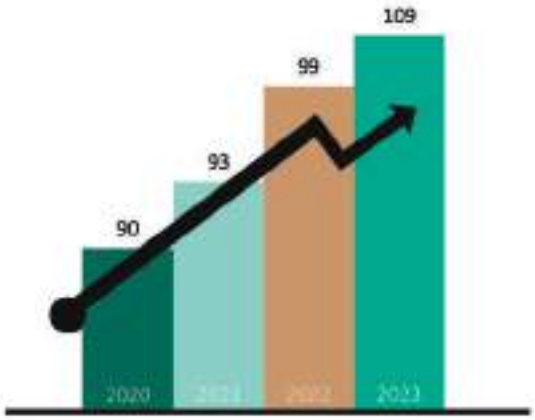


Figure 4.3: Wholesale and distribution entities supported by IED.

During 2023, the IED fulfilled its Good Distribution Practice (GDP) inspection plan where forty-six (46) GDP inspections were carried out. During 2023 four (4) new wholesale dealing licences were processed and issued by the end of the year. Forty-four (44) variation applications for wholesale dealing authorisations were processed in 2023, out of which five (5) required an onsite inspection. Also, in 2023 two (2) new applications for brokerage activity were received and eventually registered. Four (4) applications for new API import/ distribution activities were submitted, processed, and eventually registered.

CLINICAL TRIALS AND PHARMACOVIGILANCE INSPECTIONS

During 2023 in view that no new Clinical Trials applications were submitted to the MMA, no inspections for this activity were required.

Five (5) Pharmacovigilance (PhV) inspections were carried out in 2023 for local entities.

THIRD COUNTRY INSPECTIONS

During the year under review, the IED carried out twenty-four (24) GMP Inspections in countries outside the EU. 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 whilst supporting the local industry where products coming from third countries are imported and batch released by local companies. Additionally, these procedures attract new revenue to the MMA and provide exposure for the medicine inspectors of the MMA to different manufacturing facilities, thus increasing the collective corporate knowledge and experience.

Figure 4.4: Number of third-country EU-GMP inspections carried out in 2023 (N=24)

PHARMACIES, PHARMACOVIGILANCE AND SURVEILLANCE OF THE LOCAL MARKET

The Operations and Pharmacy Practice Unit within the Regulatory Operations, Medicines Intelligence and Access Directorate regulates and manages a portfolio of two hundred and fifty-three (253) licensed pharmacies, which include two hundred and thirty-eight (238) pharmacies serving patients in the community, eleven (11) hospitals and four (4) government pharmacies.

In 2023, no spot-check pharmacy inspections were carried out, eight (8) pharmacy relocations were inspected and approved, two (2) new pharmacy licences were issued and forty (40) administrative variations for pharmacy licences were processed. A total of fifty-three (53) routine inspections were carried out in 2023. Out of the total pharmacies inspected, 51% (27) were classified as high, 45% (24) as medium and 4% (2) as low risk. With these data in hand, the MMA will schedule the inspections for the following year and will ensure the prioritisation of inspections to ensure the safety of medicinal products and patients in the Maltese islands. Throughout 2023, the Unit handled forty-nine (49) queries on general procedures related to pharmacy licence, pharmacy standards and services provided at a pharmacy level.

The Operations and Pharmacy Practice Unit collaborated with colleagues from the IED and participated in an inspection at a local in-patient hospital to license the reconstitution of sterile medicinal products for chemotherapeutic applications. With the licensing of such a service, the MMA contributed to the promotion of public health by ensuring patients' access to reconstituted chemotherapy.

In a spirit of collaboration, the Unit, together with colleagues from the Office of the CEO, the ASID and the Pharmaceutical Collaboration Unit participated in care home visits (5) with the Social Care Standards Authority (SCSA) to enhance the delivery of optimal care for elderly patients and individuals with disability. The expertise of MMA officers heightened the understanding of good storage and dispensing practices for medicinal products in the elderly and disabled individuals.

As part of the government reform on inspections, the MMA continued its collaboration with the Inspection Coordination Office (ICO) towards the automation of a risk assessment model and the implementation of the Certificate of High Standard of Compliance in community pharmacies. This project ensures a coordinated approach between inspectorates and proposes a competitive scheme uplifting the standards of services provided.

The MMA collaborates with the Medicines and Healthcare Regulatory Agency (UK) (MHRA) so that the latter carries out testing in an Official Medicines Control Laboratory (OMCL) for the MMA. In this regard, the Local Market Surveillance Plan for 2022 was closed off positively. Four (4) products were identified for sampling from the local market under the national Market Surveillance plan for 2023 and two products under the European Market Surveillance plan were additionally sampled under the co-ordinated of the European Directorate for Quality of Medicines (EDQM).

ENFORCEMENT OF LEGISLATION AND JUDICIARY ACTIONS

During 2023, the IED worked on five (5) enforcement cases/investigations that were related to receiving complaints. The Enforcement Committee (a specific committee that discusses enforcement cases, chaired by the Licensing Authority) was not required to meet in 2023.

In 2023 there were no court case sittings involving IEDs.

Legal Matters

During the year under review, the Legal Unit continued to provide legal advice on a multitude of different matters, primarily revolving around the legislation, policy and guidelines that regulate the Authority. Nevertheless, the everyday activities of the Authority go beyond the laws and regulations that govern its daily operations, and the Legal Unit's remit extends to advice relating to payments, data protection, employment law, VAT law, verification of documents, and other areas that pose queries.

This Unit works closely with all the Directorates and other Units, with each request for legal assistance or advice being overseen with the utmost confidentiality and in the shortest time possible. The Unit also intervenes when there are external queries relating to licenses and authorisations issued by the Authority.

The Legal Unit takes a dynamic role in the amending and promulgation of legislative instruments under the Medicines Act, in fact during the reference year it was actively engaged in seven (7) legislative processes, which included both amendments to current legislation and the promulgation of new subsidiary legislation under the Medicines Act.

The Unit works closely with the Finance and Corporate Services Unit of the Authority in the investigation of any defaulters and takes a driving role in alerting them to redress their position. The work of this Unit extends to judicial processes, whereby it represents the legal interest of the Authority in the Maltese law courts and tribunals. It assists internally and with law enforcement in investigations to several concerns that arise, such as the setting up of online websites that offer the services of virtual doctors and obtaining a medical prescription, websites that offer the dispensing of online medicinal products and the sale of nitrous oxide on the streets, amongst a few of the subjects which the Unit is vigorously involved in.

The Legal Unit is broadly engaged in the drafting of legal letters, contracts, Memorandum of Understanding (MoUs) and other agreements wherein the Authority is a contracting party. It provides general legal assistance, including legal advice and the interpretation of laws when the need arises.

CANNABIS FOR MEDICINAL AND RESEARCH PURPOSES

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. Four (4) quality improvements have been documented throughout 2023 to streamline, facilitate and consolidate processes. Over the years, 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 externally. A member from the Unit delivered a keynote presentation during the Ditchley Group 10th Meeting in Oxfordshire, United Kingdom (UK), detailing the legal and regulatory system governing medicinal cannabis-based products and related activities in Malta (MT), with a focus on transparency and risk-based approaches. There was also participation at locally organised fora including the Med-In Pharma 2023 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.

5

TRANSLATING REGULATION INTO PATIENT-CENTRED SCIENCE

The MMA is a significant player in the global regulatory field, promoting the sharing of dynamic strategies and shaping approaches for the benefit of patients. To maintain its accomplishments and endorse further development, the MMA is continuously expanding its resources and aptitudes to mature in an evolving ecosystem. Research strategy, innovative growth and regulatory response are steered through the ASID which also encompasses the Educational Planning and Academic Development Unit, facilitating constructive synergy in commitment, effort, and outcomes.

Horizon scanning, also through involvement in the EU Innovation Network (EU-IN), is enabling the identification and evaluation of emerging trends and advancements that may have the potential to address developing concerns. For instance, external environmental factors such as climate change, as well as the risk of losing our ability to protect ourselves against infectious diseases due to anti-microbial resistance, are exposing us to new risks and threats. Engagement among the multitude of stakeholders, including industry, funders, patient organisations and research networks, alongside improved support tools, communication, as well as education and training, can accelerate the translation of promising innovations to effective interventions.

The ASID fosters far-reaching collaborations with local entities such as the MCST, Malta Enterprise (ME), the Malta Further and Higher Education Authority (MFHEA) and the University of Malta, along with other academic, regulatory and innovation partners, European and international institutions, thematic specialists, and internal experts in the relevant fields. Internal continued development is also regularly assessed and followed up through multidimensional means, including active participation in the EU-Network Training Centre (EU-NTC), advancing specialised training in diverse areas such as EU procedures, scientific advice, toxicology, pharmacovigilance, medical devices, herbal medicinal products, quality, and auditing.

Enhancing the relevant know-how in regulatory sciences across the board can mitigate delays in the development of novel strategies and improve the chances that new medical interventions will reach our clinics. The Seminar on the Management, Communication and Perception of Risk, delivered by the MMA on 10 May 2023, represents one example of an outreach activity, with over thirty-five (35) participants engaging in this interdisciplinary initiative. Regulatory science is not some detached activity performed in secluded offices but is applied by our stakeholders as an integral part of their daily work, whether thought of as regulatory intelligence or not. Educational interventions to strengthen regulatory intelligence portend substantial return on investment for the ultimate benefit of patients. This impetus has been driving the MMA Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences since its launch under the auspices of the MMA.

The MMA Academy was initially registered as a Higher Education Institution (MFHEA Licence No. 2021 – 004) whereby three (3) new courses were designed, accredited at Level 5 on the MQF, and delivered: Award in Good Manufacturing Practice, Award in Good Distribution Practice and Award in Medical Devices. In April 2023, the MMA Academy for Patient-Centred Excellence and Innovation in Regulatory Sciences was licensed by the MFHEA as a Further

and Higher Education Institution, introducing its first course accredited at MQF Level 4 – Award in Basic Regulatory Sciences. In line with the Authority's efforts to meet market demands and training needs, this programme was implemented in September 2023 with the engagement of over twenty (2) local experts who delivered material on various topics over three (3) days.

The course, leading to an Award in Basic Regulatory Sciences, brought together a total of thirty (30) local and international individuals who participated in the twenty-five-hour face-to-face programme to enhance their knowledgebase, skillset, and competencies in this dynamic sphere. Topics included legal frameworks, regulations, competent authorities, terminology, quality management, sources of information, digitalisation, and good practices.

Through this educational initiative, in conjunction with a solid theoretical grounding, participants grasped practice-oriented considerations even through networking and panel discussions on supporting pharmaceutical processes and services of excellence. The uptake was remarkable, with the course being fully subscribed - all participants completed the course and were granted a certificate. The work invested in this programme positively concluded the additional measure AM 149 (2023) under the Ministry for Active Aging, whilst also being accepted as a Good Practice Initiative (GPI) for presentation at the 28th European Association of Hospital Pharmacists (EAHP) Congress which will be held from 20 to 22 March 2024, in Bordeaux, France.

This focal milestone in the track record of the MMA Academy was pursued by the design and development of its first programme recognised at Level 6 on the Malta Qualifications Framework. The Award in Pharmacovigilance, for which accreditation (MQF Level 6) was granted in October 2023, is planned for delivery in Q1 2024 in liaison with a seasoned expert having over 30 years of experience in drug development, clinical research, drug safety and quality assurance. Such partnerships, alongside internal expertise, and experience in the relevant fields, are enabling the enrichment of courses offered by the MMA Academy. The latter resonates with our Internal Quality Assurance (IQA) Policy attesting commitment to the provision of high-quality education, continuous enhancement, and accountability, whilst ascertaining that programmes meet and exceed participants' expectations and bridge knowledge gaps identified through educational needs analysis.

Going forward, the ASID shall persevere to build on the momentum achieved by the MMA Academy for Patient-Centred, Excellence and Innovation in Regulatory Sciences which was identified by the assessment team of the BEMA 2023 as one of the main strengths of the MMA. The drive towards continued education, professional development and scientific exposure shall continue to enable the identification of innovative strategic areas and tapping into funding opportunities while supporting academic endeavours that provide a platform to exchange views, discuss opportunities, enhance competence, and overcome challenges through collaborative reasoning for mutual benefit.

Granting of Qualified Persons Status and Certification of Pharmaceutical Product

In 2023, the MMA received nineteen (19) new applications for the Qualified Person (QP) status eligibility which were processed. Thirteen (13) applicants were interviewed during 2023 with 10 being eventually approved as being eligible for QP status. Four (4) other applicants who had submitted their application in 2022 were interviewed and approved in 2023.

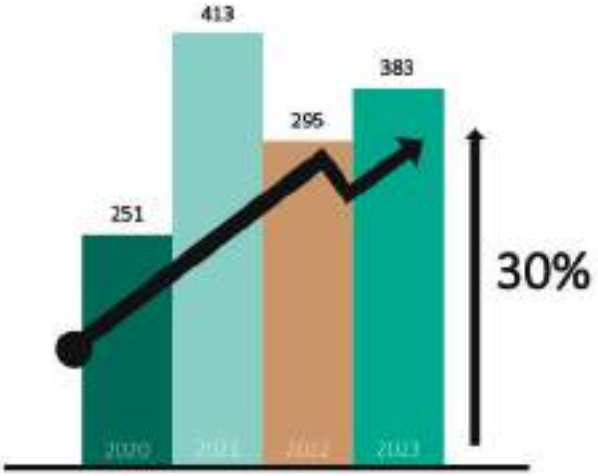


Figure 5.1: Certification of Pharmaceutical Products

IED also supports the local pharmaceutical and manufacturing industry exporting their products to developing countries which do not possess a robust regulatory framework for medicinal products, through the issuance of Certificates of Pharmaceutical Products (CPPs) based on the World Health Organisation (WHO) template and system. During the year 2023, three hundred and eighty-three (383) Certificate of Pharmaceutical Products applications were received and processed, with all certificates being issued, a 30% increase over the previous year (2022).

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 investigate the availability of other authorised products on the market.

- **PRESCRIPTION STATUS WORKING GROUP**

During 2023, 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 given 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 other sources. The Committee meets regularly, and feedback is sought from members and internal and external experts. BCC members also participate in the EDQM Borderline Products Network Meetings, held annually.

In 2023, twenty-eight (28) applications for the classification of borderline products were received, out of which twenty-five (25) were considered as non-medicinal and one (1) was considered medicinal.

Staff in the Licensing Directorate continue to fulfil the needs of meetings of Committees and working parties at the EMA and Heads of Medicines Agency (HMA) level, including the CMDh and its working groups, the Quality Working Party and the Quality Review of Documents (QRD).

- **SCIENTIFIC ADVICE AT A NATIONAL LEVEL**

Since 2018, the Authority has been engaging in EMA Scientific Advice Working Party (SAWP) advice. A representative from the Authority attends a monthly SAWP meeting at the EMA. Each month the Authority receives a list of procedures and bids for products it would like to review. Both external and internal assessors are engaged in assessing these products. In 2023, the Authority fully participated in SAWP activities, and seventeen (19) SAWP procedures were registered.

The objective of scientific advice procedures is to discuss with the MMA scientific matters regarding the development and licensing of medicinal products. In the context of national scientific advice applicants can obtain input concerning questions related to procedures that are within the remit of the MMA. For 2023, one (1) national scientific advice procedure was registered.

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

- **ELECTRONIC LABELLING PROJECT**

The Licensing Directorate has been supporting the Ministry for Health and Active Aging in their proposal to initiate a project for the inclusion of the package leaflet in electronic format. This follows the approval by the EC for a limited period of derogation from the requirements of Article 63(3) of Directive 2001/83/EC, starting as a pilot project with limited scope until the legislation is amended.

Several meetings about this project have been held with EMA, the EC, and other entities in the reporting period. The project is led by the Ministry for Health and Active Aging with the support of the Medicines Authority.

- **ELECTRONIC PRESCRIBING**

The Licensing Directorate has also been supporting the Ministry in the electronic prescribing project by assisting with access to the MMA product database and in their groundwork for the provision of information on authorised medicinal products.

CONTINUOUS PROFESSIONAL DEVELOPMENT TRAINING

The Medical Devices and Pharmaceutical Collaboration Directorate's Technical capacity was increased by the addition of four (4) personnel each undergoing internal induction training. The Directorate is committed to keeping abreast with the dynamic advancements in the field of practice and professional development 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 a site visit to an Official Medicines Control Laboratory (OMCL) in Switzerland (CH).

REGULATING MEDICAL DEVICES

Stakeholder Focus: A Patient-centred approach

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 to placing patient safety at the centre of all its regulatory activities by applying robust regulatory principles in line with national and EU legislation and embracing best practices in the field of medical devices and in-vitro diagnostics. The overarching aim of the Directorate is to enhance patient safety by overseeing procedures relating to the 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.

The Directorate strives to improve stakeholders' access to its services and supports stakeholders in reaching the requirements as laid down by EU legislation in the interest of patient safety. The Directorate encourages communication with stakeholders in the area of medical devices and in-vitro diagnostics adopting a patient-centred approach. In 2023, the Directorate addressed a total of one hundred and ninety-nine (199) queries originating from economic operators on a national and international level.

During 2023, the Directorate actively participated:

- In eighty (80) international meetings including participation in regular EC working groups, Competent Authorities for Medical Devices meetings, and the International Medical Devices Regulatory Forum,

- In one hundred and seventy-five (175) national meetings involving local governmental entities, such as CPSU, MDH, the line ministry and stakeholders involved in the medical device industry coming from the national front and/or international front.

MEDICINES INTELLIGENCE AND ACCESS

The patient-centred ethos is the foundation of the functions of the Medicines Intelligence and Access Unit where patients, healthcare professionals and patient organisations are supported in their queries with targeted recommendations to ensure sustainable access to medicines through added-value therapeutic interventions.

The MIAU handled on an individual basis one hundred and two (102) queries related to shortages, pharmacoeconomic, registration and safety issues which included cases such as the availability of atropine sulphate 0.05% eye drops, the introduction of new innovative medicines and supporting the Licensing Directorate with regards to investigating the availability of medicines on the Maltese market as shown in Figure 5.2 below. The Unit proactively addresses emerging medical needs by assisting in the sourcing and supply of new medicines. To ensure continuity of supply and access to medicines, ten (10) Named Patient Basis forms were processed by the MIAU, and a positive recommendation was sent to the Licensing Authority.

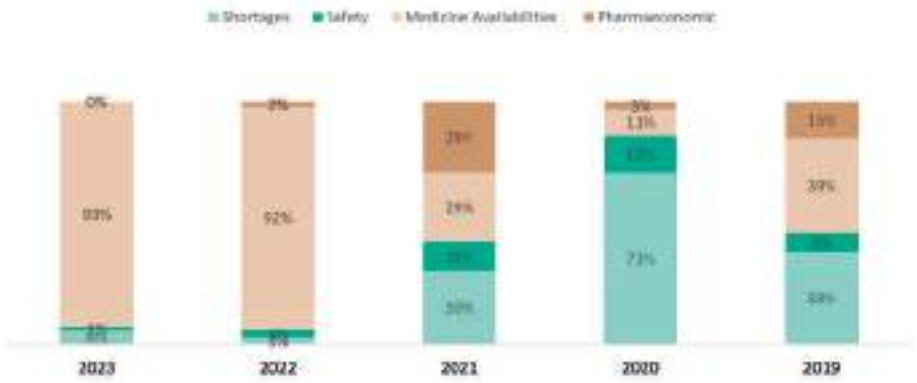


Figure 5.2: The number of interventions tackled by the MIAU during the years.

In 2023, one thousand, one hundred and eleven (1,111) applications requesting an Article 20 exemption were received with nine hundred and eighty-three (983) applications being approved given a justified public health need. The Article 20 exemption is reserved solely as a full or interim measure to counteract the risk of shortages and maintain accessibility to medicines on the local market when registration options through an MA, authorisation in line Article 126(a) of Directive 2001/83/EC and parallel importation have been exhausted as possible registration routes. The Authority liaises with the concerned public and private stakeholders during the vetting process of Article 20 exemption requests and following a thorough review, it issues a recommendation to the Licensing Authority to grant or refuse the request, together with conditions attached to the approval.

The reliance on the United Kingdom (UK) for the availability of medicines on the Maltese market is illustrated in Figure 5.3 below where 51% of the medicines approved through Article 20 exemptions are sourced from the UK. This dependence is multifactorial and may be the result of the lack of interest from EU pharmaceutical operators to market their products in small Member States like Malta, in addition to issues of labelling. Medicine packs sourced from the UK include the product information in the English language thus, there is no need for over/re-labelling. Only 28% of approved Article 20 exemption requests are sourced from EU markets which mainly result from urgent interim need demands of medicines. The Article 20 exemption was also granted to medicines sourced from Canada, Turkey, and the United States of America (USA). These countries are members of the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

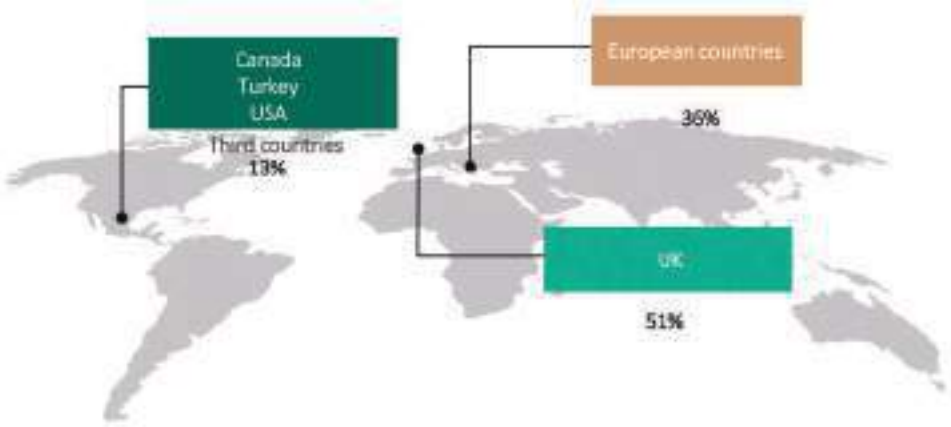


Figure 5.3: Country of source of medicinal products approved under Article 20 exemption in 2023 (N=983).

The employees within the MIAU actively participated in twelve (12) meetings of the Medicines Shortages Single Point of Contact (SPOC) Working Party, where intelligence on medicines including shortages was gathered during these meetings to prepare for disruptions in the supply of medicines that may impact Malta. The MIAU, in collaboration with fellow EU member states, engaged in a comprehensive analysis encompassing 1870 active ingredients across various pharmaceutical formulations. This exercise aimed to ascertain the market availability and criticality status of medicinal products, marking the initial phase towards establishing an EU critical medicines list. Among the examined substances, six hundred and forty-seven (647) were identified as marketed, while one thousand, two hundred and twenty-three (1223) were not. Notably, of the marketed products, five hundred nineteen (519) were deemed critical medicines, one hundred and two (102) were classified as medicinal products at risk, and twenty-six (26) fell into the category of 'other'.

The MIAU is in continuous dialogue with local and international pharmaceutical stakeholders and the Malta Competition and Consumer Affairs Authority (MCCAA) to ensure reasonable prices for medicines. In 2023, fifty-four (54) price reductions of medicines were announced and a total of ten (10) new generic medicines were introduced on the local market.

As a result, patients have access to more affordable medicines that conform to the established European standards of quality, safety, and efficacy.

The MIAU is spearheading the supervisory role of the MMA for the National implementation of the Safety Features Regulation 2016/161/EU appearing on packs of human medicines. Twenty (20) batch-specific requests for packs having safety features that do not comply with the requirements of Delegated Regulation 2016/161/EU were processed and granted to ensure the continuity of supply to patients after being evaluated and the necessary corrective and preventive actions have been implemented by the supplier.

The MIAU, in partnership with the Licensing Authority, has devised subsidiary legislation (Chapter 458.63 of the Laws of Malta) to address medicine shortages and improve access within the National Health Service (NHS). In exceptional circumstances where CPSU lacks access to any registered or medicinal product that can be registered within the required timeframe and following a request under the first proviso of Article 20 of the Act, permission may be sought from the Licensing Authority to procure and introduce an unauthorised medicinal product into the National Health Services following these regulations.

The MIAU is presently engaged in developing an internal standard operating procedure for the receipt and processing of applications under the recently enacted Subsidiary Legislation.

REGULATORY RESPONSE TO PUBLIC HEALTH EMERGENCIES

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.

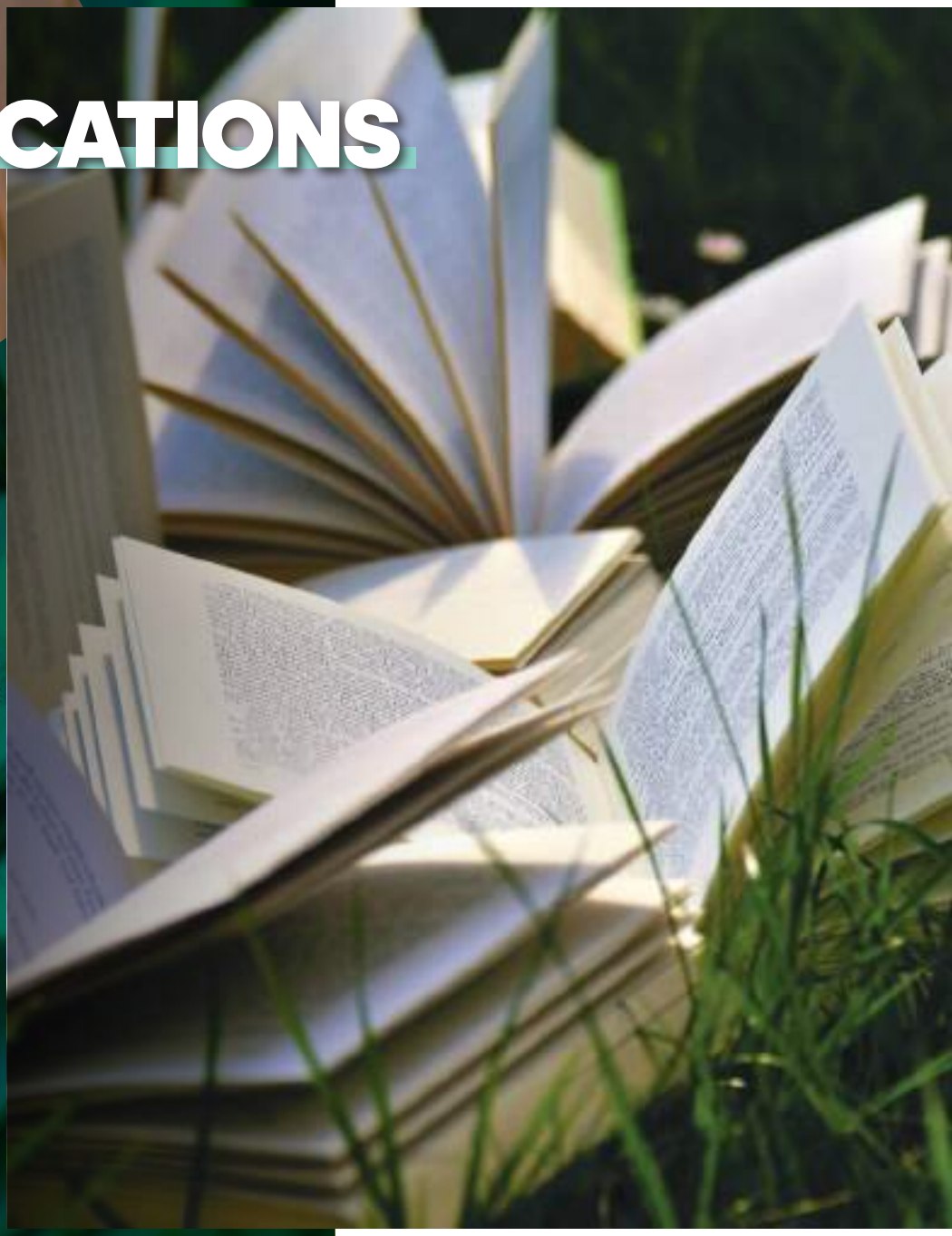
In April 2022, the EC published Directive (EU) 642/2022 extending further the derogations previously covered by Commission Notices, allowing for the granting of authorisations by Article 126(c) based on MAs granted in the UK.

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, to the National Health Service, were granted before the Brexit date.

In addition, until the end of 2022, one hundred and seventy-two (172) new authorisations were granted based on UK MAs, where availability from other Member States was not possible, based on Article 126(c) as amended by Directive (EU) 642/2022. Other derogations were granted, mainly to derogate from the need for batch testing or batch release of products in the European Union. Over sixty (60) products benefit 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.

PUBLICATIONS



Falzon S, Serracino-Inglott A, Mamo M. Development of a course leading to an Award in Basic Regulatory Sciences. 81st International Pharmaceutical Federation (FIP) Congress of Pharmacy and Pharmaceutical Sciences; 2023 Sep 24-28; Brisbane, Australia.

Falzon S, Serracino-Inglott A, Mamo M. Implementation of a Workshop on the Dimensions of Cannabis for Medicinal and Research Purposes. 81st International Pharmaceutical Federation (FIP) Congress of Pharmacy and Pharmaceutical Sciences; 2023 Sep 24-28; Brisbane, Australia.

Micallef B, Dogné JM, Sultana J, Straus SMJM, Nisticò R, Serracino-Inglott A, Borg JJ. An Exploratory Study of the Impact of COVID-19 Vaccine Spontaneous Reporting on Masking Signal Detection in EudraVigilance. Drug Saf. 2023 Nov;46(11):1089-1103. doi: 10.1007/s40264-023-01346-9. Epub 2023 Sep 14. PMID: 37707778.

Mifsud Buhagiar L, Mamo M, Abbas A, Serracino-Inglott A. Optimising the interplay between competent authorities and industry with a patient-first drive. MedInPharma Conference; 2023 Oct 19-20; Valletta, Malta.

Sammut V. Auditing in a Medicinal Regulatory Framework, FIP, Brisbane 2023.

PUBLICATIONS IN JOURNALS

Attard Pizzuto M, Grech L, Gatt Baldacchino E, Serracino-Inglott A. Developing a Risk Management Course for Forensic Professionals. *Pharmacy Education*. 2023;23(3):42.

Attard J, Grech L, Azzopardi LM. Development and validation of tools in relation to vaccination in autoimmune inflammatory rheumatic diseases patients. *Pharmacy Education*. 2023;23(6):393.

Farrugia K, Anastasi A, Grech L, Azzopardi LM. Timely designation of notified bodies within the European Union. *Pharmacy Education*. 2023;23(6):424.

Fearne J, Catania J, Grech L, Serracino-Inglott A. Developing a Patient-Centred Incident Reporting Medical Device Framework. *Pharmacy Education*. 2023;23(6):402

Gatt Baldacchino E, Grech L, Serracino-Inglott A. Challenges in establishing a sustainable Official Medicines Control Laboratory in a small member state. *Pharmacy Education*. 2023;23(6):429

Vella J, Grech L, Azzopardi LM. Challenges and concerns of type 1 diabetic patients during transitional settings: the pharmacist's role. *Pharmacy Education*. 2023;23(6):393.

Zammit Dimech D, Grech L, Serracino-Inglott A. Perception of Maltese healthcare professionals on cannabis for medicinal use. *Pharmacy Education*. 2023;23(6):402.

OTHER PUBLICATIONS

Borra J, Grech L, Azzopardi LM. Development of a course accreditation gap analysis tool to support professional development courses for the pharmaceutical workforce. EAFP annual conference, Valencia, 2023.

Grech L, Fearne J, Farrugia K, Gatt Baldacchino E, Zarb Adami M, Wirth F, Serracino-Inglott A, Azzopardi LM. Medical Devices Study Unit in the Pharmaceutical Technology Course. EAFP annual conference, Valencia, 2023.

Catania J, Fearne J, Farrugia K, Grech L, Serracino-Inglott A. Implementation of patient-centred incident reporting framework. MedinPharma, Malta, 2023.

Fearne J, Catania J, Farrugia K, Grech L, Serracino Inglott A. Establishing a patient-centred incident reporting medical device framework in Malta. MedinPharma, Malta, 2023.

Farrugia K, Anastasi A, Grech L, Azzopardi LM, Serracino Inglott A. Challenges in timely designation of notified bodies within the European Union. MedinPharma, Malta, 2023.

Farrugia K, Tanti S, Portughese A, Fearne J, Grech L, Serracino Inglott A. Development of clinical investigations and performance studies in Malta. MedinPharma, Malta, 2023.

Galea L, Farrugia K, Fearne J, Grech L, Serracino Inglott A. Identification of Medical Devices application templates in Malta. MedinPharma, Malta, 2023.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