THE MMA telegram

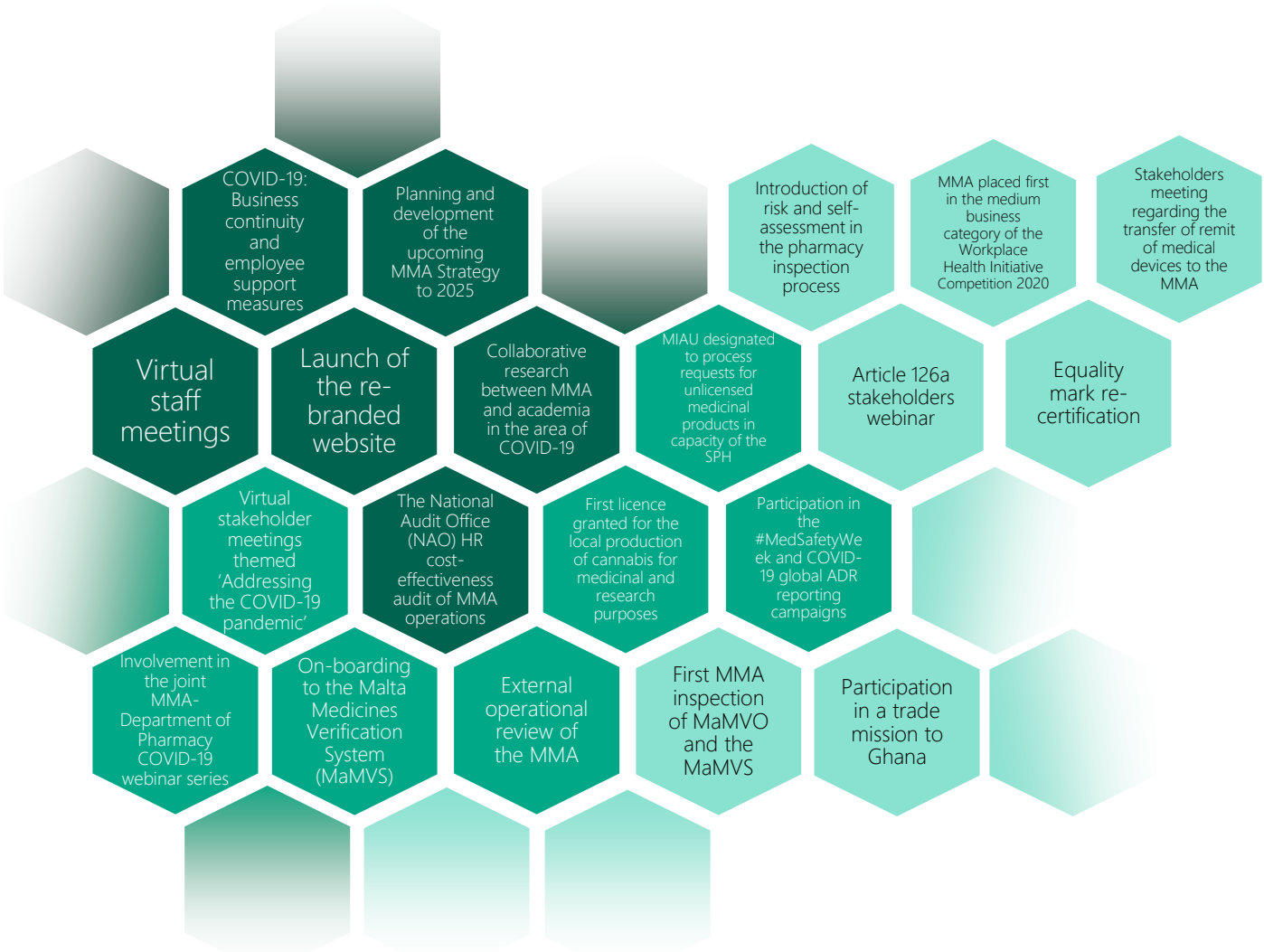
ISSUE 05- Q1 2021

EVENTS

Welcome dear colleagues for our first e-newsletter for year 2021!

A look back at 2020...and what a year!

In view of the COVID-19 pandemic and BREXIT, the Malta Medicines Authority (MMA) has faced drastic challenges and had to cope with the ever-changing regulatory environment. Amid the volatile situation, the Authority upheld its mission to protect and enhance public health through the regulation of medicinal products, medical devices and pharmaceutical activities. The Authority secured business continuity whilst prioritising the health and safety of its employees. Its steadfast commitment safeguarded the availability and affordability of medications by working in tandem with relevant stakeholders. Prominent events of year 2020 included:



Medicines Price Reductions

On the 23 of February, the Minister for Tourism and Consumer Protection, Mr Clayton Bartolo and the Parliamentary Secretary for Consumer Protection and Public Cleansing, Dr Deo Debattista, had a cordial visit at the Malta Medicines Authority where they toured the premises and engaged in dialogue with members of the Authority. During the visit an announcement was made regarding the reduction in costs of medicines indicated in the treatment and/or prevention of chronic cardiovascular diseases, schizophrenia, and hypertension as shown in the Table 1.

Medication	Indications	Original Price	New Price	Price Reduction
Procoralan®	Symptomatic treatment of chronic stable angina pectoris in coronary artery disease	€66.62	€20.02	-€46.60
Aripiprazole	Treatment of adults with schizophrenia	€22.50	€12.00	-€10.50
Rivaroxaban	Prevention of stroke, systemic embolism and pulmonary embolism and treatment of deep vein thrombosis and pulmonary embolism	€54.00	€26.40	-€27.60
Perindopril	Treatment of mild to moderate essential hypertension, mild to moderate congestive heart failure, and reduction of cardiovascular risk in individuals with hypertension or post-myocardial infarction and stable coronary disease.	€10.20	€8.31	-€1.89

Table 1: The reduction in costs of medicines indicated in the treatment and/or prevention of chronic cardiovascular diseases, schizophrenia, and hypertension

BREXIT Seminar

On the 15 of January, a virtual meeting was held on the Commission notice on the application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period.

Medicines Intelligence and Access Unit (MIAU) Seminar

A virtual meeting was held on 27 of January to discuss and identify problems and solutions on the timely provision of medicines used in Assisted Reproductive Technology (ART) services at Mater Dei Hospital. The meeting was chaired by the Chairperson and all pharmaceutical stakeholders were invited. ART includes medical procedures used primarily to address infertility, including the use of fertility medications.

Medical Devices Online Seminar

On the 28 of January 2021, the Malta Medicines Authority hosted an online seminar on medical devices which tackled the EUDAMED-Actor registration module. The European Commission has made available the Actor registration module which enables economic operators to submit, by means of an actor registration request, the information necessary to obtain a single registration number (SRN). The SRN guarantees a EU-wide unique identification for economic operators (also outside of EUDAMED). Following the assessment and approval of the request by the concerned National Competent Authority, EUDAMED generates the SRN of the economic operator to the national competent authority and transfers it to the requesting economic operator.

Annual Report 2020

In a year marked by the challenges of the global COVID-19 pandemic, the Malta Medicines Authority Annual Report 2020 reflects the strength, resilience and quality of our people and portfolio. The report shall compile milestones, statistical data and scientific initiatives achieved and pursued by the Authority during the preceding year of operation. The report is in its final stages of preparation.

The Malta Medicines Authority Budgetary and Simplification Measures for Year of Operation 2021

In its endeavour to continue to secure the protection and safety of consumers of medicines, the MMA has pledged to a budgetary commitment which shall explore the feasibility of setting up a national reference laboratory for the purpose of ensuring the quality of medicinal products on the market.

This year's simplification measure constitutes the deployment of a national electronic database which will be developed to store information on medical devices and to facilitate transactions with economic operators. This measure will ensure conformity to local and European regulations through a robust registration process of medical devices with the National Competent Authority. The database shall interface with the Authority's website where economic operators can directly access the registration platform for devices. The development of this database is intended to instil greater confidence in the operations involved in the regulation of medical devices.

Update on Preparations for ISO Certification on Information Security Management

The Scientific and Regulatory Operations Directorate is working in tandem with the Quality, Continuous Improvement and Internal Audit Unit for the implementation of security markings to documented information at the Malta Medicines Authority, which is a requirement to the ISO standard on Information Security Management Systems. The ISO/IEC 27001:2013 provides high quality international standards which assists organisations in retaining securely their information assets and the customers' data against any threats and vulnerabilities. It provides the responsibilities incurred by the organisation to establish, implement, maintain and improve continuously an information security management system. Having an effective information security system in place assures both the management and stakeholders that the Authority's assets are safe. In view of this, internal consultations are ongoing regarding further preparations on documentation handling and control for certification in this Standard.

DID YOU KNOW?

Fun Facts!

Can seeing the glass half full help you live longer? Studies have found that there is a correlation between increasing levels of optimism with decreasing levels of death from cancer, disease, infection and stroke. This is particularly true for cases of cardiovascular disease.

So Remember, be optimistic if you want to live longer!

Regulatory Considerations for Therapeutics Indicated in COVID-19

Owing to hopes of mitigating the COVID-19 pandemic, the first quarter of 2021 heralded international interest in vaccinology, including regulatory approaches to vaccines and their mode of action. The Conditional Marketing Authorisation (CMA) is a fast-track authorisation mechanism which is used by the European Medicines Agency (EMA) to expedite the approval of therapeutics, including vaccines, in response to unmet medical needs, in particular those to be used in emergency situations presenting as public health threats recognised by the WHO or the EU. In a CMA application, the clinical data package submitted by the applicant is less comprehensive than required in an application for a standard Marketing Authorisation however it must still demonstrate that the benefit of the immediate availability of the medicine outweighs any risks that may be potentially identified through the collation of additional data. The grant of the CMA follows a positive scientific recommendation by EMA, which is then endorsed by the Commission.

The rolling review is a regulatory procedure characterised by interaction between the EMA and the developer during the development stages. The EMA begins assessing data as its becomes available during the development process with the aim to expedite the subsequent formal marketing authorisation application assessment even further (Figure 1). The EMA's human medicines committee (CHMP) decision to start the rolling review is based on preliminary results from laboratory and early clinical studies. Thus, the CHMP assesses the clinical safety data, quality data and data from laboratory studies and facilitates quick and coordinated regulatory action.

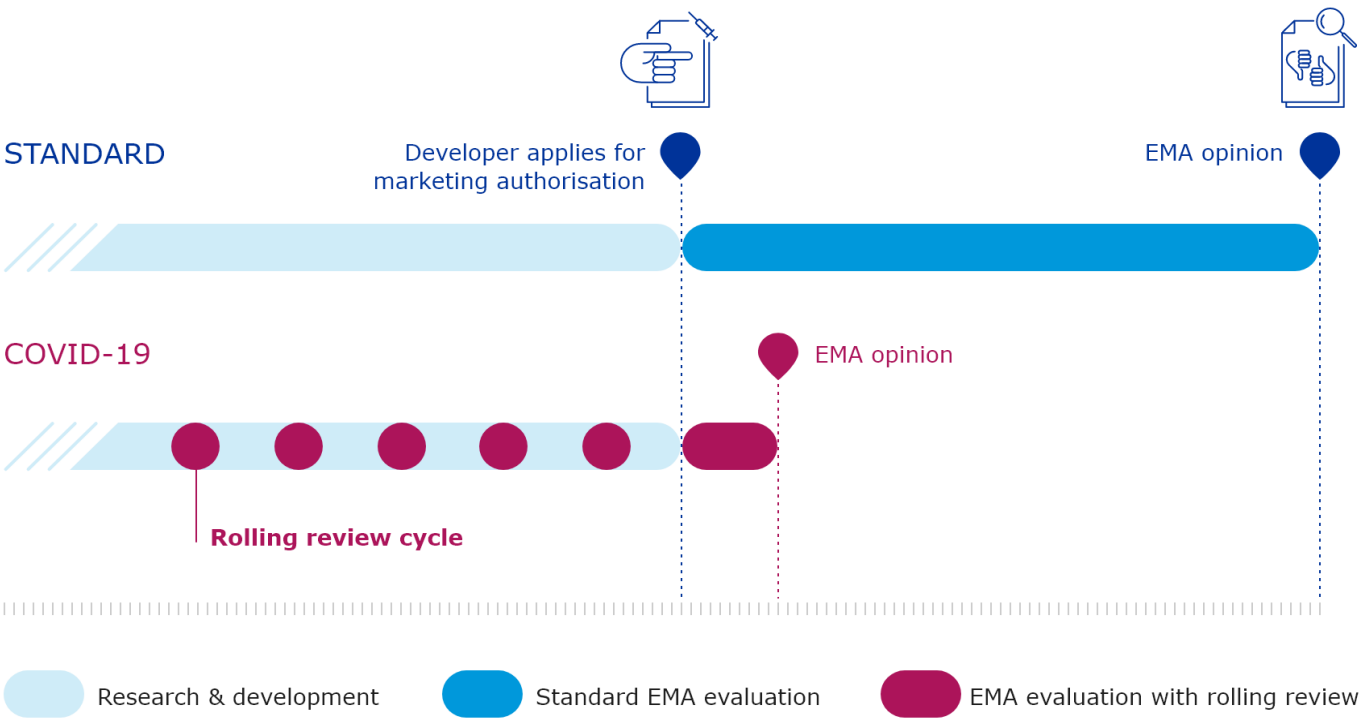


Figure 1: Standard evaluation process versus the rolling review concept for COVID-19 therapeutics.

Image source: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring

COVID-19 Vaccines: An Era of Advanced Pharmaceutical Technology

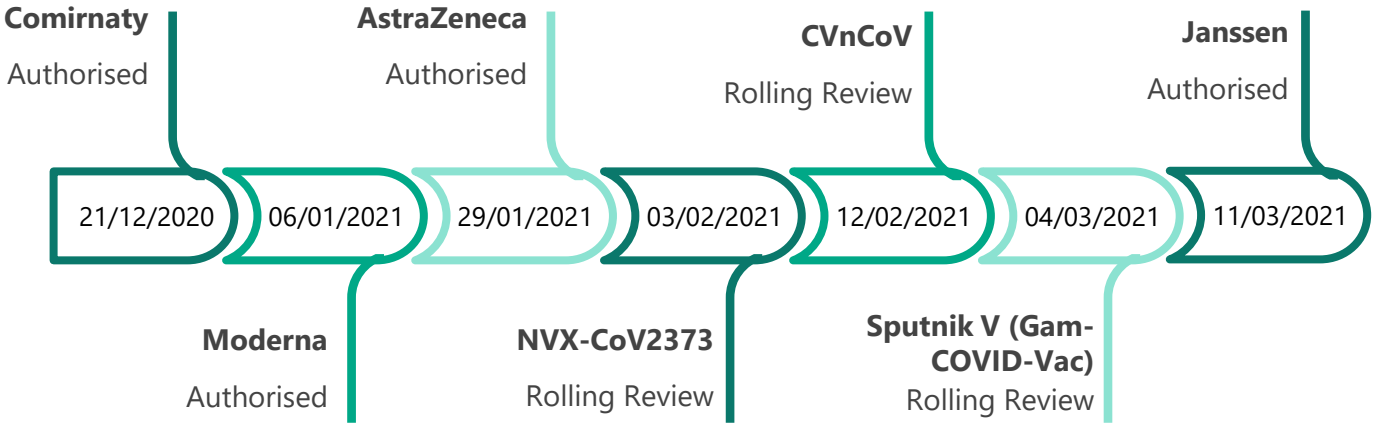


Figure 2: Timeline on the current centralised authorisation status of COVID-19 vaccines in the EU.

Four (4) COVID-19 vaccines, which include the *Pfizer-BioNtech (Comirnaty)*, *Moderna*, *Oxford-AstraZeneca (Vaxzevria)* and *Janssen* vaccines, have been centrally authorised in the EU and make up the pharmacotherapeutic armamentarium Member States are using to combat the COVID-19 pandemic. A further three (3) vaccines are currently under rolling review by the EMA (Figure 2).

The concept of novel approach technology (Figure 3) is mainly adopted for the development of the vaccines to prevent COVID-19 which include viral vector vaccines and mRNA and DNA vaccines. The vector vaccines use adenovirus of human or non-human primate origin which are harmless and non-replicating viruses that enter cells to deliver the genetic code for SARS-CoV-2 spike protein antigen (*Oxford-AstraZeneca* and *Janssen* vaccines use this technology). The mRNA vaccines are often encapsulated into lipid nanoparticles which allow mRNA to fuse into the cytoplasm without being degraded (*Moderna*, *BioNTech/Pfizer's*, *CureVac*, and the *Sputnik V (Gam-COVID-Vac)* vaccines adopt this technology).

The *Novavax* vaccine is the only protein-based vaccine which contains tiny particles made from laboratory-grown version of the spike protein found on the surface of SARS-CoV-2 coronavirus. It also contains an 'adjuvant', a substance to help strengthen the immune responses to the vaccine.

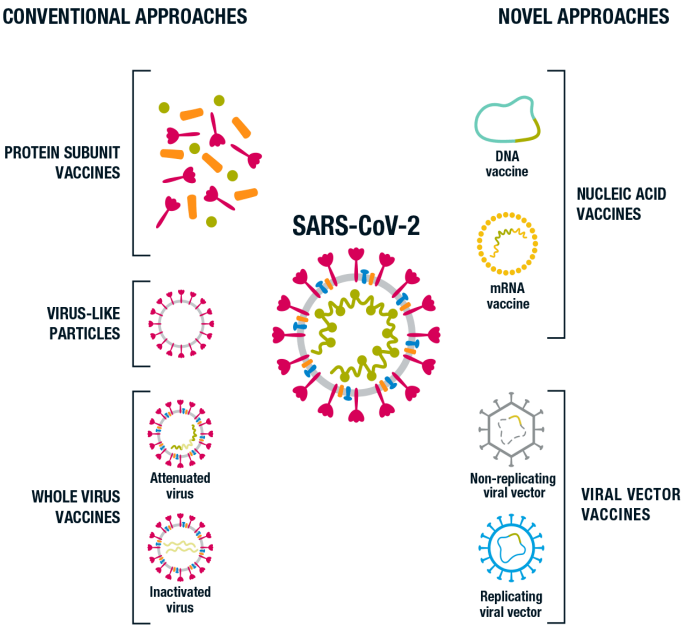


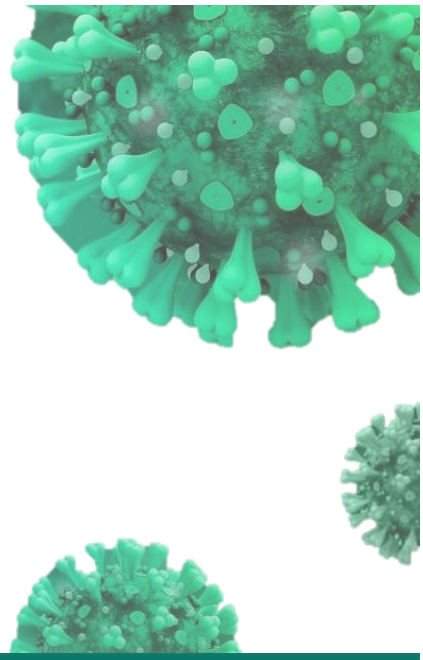
Figure 3: Approaches being used to develop vaccines for active immunisation to prevent COVID-19 caused by SARS-CoV-2.

Image source: https://www.nps.org.au

Table 2 is a comparison of the four (4) vaccines which were granted a centralised conditional marketing authorisation in the EU. Common side-effects which can be experienced with the use of these vaccines include: local pain, swelling, fever, chills, muscle pains and headache. These effects can last up to 24 to 48 hours. No risk from breast-feeding is expected but pregnancy is not recommended.

Vaccine	Vaccine Developer	Vaccine Type	Doses	Dose Interval	Storage	Age
Comirnaty	BioNTech/ Pfizer (Germany, USA)	mRNA (lipid nanoparticle)	x 2	3 weeks	-70℃	16+
COVID-19 Vaccine Moderna	Moderna/ NIAID (USA)	mRNA (lipid nanoparticle)	x 2	4 weeks	-20℃ up to 6 months	18+
Vaxzevria	University of Oxford/ AstraZeneca (UK)	Viral vector (chimpanzee adenovirus vector)	x 2	8-12 weeks	2-8℃	18-70
COVID-19 Vaccine Janssen	Janssen-Cilag International N.V.	Viral vector (human adenovirus type 26)	x 1	N/A	2-8℃	18+

Table 2: Comparison of vaccines to prevent COVID-19 which have been granted a centralised marketing authorisation in the EU.



COVID-19 Therapeutics Under Evaluation

EMA's CHMP is currently evaluating six (6) COVID-19 therapeutics as highlighted in Table 3.

Therapeutic modalities from *Regeneron*, *Celltrion* and *Eli Lilly* are all made up of monoclonal antibodies that have been designed to recognise and attach to the spike protein of SARS-CoV-2. When they bind to the spike protein, the virus cannot enter the body's cells. When the treatment is available as a combination of two (2) monoclonal antibodies, they attach at two (2) different sites of the spike protein and elicit a synergistic effect, thus having a greater effect than when either is used alone.

Medicine	Developer	Type of Medicine	Start of rolling review
REGN-COV2 antibody combination (casirivimab/ imdevimab)	Regeneron Pharmaceuticals, Inc. and F. Hoffman-La Roche, Ltd (Roche)	Monoclonal antibodies	01/01/2021
NVX-CoV2373	Novavax CZ AS	Protein lipid nanoparticle with Matrix M adjuvant	03/02/2021
CVnCoV	CureVac AG	mRNA	12/02/2021
Monoclonal antibody regdanvimab	Celltrion	Monoclonal antibody	24/02/2021
Sputnik V (Gam-COVID-Vac)	Russia's Gamaleya National Centre of Epidemiology and Microbiology	Viral vector	04/03/2021
Monoclonal antibodies bamlanivimab and etesevimab	Eli Lilly	Monoclonal antibodies	11/03/2021

Table 3: COVID-19 therapeutics which are under rolling review by the EMA.