ANNEX TO THE WORKING ARRANGEMENT

BETWEEN

THE EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

AND

THE EUROPEAN MEDICINES AGENCY

ON THE VACCINES MONITORING PLATFORM

Having regard to:

i. the "Working arrangement Between the European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC)", Article 6, second paragraph, of which foresees that "*This working arrangement will be implemented through technical procedures annexed to this document after mutual agreement*".

ii. Regulation (EU) 2022/123 of the European Parliament and of the Council of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices, Article 20, *in fine*, of which foresees that the co-ordination of independent monitoring studies on the use, effectiveness and safety of vaccines shall be conducted by the EMA in conjunction with the ECDC;

iii. Regulation (EU) 2022/2370 of the European Parliament and of the Council of 23 November 2022 amending Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control, Article 5a, providing for the coordination by ECDC of vaccine effectiveness and safety monitoring studies through collecting new information and/or using the relevant data collected by Member States, including via a new vaccine monitoring platform.

Whereas:

(A) The following acronyms are defined herewith:

EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EU	European Union
IVMAB	EU Immunisation and Vaccine Monitoring Advisory Board
JAB	Joint Advisory Board
JS	Joint Secretariat
RWE	Real-world evidence
RMP	Risk Management Plan

TA	Technical Annex
VMP	Vaccine Monitoring Platform

(B) The ECDC, under Regulation (EC) No 851/2004, as amended by Regulation (EU) 2022/2370, is responsible for enhancing the capacity of the Union and the Member States to protect human health through the prevention and control of communicable diseases in humans, through identifying, assessing and reporting on current and emerging threats to human health from communicable diseases and related special health issues, and, provision of information thereon. ECDC's mission entails provision of scientific expertise, including recommendations, and support to defining research priorities and preparedness planning in the Union, including through existing Union activities in the public health sector, with regard to the prevention and control of communicable diseases, epidemiological surveillance, training programmes and early warning and response mechanisms, and the exchange of best practices and experience with regard to vaccination programmes. Furthermore, ECDC is responsible for coordinating scientific and technical data collection, validation, analysis and dissemination of data at Union level, including on vaccination strategies. ECDC's activities in the area of vaccination were recently extended via the revised mandate, including in regards to the coordination of independent, post-marketing monitoring studies and the new vaccine monitoring platform referred to in Recital iii above, and recognition of ECDC's role in facilitating the fight against vaccination misinformation vaccination and against the causes of vaccine hesitancy.

(C) The EMA, under Regulation (EC) No 726/2004, is responsible for supporting the development of medicinal products including vaccines and for the evaluation of applications for the granting of a Union marketing authorisation for human medicines, including vaccines. This evaluation includes the assessment of the efficacy, safety and immunogenicity of vaccines, inter alia, on the basis of clinical trials, observational studies and other studies, and risk management plans ("RMPs") submitted by marketing authorisation applicants. RMPs may include additional effectiveness and safety studies and additional pharmacovigilance activities (e.g., disease registries, post-authorisation safety studies). EMA, in collaboration with the National Competent Authorities for medicines also has responsibility for monitoring the benefits and risks of medicines including vaccines on the market and this includes collected reports of suspected adverse reaction reports and the initiation, conduct and interpretation of studies. Under Article 20 (b) of Regulation EU 2022/123, the Agency shall coordinate independent monitoring studies on the use, effectiveness and safety of medicinal products intended to treat, prevent or diagnose diseases related to the public health emergency, using relevant data, including, where relevant, data held by public authorities. For these purposes, coordination as regards vaccines shall be conducted in conjunction with the ECDC.

(D) The mission and aims of both organisations present relevant synergies and areas for collaboration, specifically in the area of independent monitoring of the effectiveness and safety of vaccines approved for use in immunisation programmes in the EU in the post-authorisation phase.

(E) In November 2020, the European Commission (EC) proposed to the European Parliament and the Council a change to EMA's and ECDC's mandates in the context of its COVID-19 lessons learnt package and the creation of a European Health Union to strengthen pandemic preparedness and response. The revised mandates of EMA and ECDC require a Vaccine Monitoring Platform (VMP) to be delivered collaboratively between ECDC and EMA.

(F) Linked to the Health Union legislative proposals, the EC made funding available to ECDC and EMA in 2021, with 7 million and 5 million Euros allocated to ECDC and EMA, respectively, to implement, as a priority, a programme of COVID-19 vaccine safety and effectiveness studies. A Joint Advisory Board (JAB) jointly coordinated by ECDC and EMA was set up to provide a forum for discussion and advice to both Agencies on the COVID-19 studies. The COVID-19 studies and the implementation of the JAB should be seen as a pilot for the VMP.

(G) Building on the collaboration on COVID-19 studies and through strengthening their collaboration, the two Agencies aim to establish, in line with their mandates, an effective mechanism for the independent monitoring of vaccine safety and effectiveness in the post-authorisation phase

(H) The VMP shall provide timely generation of real-world evidence (RWE) on the safety and effectiveness of vaccines. This will inform regulatory as well as public health action. The VMP is intended as a collaborative space between the two agencies, ECDC and EMA, aimed to address specific research questions through independent studies, and to facilitate the exchange of independent scientific evidence, information and experience on vaccine effectiveness and safety monitoring in the EU in the post-authorisation phase. The VMP shall comprise:

a. A structure for governance,
b. A set of business processes,
c. A scientific advisory board: the EU Immunisation and Vaccine Monitoring Advisory Board (IVMAB),
d. A framework for the conduct of studies and networks,
e. Funding mechanisms,
f. Communication and transparency tools.

EMA and ECDC have thus agreed to the following:

Section 1: Aim

This Technical Annex aims to provide a framework for the collaboration of the Agencies in respect of the post-authorisation monitoring of vaccines. This shall include the establishment of a VMP, which shall have the purpose of facilitating post-authorisation studies on vaccines in connection with their effectiveness and safety in the EU. The platform will be jointly co-ordinated by the ECDC and EMA.

The agencies will coordinate and divide work and responsibilities in the areas of vaccine effectiveness and vaccine safety monitoring. In this regard, this Annex sets-out principles of collaboration as well as principles of division of work as detailed below.

Section 2: Principles of collaboration and division of work

Principles of collaboration and governance

1. The ECDC and EMA will create a collaborative VMP supported by an EU Immunisation and Vaccine Monitoring and Advisory Board (IVMAB). The IVMAB will comprise vaccine regulatory and safety experts, as well as representatives from public health authorities in all Member States to maximise scientific and operational input into the work of the VMP. The VMP will be operationally led by a Steering Group and a Joint Secretariat with representatives of both Agencies. Their meetings will be the basis for sharing evidence, scientific information and experience on vaccine effectiveness and safety in the post-authorisation phase;
2. The VMP will be managed and coordinated jointly by the two Agencies; the studies necessary to fulfil the mission and objectives of the platform will be conducted separately or jointly by the ECDC and EMA, each within its financial means, based on needs and technical agreement between the two agencies;
3. The IVMAB to the VMP will have a consultative role on the decision-making from both the ECDC and EMA regarding the running of the platform;
4. The evidence generated by ECDC and EMA is aimed to inform public health vaccination strategies and/or regulatory actions in regard to the vaccines concerned. Both Agencies will endeavour to work together to foster early exchange and consultation between their respective technical experts and competent networks in order to ensure consistency in the conclusions reached with regard to the interpretation of such evidence aimed to inform future vaccination strategies;
5. Both agencies endeavour to strengthen the bridge between public health and regulatory dimensions of vaccine assessments, monitoring and evaluation in the post-authorisation phase, with a view to promoting a sustainable and mutually beneficial exchange of know-how and expertise from across the Agencies' respective public health and regulatory networks; Both Agencies endeavour to work together and provide timely and mutually beneficial input to technical meetings, documents, guidance or recommendations being issued on topics of common interest in the area covered by this TA;
6. Both Agencies will strive to foster early technical consultation and exchange of work plans in areas that may overlap with work conducted by one or the other Agency, in relation to the launch and implementation of post-authorisation studies on both vaccine effectiveness and safety monitoring;
7. Both agencies commit to eliminate the risk of duplication of efforts including duplication in the use of EU funds, as well as burdening demands for data reporting on the EU Member States when it comes to the collection and generation of evidence on vaccine effectiveness and safety in the post-authorisation phase;
8. Both agencies also agree to issue joint communications and/or recommendations on key vaccines/immunisation topics that span across the public health/regulatory dimensions, were appropriate, learning from the experience gained throughout the COVID-19 pandemic. The VMP shall comprise a set of business processes agreed between the two Agencies and operated by the Joint Secretariat. These processes shall include:
    a. Identification of gaps in the infrastructure for studies,
    b. Identification of evidence gaps requiring studies,
    c. Prioritisation of evidence needs,
    d. Assessment of the feasibility of studies,
    e. Procurement of studies,
    f. Coordination of studies,

g. Interpretation of study results,
h. Dissemination of evidence generated by the studies,
i. Communication and transparency measures, including updates to the European Commission and the EU budgetary authorities as appropriate,
j. Maintenance of a web content.

Principles of division of work

1. ECDC will be primarily, but not exclusively, responsible for the collection and generation of independent data/evidence on vaccine effectiveness;
2. EMA will be primarily, but not exclusively, responsible for the collection and generation of independent data/evidence on vaccine safety;
3. Any additional efforts undertaken by the Agencies in the areas of vaccine effectiveness and/or safety monitoring should be complementary to work already undertaken by the lead Agency in the respective field;
4. The above-outlined division of work is without prejudice to the discretion of each Agency to work independently on the generation of evidence concerning both the effectiveness and safety of priority vaccines beyond the scope of this TA, in accordance with its respective mandate and its strategic and business needs;
5. Each Agency will act as the main and single contact point with their respective networks and, as such, any requests for input or involvement of such networks should be channelled through and implemented by the Agency responsible for such network.

Section 3: Modalities of cooperation

1. The VMP shall be built and operated by a Joint Secretariat comprising staff members of both Agencies. The operations of the VMP shall be included in the multi-annual work plan of both Agencies and reported in their respective annual reports. Both ECDC and EMA will designate liaison persons to ensure a smooth implementation of the cooperation. The liaison persons will meet regularly and on an annual basis will identify joint and/or synergetic activities that will comprise an annual workplan.

2. For those cooperation activities covered by this TA, each agency will bear its own costs and identify the most suitable modalities of operational implementation, including exploring possible synergies, for the concerned studies.

3. Any intellectual property resulting from joint collaboration activities will be agreed upon in advance for each specific activity, with due consideration to obligations on the exploitation of results stemming from relevant contracts entered into by each Agency. As a principle, and notwithstanding any contractual obligation to the contrary, final results of the independent studies discussed and agreed via the VMP should be made publicly available.

4. Before any external communication about joint activities under the vaccine monitoring platform, the ECDC and EMA will coordinate the content of the communication and the method of communication.

5. The implementation of vaccine studies will build on the existing experience of ECDC and EMA in generating evidence on vaccines. The studies will either be procured individually by each Agency under existing contract(s) or procured under future contracts to be awarded via tendering procedure(s); such procedure(s) may be organised individually by each

Agency, or jointly. The aforementioned is without prejudice to any cooperation at working level between the Agencies when preparing requests for individual studies.

6. The approach for studies will include use of large electronic health care databases in several EU/EAA Member States or primary data collection. Data sources may also include public health surveillance databases maintained by ECDC or EMA in-house databases, according to the individual governance of each of these data sources. Any additional conditions on access and use of these data sources shall be agreed separately between ECDC and EMA, as required.

7. Oversight and coordination of individual studies will be done by each Agency based on responsibility, as provided for in the respective mandates or as determined by the Steering Group, with regular information sharing and discussion at the level of the Joint Secretariat.

8. For joint studies, the Joint Secretariat (JS) will coordinate and monitor the progress of the studies which are of mutual interest to the Agencies and ensure the validity of their results through assessment of proposals and deliverables. Notwithstanding any contractual obligation to the contrary, the JS will also ensure that results are disseminated and made available to EU and national decision-makers.

Section 4: Conflict of interest

Each Party will apply its own policy on competing interests to experts involved in its own activities. However, for the purpose of avoiding conflicts of interest in the context of the IVMAB, nominated experts should comply with the policies on competing interests of both Parties. To facilitate compliance with the foregoing policies, the nominated experts should submit one declaration of interests to EMA, completed in accordance with EMA's policy on competing interests; and one declaration of interests to ECDC, completed in accordance with ECDC's policy on competing interests. Each Party will be responsible for checking that the declaration of interests submitted to it is in compliance with its own policy on competing interests. In the event of a conflict of interest being identified, the Parties agree to taking any necessary action, including mitigation measures where appropriate, as provided for in the relevant policy.

Section 5: Limitations to the cooperation

Both Agencies acknowledge that the cooperation between them in the context of the TA is contingent on their available resources. The TA is not intended to create obligations or rights for any of the Agencies. At no time shall one of the agencies represent the other or behave in any way which would give such an impression.

Section 6: Amendment and Termination

The terms of this TA can be amended at any time by mutual written agreement of the Agencies. This TA can be terminated by either Agency upon the service of a 3-month written notice to the other Agency. Both Parties will take appropriate measures to ensure that any adverse consequences to ongoing technical collaboration, that could result from the decision to terminate this TA are minimsed to the extent reasonably possible.

Section 7: Duration and entry into force

This TA comes into force upon signature by both Agencies. Without prejudice to Section 6, it shall remain in force until further notice. The need for this TA may be reviewed at the end of the current Multi-annual Financial Framework in force until 2027, and in light of the new budgetary contribution from the Union to the Agencies, specifically for the conduct of the studies facilitated in the context of the vaccines monitoring platform.

For: European Centre for Disease Prevention and Control		For: European Medicines Agency	
Name:	[signature on file]	**Name:**	[signature on file]
Title:		**Title:**	
Date:	23-02-2023	**Date:**	23-02-2023