

# VAC4EU: a pan-European research network for collaborative post-authorization vaccine safety and benefit monitoring

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## Background

VAC4EU (Vaccine monitoring Collaboration for Europe) is a not-for profit international association with 25 member organizations specialised in the collaborative generation of real-world evidence on coverage, safety, and efficacy of vaccines in Europe. VAC4EU was established as a result of the IMI-ADVANCE project with the aim to enable, coordinate and accelerate the creation of the best evidence at European level on vaccine effects. In the past two years, VAC4EU has proven preparedness and efficiency in designing post-authorization monitoring for COVID-19 vaccines responding to the requests of both the European Medicines Agency (EMA) and vaccine manufacturers.

## Objectives

To describe the VAC4EU organization, data, tools and the accomplishments made towards the generation of real-world evidence on vaccine benefit-risk evaluation.

## Results

Since its creation in October 2019, VAC4EU has established a large research network composed of 25 institutions from 9 European countries (BE, DE, DK, FR, IT, NL, NO, ES, UK) providing access to 15 health care data sources covering more than 150 million European citizens [FIGURE 1] [TABLE 1]

VAC4EU has implemented a research infrastructure including a catalogue, a codemapper tool, a sharepoint, Github, digital research environment (DRE), a phenotype library of more than 100 variables with definitions and a Zenodo community to facilitate collaboration, transparency, and federated data analysis [FIGURE 2]. VAC4EU has adopted the ConcePTION common data model as a basis for the structural harmonization of electronic health data, but it also allows for primary data collection

VAC4EU has consolidated its governance structure for implementation of pharmacovigilance studies on vaccines [FIGURE 3] and successfully participated in four public tenders regarding vaccines safety and effectiveness launched by the European Medicines Agency (EMA)<sup>1, 2, 3, 4</sup> as well as four required post-authorization safety studies on COVID-19 vaccines sponsored by vaccine manufacturers<sup>5, 6, 7, 8</sup>, and other studies promoted by the Global Vaccine Data Network [FIGURE 4]. All protocols developed within VAC4EU are registered in the EU PAS register, and results are published in the open science VAC4EU Zenodo community.

## Conclusions

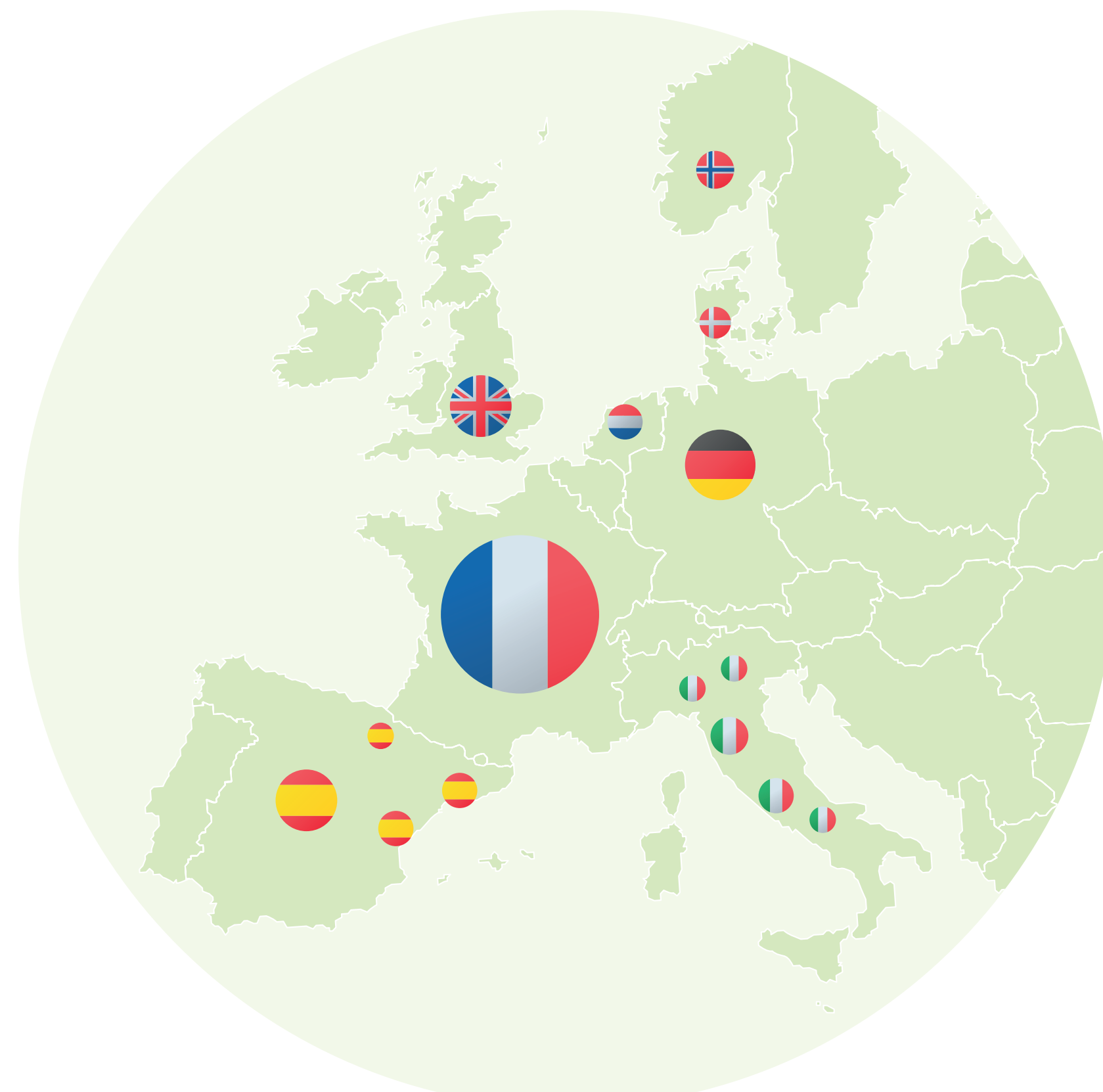
We know already from the H1N1 pandemic that collaboration is needed to study vaccine effects. This collaboration was designed and tested in the IMI-ADVANCE project and implemented in VAC4EU. VAC4EU has demonstrated readiness of its research framework making a key difference in COVID-19 vaccine monitoring in Europe. Research and public health organizations can join the initiative.

## Declaration of interest

The authors and their departments conduct research for government, public, and private organizations, including pharmaceutical companies, according to the ENCePP code of conduct.

## References

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- An Observational Post-Authorization Safety Study to Assess the Safety of Ad26.COV2.S Using European Healthcare Data through VAC4EU (COVID-19) <https://www.encepp.eu/encepp/viewResource.htm?id=46985>
- Cohort monitoring of Adverse Events of Special Interest and COVID-19 diagnoses prior to and after COVID-19 vaccination <https://www.encepp.eu/encepp/viewResource.htm?id=44372>
- Rapid Safety Assessment of SARS-CoV-2 vaccines in EU Member States using electronic health care datasources <https://www.encepp.eu/encepp/viewResource.htm?id=42637>
- Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine <https://www.encepp.eu/encepp/viewResource.htm?id=46939>
- A post-authorisation/post-marketing observational study to evaluate the association between exposure to AZD1222 and safety concerns using existing secondary health data sources (COVID-19) <https://www.encepp.eu/encepp/viewResource.htm?id=47086>
- Monitoring safety of Spikevax in pregnancy: an observational study using routinely collected health data in five European countries (COVID-19) <https://www.encepp.eu/encepp/viewResource.htm?id=45467>
- Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of Spikevax in Europe (COVID-19) <https://www.encepp.eu/encepp/viewResource.htm?id=45470>



NORWAY	DENMARK
Norwegian electronic health care registries (~5.3M) DAP: University of Oslo	Danish Health Registers Denmark (~5.8M) DAP: Aarhus University
UK	THE NETHERLANDS
CPRD (Aurum: ~13 M; Cold: ~3M) DAPs: DSRU, UMCU, RTI-HS	PHARMO Database Network (~4M) DAP: PHARMO
FRANCE	GERMANY
SNDS database (~66M) DAPs: BPE, PeLyon	CePaRD (~17.5M) DAP: Leibniz Institute for Prevention Research and Epidemiology – BIPS
SPAIN	ITALY
The EpiChron Cohort (~1.3M) DAP: IACS	Caserta Record Linkage Database (~0.9M) DAP: University of Verona
BIFAP (~14M) DAP: AEMPS	PEDIANET (~0.2M) DAP: SoSeTe/Società Servizi Telematici
SIDIAP (~5.7M) DAP: IDIAP Jordi Gol	Tuscany Regional Database (~3.6M) DAP: ARS Toscana
VID (~5M) DAP: FISABIO	HSD: ~2 million DAP: SIMG
	Lazio Regional Database (~3.6M) DAP: DEP Lazio

Figure 1: VAC4EU data sources and data access providers per country

INSTITUTION	DESCRIPTION
Agenzia Regionale di Sanità (ARS) Toscana.	Regional public health agency. Expertise in vaccine studies and COVID-19 studies, access to administrative health care data (mortality, hospital admissions, ER access, drug claims & vaccines, health care assistance), in Tuscany region (3.5 million residents). <a href="https://www.ars.toscana.it">https://www.ars.toscana.it</a>
Bordeaux PharmacoEpi (BPE)	A research platform of the Université de Bordeaux specialized in real world evidence with extensive experience in conducting fields studies and studies based on the French national healthcare database (SNDS). <a href="https://www.bordeauxpharmacoepi.eu">https://www.bordeauxpharmacoepi.eu</a>
Drug Safety Research Unit (DSRU)	The DSRU is a private research organization in the UK which monitors the safety of medicines and vaccines and uses UK databases. <a href="https://www.dsrug.org/">https://www.dsrug.org/</a>
FISABIO	The Foundation for the Promotion of Health and Biomedical Research of Valencia Region has access to regional health and vaccine data. <a href="http://fisabio.san.gva.es/">http://fisabio.san.gva.es/</a>
IDIAP-Jordi Gol	A public primary health care research organization. Home to the SIDIAP database, Information System for Research in Primary Care, electronic health data. <a href="https://www.idiapjg.org/index.php/en/">https://www.idiapjg.org/index.php/en/</a>
Instituto Aragonés de Ciencias de la Salud (IACS)	Providing access to the EpiChron Cohort Study of all the inhabitants of Aragón comprising, about 2M subjects with historic data, and 1.3 M active population subjects.
Julius Clinical Research BV	Science contract research organization that manages global clinical drug trials & real-world evidence studies. <a href="https://www.juliusclinical.com">https://www.juliusclinical.com</a>
LAREB	Netherlands national pharmacovigilance center, ample expertise in regular pharmacovigilance and intensive monitoring of influenza and pneumococcal vaccines. <a href="http://www.lareb.nl">www.lareb.nl</a>
Lazio Regional Health Service	Regional public health agency. Expertise in vaccine studies and COVID-19 studies, access to administrative health care data (mortality, hospital admissions, ER access, drug claims & vaccines, health care assistance), in Lazio region (6 million residents). <a href="https://www.deplazio.net/en">https://www.deplazio.net/en</a>
Leibniz Institute for Prevention Research and Epidemiology – BIPS	Home to the German Pharmacoepidemiologic Research Database (CePaRD), claims data from statutory health insurance providers and currently includes information on about 25 million persons. <a href="https://www.bips-institut.de">https://www.bips-institut.de</a>
Penta foundation	A private non-for-profit foundation hosting a global pediatric research network, which has coordinated hundreds of multisite clinical trials and cohort studies in infectious diseases in the past 30 years. <a href="https://penta-id.org/">https://penta-id.org/</a>

Table 1: VAC4EU members

INSTITUTION	DESCRIPTION
Pharmaco Epidemiologie Lyon (PELyon)	Private research organization able to provide access to public (SNDS) and private (IQVIA) French databases. <a href="https://www.pelyon.fr/">https://www.pelyon.fr/</a>
PHARMO Institute	A private research organization conducting studies on use and effects of medicinal products. Home to the PHARMO data network, is a population-based network from different primary and secondary healthcare settings in the Netherlands. <a href="http://www.pharmo.nl">www.pharmo.nl</a>
Research Triangle Institute Health Solutions (RTI-HS)	A private non-for-profit research organization. Pharmacoepidemiology and Risk Management expertise including EMA-mandated safety and utilization studies. <a href="https://www.rtihs.org/">https://www.rtihs.org/</a>
RIVM	The Dutch national public health institute, ample expertise in vaccine coverage, effectiveness and safety studies with primary data collection and secondary use of data. <a href="https://www.rivm.nl">https://www.rivm.nl</a>
Royal College for Primary Care physicians (SIMG)	Data access provider to Italian GP network and the Health Search Data network, a GP based data collection. <a href="https://www.simg.it/">https://www.simg.it/</a>
Sciensano	National public health agency Belgium, with ample expertise in vaccine studies, pre-licensure and post-licensure. <a href="https://www.sciensano.be">https://www.sciensano.be</a>
Società Servizi Telematici	Home to the PEDIANET database covering primary care pediatricians in Italy. <a href="http://pedianet.it/en/primary-health-care-project">http://pedianet.it/en/primary-health-care-project</a>
Teamit Institute, S.L.U.	Company specialized in scientific project management of pharmacoepidemiology research and regulatory science initiatives for the advancement of global health. <a href="https://www.teamitresearch.com/teamit-institute/">https://www.teamitresearch.com/teamit-institute/</a>
The Spanish Agency of Medicines and Medical Devices (AEMPS)	National agency providing access to BIFAP (Base de Datos para la Investigación Farmacoepidemiológica en Atención Primaria). <a href="http://bifap.aemps.es">http://bifap.aemps.es</a>
University Aarhus	Academic research organization, having access to national Danish health registers
University Medical Centre Utrecht (UMCU)	Academic medical center with ample expertise in vaccine studies, pre-licensure and post-licensure. Host of the VAC4EU secretariat. <a href="https://www.umcutrecht.nl/en">https://www.umcutrecht.nl/en</a>
University Oslo	Public academic research organization. Access to Norwegian health and vaccine data.
University Verona	An academic research organization and important regional pharmacovigilance center for Italy.
Vall d'Hebron Hospital	Clinical Pharmacology Unit, provides expertise in primary data collection and clinical research.

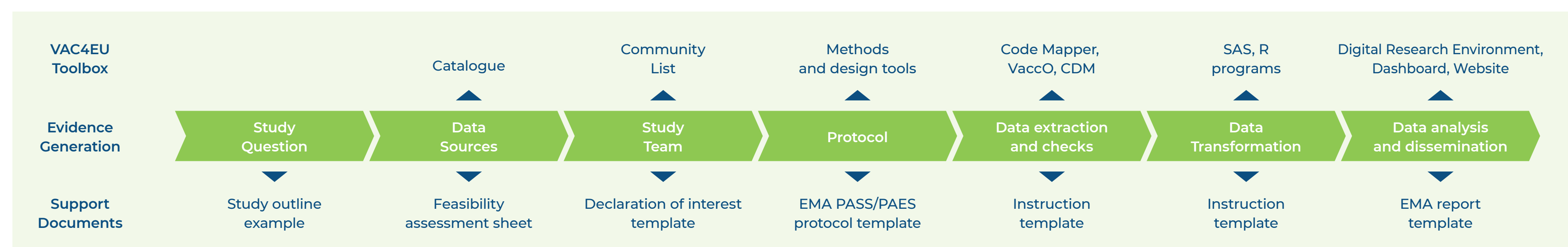


Figure 2: VAC4EU research infrastructure

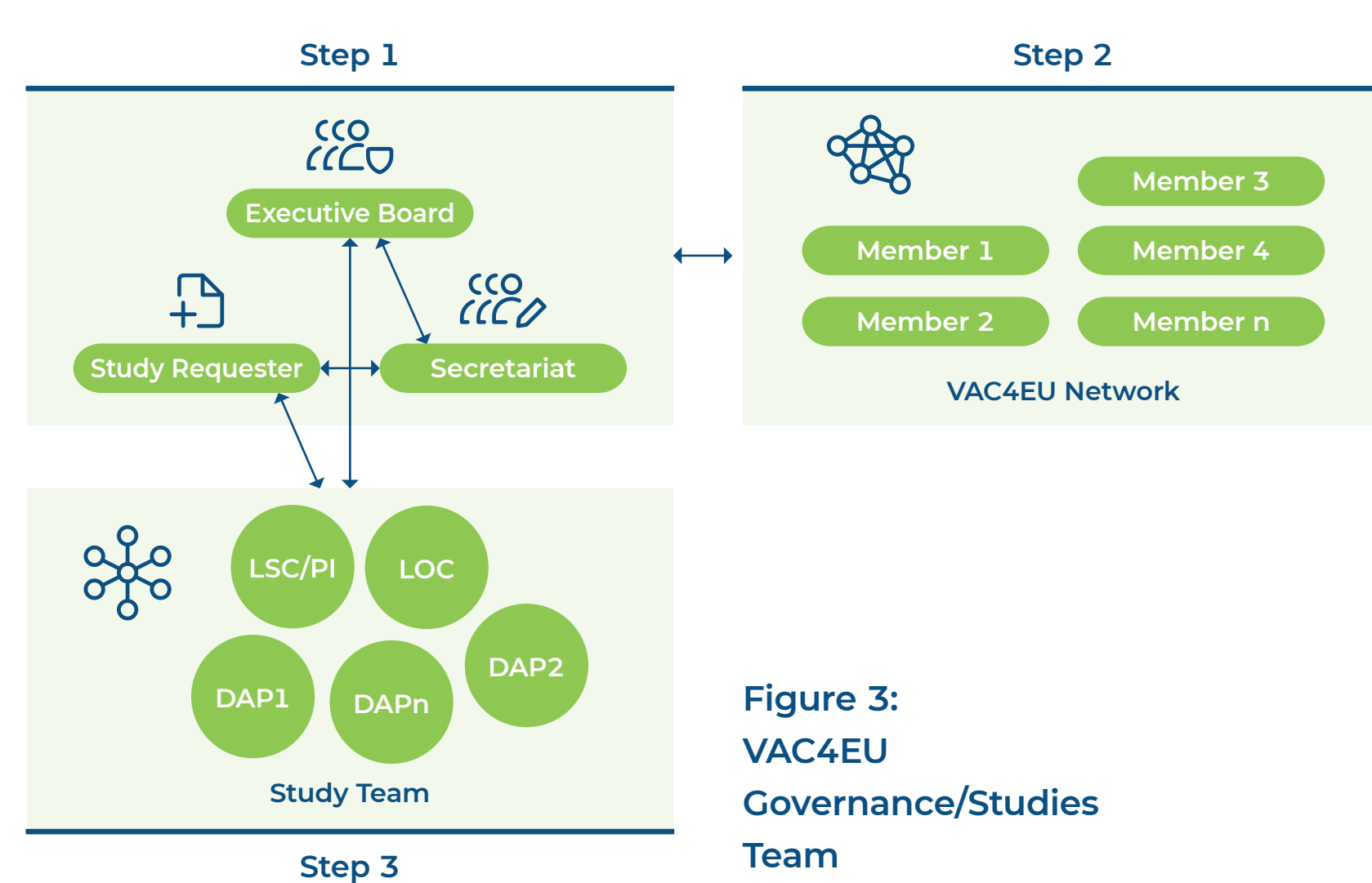


Figure 3: VAC4EU Governance/Studies Team

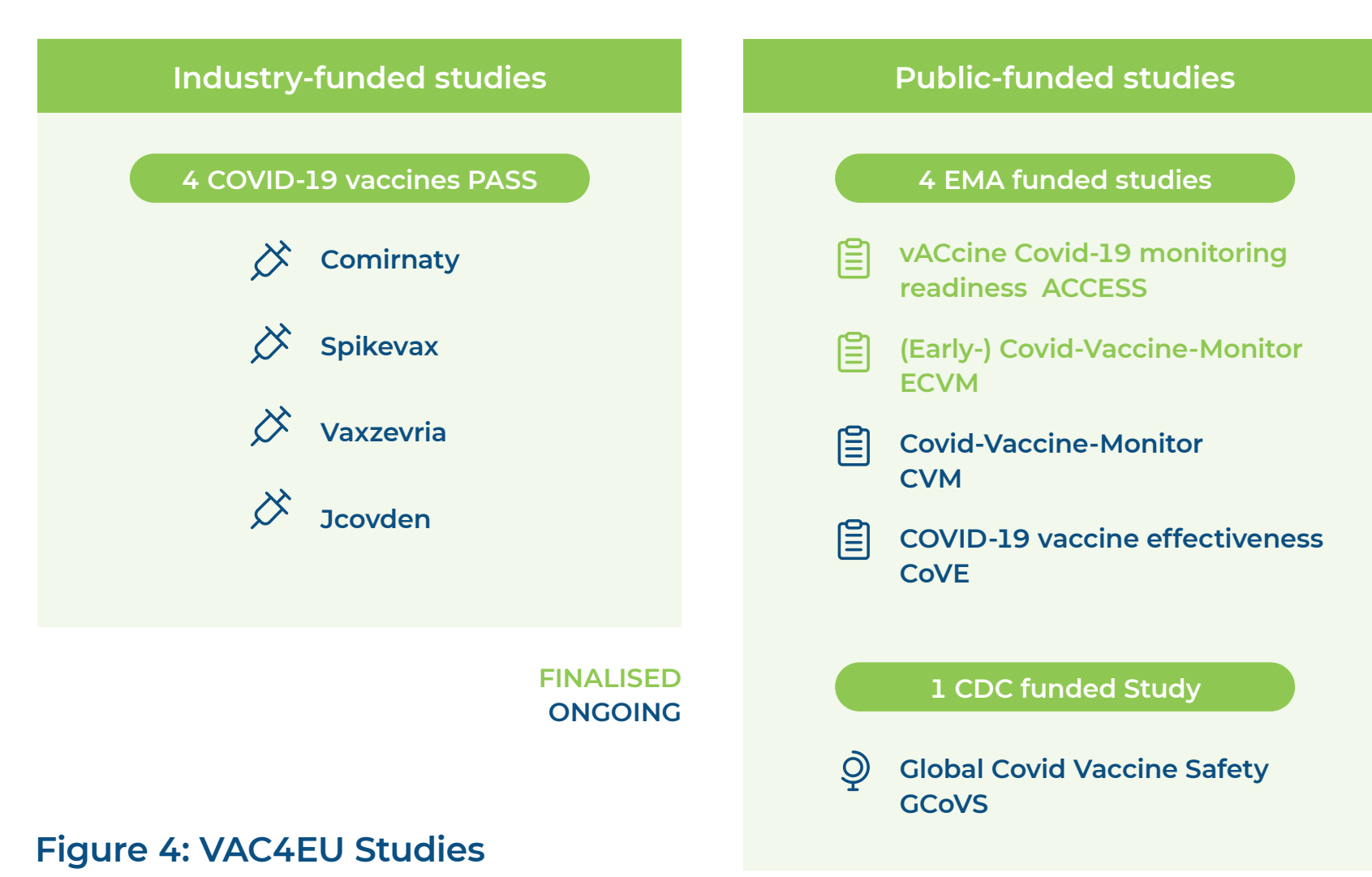


Figure 4: VAC4EU Studies