Vaccine 41 (2023) 3915–3922

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

VACCELERATE Site Network: Real-time definition of clinical study capacity in Europe

Jon Salmanton-García [a,b,c], Pauline Wipfler [a,b], Paula Valle-Simón [d,e], Christina Merakou [f], Ioannis Kopsidas [f], Ullrich Bethe [a,b], Angela Steinbach [a,b], Orly Spivak [g], Lenka Součková [h], Maria Amélia Mendonça [i], Markela Koniordou [f], Margot Hellemans [j], Jesus Frías-Iniesta [d,e], Ruth Joanna Davis [k], Imre Barta [l], Anna Maria Azzini [k], Helena H. Askling [m], Christos D. Argyropoulos [n], Elena Álvarez-Barco [o], Murat Akova [p], Marc M.J. Bonten [q,r], Miriam Cohen-Kandli [g], Rebecca Jane Cox [s], Robert Flisiak [t], Petr Husa [h], Ligita Jancoriene [u], Alena Koscalova [v], Odile Launay [w], Jens Lundgren [x], Patrick Mallon [o], Laura Marques [i], Pontus Nauclér [m], Jordi Ochando [y], Zoi-Dorothea Pana [n], Evelina Tacconelli [k], Krisztina Tóth [l], Sven Trelle [z], Pierre van Damme [j], Theoklis E. Zaoutis [f], Markus Zeitlinger [aa], Kerstin Albus [a,b], Fiona A. Stewart [a,b], Sanne H.I. Hofstraat [ab], Patricia Bruijning-Verhagen [ab], Oliver A. Cornely [a,b,c,ac,*], on behalf of the VACCELERATE Consortium

[a] University of Cologne, Faculty of Medicine and University Hospital Cologne, Institute of Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Cologne, Germany
[b] University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), Cologne, Germany
[c] German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany
[d] Hospital La Paz Institute for Health Research (IdiPAZ), Madrid, Spain
[e] Servicio Madrileño de Salud, Madrid, Spain
[f] Collaborative Center for Clinical Epidemiology and Outcomes Research (CLEO), Athens, Greece
[g] Ministry of Health of Israel, Jerusalem, Israel
[h] Masaryk University, Brno, Czech Republic
[i] Centro Hospitalar Universitário do Porto, Porto, Portugal
[j] Universiteit Antwerpen, Faculty of Medicine and Health Science, VAXINFECTIO, Centre of Evaluation of Vaccination, Antwerp, Belgium
[k] University of Verona, Infectious Diseases Division, Department of Diagnostic and Public Health, Verona, Italy
[l] National Koranyi Institute for Pulmonology, Budapest, Hungary
[m] Karolinska University Hospital, Stockholm, Sweden
[n] European University of Cyprus, Nicosia, Republic of Cyprus
[o] University College Dublin, National University of Ireland, Dublin, Ireland
[p] Hacettepe University, Ankara, Turkey
[q] Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht University, Utrecht, Netherlands
[r] Department of Medical Microbiology, University Medical Centre Utrecht, Utrecht, Netherlands
[s] University of Bergen, Bergen, Norway
[t] Department of Infectious Diseases and Hepatology, Medical University of Bialystok, Białystok, Poland
[u] Institute of Clinical Medicine, Medical Faculty, Vilnius University, Vilnius University Hospital Santaros klinikos, Vilnius, Lithuania
[v] Biomedical Research Center of the Slovak Academy of Sciences, Bratislava, Slovakia
[w] Institut National de la Santé et de la Recherche Médicale-ANRS Maladies Infectieuses Émergentes, Paris, France
[x] Centre of Excellence for Health, Immunity and Infections (CHIP), Rigshospitalet, Copenhagen, Denmark
[y] Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Madrid, Spain
[z] Universitaet Bern, Bern, Switzerland
[aa] Medizinische Universität Wien, Vienna, Austria
[ab] University Medical Centre Utrecht, Utrecht University, Utrecht, Netherlands
[ac] University of Cologne, Faculty of Medicine and University Hospital Cologne, Clinical Trials Centre Cologne (ZKS Köln), Cologne, Germany

ARTICLE INFO

Article history:
Received 7 December 2022
Received in revised form 11 April 2023

ABSTRACT

Background: The inconsistent European vaccine trial landscape rendered the continent of limited interest for vaccine developers. The VACCELERATE consortium created a network of capable clinical trial sites throughout Europe. VACCELERATE identifies and provides access to state-of-the-art vaccine trial sites to accelerate clinical development of vaccines.

* Corresponding author at: University of Cologne, Faculty of Medicine and University Hospital Cologne, Institute of Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Cologne, Germany.
E-mail addresses: Oliver.Cornely@uk-koeln.de (O.A. Cornely), trialsites@vaccelerate.eu.

https://doi.org/10.1016/j.vaccine.2023.05.006

Accepted 1 May 2023
Available online 18 May 2023

Keywords:
SARS-CoV-2
Registry
Pandemic preparedness
Vaccine trial
Site
Clinical network

Methods: Login details for the VACCELERATE Site Network (vaccelerate.eu/site-network/) questionnaire can be obtained after sending an email to. Interested sites provide basic information, such as contact details, affiliation with infectious disease networks, main area of expertise, previous vaccine trial experience, site infrastructure and preferred vaccine trial settings. In addition, sites can recommend other clinical researchers for registration in the network. If directly requested by a sponsor or sponsor representative, the VACCELERATE Site Network pre-selects vaccine trial sites and shares basic study characteristics provided by the sponsor. Interested sites provide feedback with short surveys and feasibility questionnaires developed by VACCELERATE and are connected with the sponsor to initiate the site selection process.
Results: As of April 2023, 481 sites from 39 European countries have registered in the VACCELERATE Site Network. Of these, 137 (28.5 %) sites have previous experience conducting phase I trials, 259 (53.8 %) with phase II, 340 (70.7 %) with phase III, and 205 (42.6 %) with phase IV trials, respectively. Infectious diseases were reported as main area of expertise by 274 sites (57.0 %), followed by any kind of immunosuppression by 141 (29.3 %) sites. Numbers are super additive as sites may report clinical trial experience in several indications. Two hundred and thirty-one (47.0 %) sites have the expertise and capacity to enrol paediatric populations and 391 (79.6 %) adult populations. Since its launch in October 2020, the VACCELERATE Site Network has been used 21 times for academic and industry trials, mostly interventional studies, focusing on different pathogens such as fungi, monkeypox virus, *Orthomyxoviridae*/influenza viruses, SARS-CoV-2, or *Streptococcus pneumoniae*/pneumococcus.
Conclusions: The VACCELERATE Site Network enables a constantly updated Europe-wide mapping of experienced clinical sites interested in executing vaccine trials. The network is already in use as a rapid-turnaround single contact point for the identification of vaccine trials sites in Europe.

1. Introduction

Before the coronavirus disease 2019 (COVID-19) pandemic was declared in March 2020 [1]. Europe was not the preferred option for global vaccine trial developers, as compared to other regions [2–5], due to its fractured clinical trial infrastructure [6–9]. While regional and international networks were attempting to boost clinical trial and study performance on the continent, none of them was focused on vaccine development [10,11].

In January 2021 the VACCELERATE consortium was set up [12], to harmonize vaccine trial initiative across Europe and create a network in which vaccine trials can be rapidly deployed for early evidence generation and addressing public health needs [13]. Within VACCELERATE, one of its core objectives was to describe the capacity mapping of vaccine trials sites in Europe, in order to facilitate rapid clinical trial site identification, selection and initiation of joint European vaccine trials. Nevertheless, while primarily set up as a vaccine trial network, the network is also ready to participate in epidemiological studies, surveys and other projects and initiatives related to vaccine topics.

Additionally, the VACCELERATE Site Network offers and provides access to the VACCELERATE Academy where investigators can register for educational courses such as good clinical practice (GCP) a training course specific on vaccine trials and a course on conduct of multinational trials. A study nurse course is currently also under development. The VACCELERATE Academy will support capacity building of European sites with limited previous experience in vaccine trials. Altogether, VACCELERATE Site Network will enable to keep sites updated on regulatory developments and state-of-the-art operational procedures.

2. Methods

The VACCELERATE Site Network (vaccelerate.eu/site-network/) [14] collects information on basic contact and site details, main point of contact, prior vaccine trial experience, available infrastructure as well as preferred parameters for study participation (Table 1). Interested sites can initiate their registration through trialsites@vaccelerate.eu. The VACCELERATE Coordination Office (CO) provides the designated point(s) of contact with individual access details to the online platform to complete the site questionnaire. Registration in the VACCELERATE Site Network does not guarantee participation in a vaccine trial sponsored by the VACCELERATE consortium or by third parties. With the aim to enlarge the Site Network by reaching the largest number of vaccine trial sites in Europe, the VACCELERATE National Coordinators (NC) have a key role within the network. They are local liaison partners of the Consortium in their respective countries, being in charge of the guidance for the most appropriate approach to involve new sites and for the local expansion of the network (see Table 2 and Table 3).

The VACCELERATE CO can be approached by vaccine developers or sponsors during clinical trial planning but also while the trial is already active and the need for additional sites arises. The developer/sponsor provides basic information regarding the vaccine trial (i.e., study population, country, study phase…) and defines basic needs and requirements regarding the sites. The registry is then filtered for sites fulfilling these criteria. Registered sites will be identified using information collected in the VACCELERATE Site Management System (ClinicalSite) [15]. Matching registered sites are informed about the clinical trial opportunity per e-mail by VACCELERATE. If desired, sponsors/developers can opt to include further trial information and or (pre-)feasibility questionnaires in the e-mail. VACCELERATE NC can be involved to discuss potential country-specific requirements or challenges and promote the trial in their country-specific VACCELERATE site network. Sites will decide whether they are interested in participating. Refusing to participate in any offered vaccine trial opportunity does not impact registration in the network. Vaccine trial sites keep their decision independence throughout the whole process (Fig. 1). The sponsor then receives the contact details of interested sites and a feasibility and site selection process is to be done by the sponsor or their representative unless VACCELERATE is delegated/contracted to do this for them.

For the cases when VACCELERATE is in charge of the site feasibility, a transparent site selection procedure tool was created to select the best qualified sites for individual studies, both for adult and paediatric trials. First, an online baseline feasibility questionnaire is sent out to a selection of sites that could qualify based on an initial match between the trial site information entered at registration in the Site Network and the specific trial requirements. Feasibility questions address the following categories: general site

Table 1
VACCELERATE Site Network: Survey Captured.

Vaccine Trial Site/Network	
Site name	
Type of institution *(multiple answers possible)*	
Academic research organization	*Pathology Department*
Clinic	*Pharma company/Medical device manufacturer*
Comprehensive cancer centre	*Practice*
Contract research organization	*Society/association*
Ethics committee	*Study office*
Institute/University institution	*Study Group*
Institution	*Trials unit*
Laboratory	*University*
Medical centre	*Working Group*
Network/Consortium	*Pathology Department*
Address	
Street and number	
Postal code	
City/Town	
Country	
Part of national infectious disease network/s?	
Main site for communication	
Name of contact person	
Academic Title | Function	
MD	*Primary care network coordinator*
Microbiologist	*Study nurse*
MSc	*Study physician*
Pharmacist	*Virologist*
PhD	*Other. Please specify*
PI	
Phone number (direct line)	
Email	
Prior clinical trial experience	
Number of trials per centre < 5 years	
Number of subjects per centre < 5 years	
Main focus *(multiple answers possible)*	
Phase I (includes I/II)	
Phase II	
Phase III	
Phase IV	
Observational	
No previous experience	
Previous experience conducting vaccine studies?	
If yes,	
Number of trials per centre < 2 years	
Number of subjects per trial < 2 years	
Main disease area/indication	
Phases	
Phase I	
Phase II	
Phase III	
Phase IV	
Main disease area/indication. Please specify	
Infrastructure	
Dedicated Phase-I-Unit available?	
If yes, number of subjects who can be enrolled in parallel at any given time	
Site pharmacy has prior experience with blinded investigational product?	
Site pharmacy has prior experience with vaccines as investigational product?	
Site pharmacy has prior experience with genetically modified organisms as investigational product?	
Is PCR for SARS-CoV-2 carried out by a lab at your institution?	
No, i.e., by external lab. Please indicate who carries out these PCR for your site	
Yes, i.e., in-house	
Please indicate maximum turn-around time for SARS-CoV-2 PCR at your site? (time from swab to results, regardless of whether done in-house or externally)	
24–48 h	
>48 h	
Preferred parameters for study participation	
Study population	
Healthy subjects	
Adults (≥18)?	
Adolescents and children (<18)?	
Seropositive subjects	
Adults (≥18)?	
Adolescents and children (<18)?	

(*continued on next page*)

Table 1 (*continued*)

Vaccine Trial Site/Network
Clinical setting
Phase-I-Unit
Outpatient setting
Inpatient setting
Interest in participating in trials for other than SARS-CoV-2/COVID-19?
I would like to recommend the following site(s)/network(s) for the platform (e.g., site name, PI name, email address…)

COVID-19, coronavirus diseases 2019; **MD**, Medical Doctor; **MSc**, Master of Science; **PCR**, polymerase chain reaction; **PhD**, Doctor of Philosophy; **PI**, principal investigator; **SARS-CoV-2**, severe acute respiratory syndrome coronavirus 2.

Table 2
Registered sites in the VACCELERATE Site Network as of April 2023.

	Paediatric			Adults			Total		
	n	% over total	centres/1M hab	n	% over total	centres/1M hab	n	% over total	centres/1M hab
Total	**231**	100.00 %	0.3	**388**	100.00 %	0.6	**481**	100.00 %	0.7
Albania	1	0.43 %	0.3	1	0.26 %	0.3	1	0.21 %	0.3
Austria	4	1.73 %	0.5	9	2.32 %	1.0	11	2.29 %	1.2
Azerbaijan	1	0.43 %	0.1	2	0.52 %	0.2	2	0.42 %	0.2
Belgium	5	2.16 %	0.4	13	3.35 %	1.1	15	3.13 %	1.3
Bulgaria	5	2.16 %	0.7	16	4.12 %	2.3	16	3.33 %	2.3
Croatia	1	0.43 %	0.2	1	0.26 %	0.2	1	0.21 %	0.2
Cyprus	3	1.30 %	2.6	6	1.55 %	5.1	9	1.88 %	7.7
Czech Republic	1	0.43 %	0.1	8	2.06 %	0.8	8	1.67 %	0.8
Denmark	10	4.33 %	1.7	14	3.61 %	2.4	20	4.17 %	3.5
Estonia	1	0.43 %	0.8	0	0.00 %	0.0	2	0.42 %	0.8
Finland	0	0.00 %	0.0	1	0.26 %	0.2	1	0.21 %	0.2
France	36	15.58 %	0.5	38	9.79 %	0.6	39	8.13 %	0.6
Georgia	1	0.43 %	0.3	1	0.26 %	0.3	1	0.21 %	0.3
Germany	18	7.79 %	0.2	47	12.11 %	0.6	56	11.67 %	0.7
Greece	16	6.93 %	1.5	15	3.87 %	1.4	26	5.42 %	2.4
Hungary	3	1.30 %	0.3	8	2.06 %	0.8	8	1.67 %	0.8
Iceland	1	0.43 %	2.9	0	0.00 %	0.0	1	0.21 %	2.9
Ireland	6	2.60 %	1.3	15	3.87 %	3.2	19	3.96 %	4.0
Israel	3	1.30 %	0.3	7	1.80 %	0.8	7	1.46 %	0.8
Italy	14	6.06 %	0.2	27	6.96 %	0.4	35	7.29 %	0.6
Latvia	1	0.43 %	0.5	0	0.00 %	0.0	1	0.21 %	0.5
Lithuania	4	1.73 %	1.4	6	1.55 %	2.1	8	1.67 %	2.9
Luxembourg	1	0.43 %	1.7	1	0.26 %	1.7	2	0.42 %	3.3
Malta	2	0.87 %	4.5	0	0.00 %	0.0	2	0.42 %	4.5
Netherlands	5	2.16 %	0.3	10	2.58 %	0.6	11	2.29 %	0.6
North Macedonia	1	25.00 %	0.5	0	0.00 %	0.0	1	9.09 %	0.5
Norway	7	3.03 %	1.3	5	1.29 %	0.9	7	1.46 %	1.3
Poland	7	3.03 %	0.2	16	4.12 %	0.4	17	3.54 %	0.4
Portugal	13	5.63 %	1.3	9	2.32 %	0.9	18	3.75 %	1.7
Romania	1	0.43 %	0.1	2	0.52 %	0.1	3	0.63 %	0.2
Serbia	0	0.00 %	0.0	1	0.26 %	0.1	2	0.42 %	0.3
Slovakia	1	0.43 %	0.2	3	0.77 %	0.6	4	0.83 %	0.7
Slovenia	0	0.00 %	0.0	1	0.26 %	0.5	1	0.21 %	0.5
Spain	27	11.69 %	0.6	56	14.43 %	1.2	62	12.92 %	1.3
Sweden	12	5.19 %	1.2	11	2.84 %	1.1	20	4.17 %	2.0
Switzerland	3	1.30 %	0.4	10	2.58 %	1.2	10	2.08 %	1.2
Turkey	7	3.03 %	0.1	8	2.06 %	0.1	11	2.29 %	0.1
Ukraine	2	0.87 %	0.0	8	2.06 %	0.2	8	1.67 %	0.2
United Kingdom	7	3.03 %	0.1	12	3.09 %	0.2	15	3.13 %	0.2

hab, habitant**s; M**, million.

information, prior experience in clinical vaccine trials, access to study population, site staff expertise and qualifications, (laboratory) facilities and equipment, and local ethics approval and contracting processes. The information from the baseline feasibility questionnaire is compiled in feasibility reports and this information is used as site selection tool by the Site Selection Board (SSB). The main objectives of the SSB are to agree on site selection criteria for trials, review answers from feasibility questionnaires provided by potential sites against these criteria, and to select the more suitable trial sites across Europe. The information collected by the site selection tool is used as an initial pre-selection filter. Pre-selected sites receive a second feasibility questionnaire detailing trial specific needs and requirements. Combined, the information from baseline and trial-specific feasibility questionnaires is compiled and used for final site selection procedure by the Board.

2.1. Site management system: added value

VACCELERATE Site Network data are stored on the online platform Clinicalsite.org (Healex GmbH, Cologne, Germany) [15]. Clinicalsite.org also permits document uploads, such as curricula vitae of designated clinical trial personnel, reports of previous experience in trials, GCP certificates and other relevant clinical trial training certification.

To further harmonise VACCELERATE standards and processes, minimum good quality standards, key performance indicators and site assessment procedures were also developed by the coordi-

Table 3
Description of the VACCELERATE Site Network.

	Overall *(n = 481)*		**Children** *(n = 231)*		**Adults** *(n = 390)*	
	n	*%*	*n*	*%*	*n*	*%*
Research topic						
Infectious Diseases	274	57.0	132	57.1	217	55.6
Immunodefficiencies	141	29.3	37	16.0	127	32.6
Diabetes mellitus	10	2.1	7	3.0	7	1.8
Any disease	64	13.3	50	21.6	60	15.4
Prior vaccine trial experience	418	86.9	184	79.7	334	85.6
Number of trials per centre < 5 years	12 (5–30) [0–999]		10 (5–30) [0–960]		15 (7–35) [0–999]	
Number of subjects per centre < 5 years	200 (50–617) [0–100000]		200 (50–1000) [0–100000]		285 (80–825) [0–100000]	
Trial phase						
Phase I	137	28.5	63	27.3	120	30.8
Phase II	259	53.8	119	51.5	222	56.9
Phase III	340	70.7	147	63.6	282	72.3
Phase IV	205	42.6	92	39.8	172	44.1
Observational studies	253	52.6	115	49.8	208	53.3
Previous vaccine trial experience	229	47.6	115	49.8	181	46.4
Number of trials per centre < 2 years	3 (2–5) [0–15]		1 (0–2)[0–2]		4 (2–5) [1–15]	
Number of subjects per trial < 2 years	152 (20–600) [6–1000]		20 (6–203) [6–203]		402 (152–800) [100–1000]	
Trial phase						
Phase I	61	12.7	30	13.0	57	14.6
Phase II	107	22.2	52	22.5	87	22.3
Phase III	164	34.1	88	38.1	128	32.8
Phase IV	69	14.3	38	16.5	56	14.4
Infrastructure						
Pharmacy experience with blinded products	391	81.3	165	71.4	322	82.6
Pharmacy experience with vaccines	280	58.2	125	54.1	236	60.5
Pharmacy experience with GMO	177	36.8	85	36.8	156	40.0
PCR access	443	92.1	196	84.8	353	90.5
Onsite	382	79.4	175	75.8	297	76.2
Outsourced	61	12.7	17	7.4	47	12.1
24–48 h	12	2.5	3	1.3	10	2.6
>48 h	431	89.6	193	83.5	343	87.9
Preferred parameters						
Healthy subjects	418	86.9	193	83.5	110	28.2
Seropositive subjects	344	71.5	144	62.3	93	23.8
Clinical setting						
Phase-I-Unit	129	26.8	49	21.2	119	30.5
Outpatient setting	393	81.7	180	77.9	315	80.8
Inpatient setting	295	61.3	142	61.5	227	58.2

GMO, genetically modified organism; **PCR**, polymerase chain reaction.

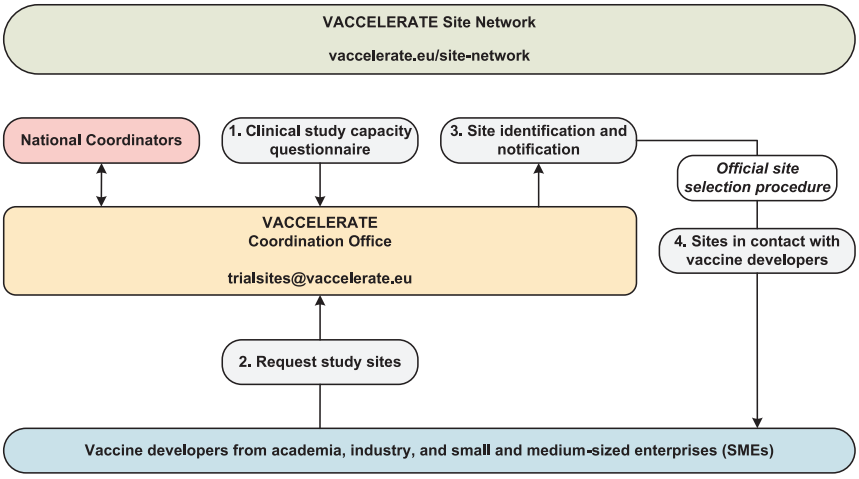

Fig. 1. Management of the VACCELERATE Site Network (1) Potential sites may register after sending an email to trialsites@vaccelerate.eu. Login data to access the online platform where data are stored will be provided. (2) Vaccine developers interested in performing vaccine trials might contact the VACCELERATE Coordination Office with a participant request. (3) Potential sites are identified and filtered according to the vaccine developers, and briefly informed about the vaccine trial, including sometimes a specific feasibility questionnaire, via e-mail. (4) Interested sites can independently decide whether they eventually participate the vaccine trial.

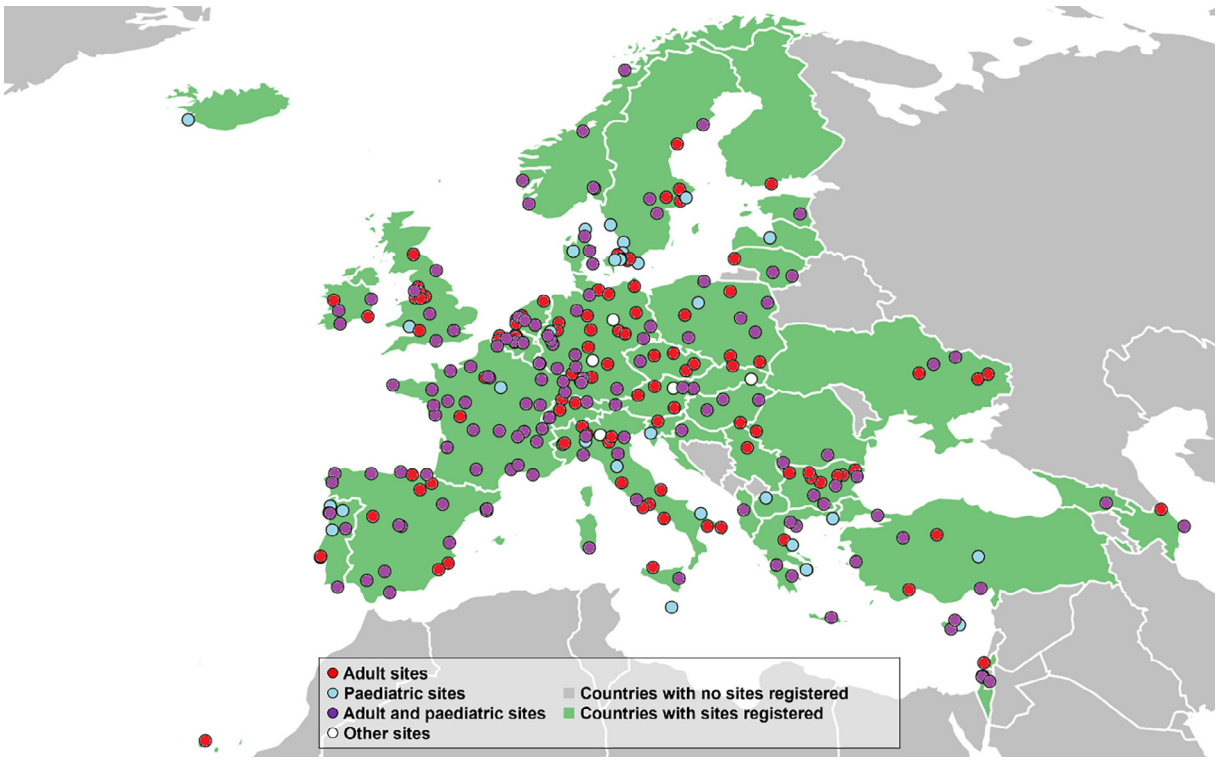

Fig. 2. Current Site Mapping of the VACCELERATE Site Network **Overall registered sites**: Spain (n = 62), Germany (n = 56), France (n = 39), Italy (n = 35), Greece (n = 26), Denmark and Sweden (n = 20, each), Ireland (n = 19), Portugal (n = 18), Poland and United Kingdom (n = 17, each), Bulgaria (n = 16), Belgium (n = 15), Austria, Netherlands, and Turkey (n = 11, each), Cyprus and Switzerland (n = 9, each), Czech Republic, Hungary, Lithuania, and Ukraine (n = 8, each), Israel and Norway (n = 7, each), Slovakia (n = 4), Romania (n = 3), Azerbaijan, Estonia, Luxembourg, and Malta (n = 2, each), and Albania, Croatia, Finland, Georgia, Iceland, Latvia, North Macedonia, Serbia, and Slovenia (n = 1, each).

nation team of the VACCELERATE Site Network. Within ClinicalSite, a certification status was created that can be used to identify experienced and qualified sites. A distinction is made between the following statuses: green, bronze, silver and gold. The obtained status depends on the qualification of the site and staff (sites uploaded GCP and study nurse course certificates, as well as CVs of Principal Investigator/site personnel), as well as their previous experience (participation in at least one phase 2/3 vaccine trial) and if the site implemented VACCELERATE SOPs.

In addition to this certification status, a quality assessment tool was created focussed on criteria related to the previous experience of VACCELERATE sites (i.e., vaccine trial experience, trained PI and staff), indicating capacity building needs. Over the course of the VACCELERATE project, this tool will be able to show the progress of the network and capacity building efforts. For each parameter (experience with vaccine trials, experience PI and experience study coordinator), a site will be classified in one of four categories. The categories all have their own score. The site data for each category can be retrieved from ClinicalSite or the baseline feasibility questionnaire. All information on these parameters can be combined and plotted in a heat map with sites on the y-axis and the different parameters on the x-axis. Sites can move to a new category when they follow the training courses developed in VACCELERATE. Additionally, a total score can be calculated based on the scores of the site for each of the parameters using the assessment tool. Based on the total scores for each site, a gradient scale can be generated and added to the heat map. Besides the assessment tool, performance indicators were also defined in order to measure a VACCELERATE site's performance in trials. The objectives of these performance indicators are to a) aid the selection of sites into studies based on their infrastructure and performance in VACCELERATE studies, b) identify challenges within less well performing organisations requiring extra support/training and plan improvement activities for these sites, and c) monitor and report progress of the VACCELERATE project in improving these indicators.

The following performance indicators were selected because they were considered relevant, objectively measurable, and amenable to improvement by participating sites: a) enrolment/randomisation rates (number of subjects randomised / planned number of subjects randomised), b) subject completion rates (number of subjects completed / enrolled), c) turnaround time for IEC/IRB approval (number of days between submission to ethics committee and approval from ethics committee), d) turnaround time for contract agreement (number of days between first contract sent and all contracts signed), e) completion time of electronic case report forms (eCRFs), and f) response time to electronic case report form (eCRFs) queries.

The above-mentioned performance indicators will be used for both sites that participate in trials with an adult or a paediatric study population. The ClinicalSite data, performance data and assessment tool outcomes can be combined to create a well-rounded quality assessment of sites, distinguishing between sites that performed adult and paediatric trials.

2.2. Data privacy and data protection

The processing of personal data, such as name(s) and surname (s), address, e-mail address, telephone number or curriculum vitae of the person concerned, is always carried out in accordance with the General Data Protection Regulation (EU GDPR) and in accordance with the country-specific data protection regulations applicable to Healex GmbH (Cologne, Germany). Furthermore, participants are informed of the rights to which they are entitled by means of this data protection declaration. Registered points of

Table 4
VACCELERATE Site Network utilisation since set up.

Utilisation date	Pathogen	User	Purpose
October 2020	SARS-CoV-2	Industry trial	Vaccine trial
October 2020	SARS-CoV-2	Industry trial	Vaccine trial
February 2021	SARS-CoV-2	Industry trial	Vaccine trial
February 2021	SARS-CoV-2	Industry trial	Vaccine trial
February 2021	*Orthomyxoviridae*	Industry trial	Vaccine trial
March 2021	SARS-CoV-2	Industry trial	Vaccine trial
March 2021	SARS-CoV-2	Industry trial	Vaccine trial
July 2021	SARS-CoV-2	Industry trial	Vaccine trial
July 2021	SARS-CoV-2	Industry trial	Vaccine trial
August 2021	SARS-CoV-2	Academic trial	Vaccine trial
August 2021	SARS-CoV-2	Academic trial	Vaccine trial
August 2021	SARS-CoV-2	Academic trial	Vaccine trial
September 2021	Fungi	Academic epidemiological study	IFI diagnostic and treatment capacity mapping [18]
March 2022	*Streptococcus pneumoniae*	Industry trial	Vaccine trial
April 2022	*Streptococcus pneumoniae*	Industry trial	Vaccine trial
May 2022	*Orthomyxoviridae*	Industry trial	Vaccine trial
May 2022	Monkeypox virus	Academic epidemiological study	Monkeypox diagnostic and treatment capacity mapping [17]
June 2022	Monkeypox virus	Academic epidemiological study	Status of monkeypox-related clinical trials in Germany
June 2022	Monkeypox virus	Academic epidemiological study	Status of monkeypox-related clinical trials in Europe
July 2022	Monkeypox virus	Academic epidemiological study	Monkeypox epidemiology in children and adult women at outbreak onset [16]
August 2022	NA	Academic epidemiological study	Status of Study Nurse courses in Europe
February 2023	Monkeypox virus	Industrail trial	Feasibility to participate in observational monkeypox paediatric studies
February 2023	Any	Academic epidemiological study	Priority list of pathogens of interest
February 2023	SARS-CoV-2	Academic epidemiological study	Long-COVID treatment and follow up capacity mapping
March 2023	NA	Other	Invitation to study nurse course

IFI, invasive fungal infection; **NA**, not applicable; **SARS-CoV-2**, severe acute respiratory syndrome coronavirus 2.

contact for the sites consent to the transfer of their names and contact details to the sponsor/sponsor representative, in case of a matching and their interest in trial participation as a site with the e-mail expressing their interest.

3. Results

As of April 2023, the VACCELERATE Site Network has collected information from up to 481 institutions from 39 European countries (Fig. 2). Of these, in 274 (57.0 %) the main topic for research was reported to be infectious diseases, in 141 (29.3 %) immunodeficiencies, either acquired or autoimmune, and 64 (13.3 %) sites are open to research in any disease.

More than 400 sites (n = 418, 86.9 %) reported previous experience in vaccine trials, with a median of 12 (IQR 5–30) trials performed per centre in the previous 5 years before the registration, and a median of 200 (IQR 50–617) subjects participating in them. Focusing on the trial phase, most sites (n = 340, 70.7 %) have already participated in phase III trials; with only 137 (28.5 %) sites reporting experience in phase I trials. Specifically for vaccine trials, 229 (47.6 %) claimed having participated in such studies in the past, mainly in phase III (n = 164, 34.1 %) and phase II (n = 107, 22.2 %).

Four in five hospital pharmacies (n = 391, 81.3 %) had experience handling blinded products for research, 280 (58.2 %) vaccines and 177 (36.8 %) genetically modified organisms. Polymerase chain reaction tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were available in 443 (92.1 %) of the participating sites, mainly on-site (n = 382, 79.4 %). Participant-wise, 418 (86.9 %) institutions were open to perform vaccine trials with healthy subjects, while 344 (71.5 %) with infected subjects. Specific data for paediatric and adult populations are depicted in table 2 and 3.

Since its inception in October 2020, the VACCELERATE Site Network has provided access to European sites up to 25 times for different initiatives, such as academic and industry interventional clinical trials or epidemiological studies: two (8.0 %) in 2020, 11 (44.0 %) in 2021, eight (32.0 %) in 2022, and four (16.0 %) until April 2023. Of all the initiatives, 12 (48.0 %) were focused on SARS-CoV-2 initiatives, five (20.0 %) on monkeypox virus and two (8.0 %) on *Orthomyxoviridae*/influenza viruses *Streptococcus pneumoniae*/pneumococcus each (Table 4) [16–18].

3.1. Outlook

The VACCELERATE Site Network serves as a platform where vaccine trial sites, regardless of any previous experience, can register in order to eventually participate in vaccine trials in Europe. In fact, the VACCELERATE consortium itself can ensure capacity building to trial centres that lack the necessary experience, by providing certified courses on different aspects, such as GCP or study nurse courses. Initiated at COVID-19 pandemic onset, the network is open to any vaccine trial that could be accelerated by participating institutions. Additionally, it has also proved to be an excellent initiative to run flash surveys. for timely relevant aspects that could potentially evolve into vaccine trials, and epidemiological studies in Europe [16–18].

Currently, the enrolment in the VACCELERATE Site Network is open to any vaccine trial centre in Europe and reach out to other world regions has begun.

4. Funding statement

The VACCELERATE Site Network has received funding from the European Union's Horizon 2020 research and innovation programme (grant agreement No 101037867) and the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung [BMBF]) (grant agreement No BMBF01KX2040).

5. Contribution statement

OAC conceived the network idea and is the coordinator of the VACCELERATE Consortium. JSG, AS and UB developed and pro-

grammed the software containing the variables collected for the VACCELERATE Site Network. JSG and PW manage the VACCELERATE Site Network. PVS, CM and IK developed specific strategies and tools to enlarge the VACCELERATE Site Network. JSG performed the analysis, created the figures and wrote the initial manuscript. SHIH and PBV coordinate the work package in which the VACCELERATE Site Network is placed within the VACCELERATE Consortium. All authors worked for the dissemination, enlargement and promotion of the VACCELERATE Site Network and reviewed and approved the final manuscript.

6. Ethics approval

Not applicable.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: VACCELERATE Consortium reports financial support was provided by European Union. VACCELERATE Consortium reports financial support was provided by Federal Ministry of Education and Research Bonn Office.

Acknowledgements

We would like to thank for their registration to all institution members of the VACCELERATE Site Network.

Data availability

Data can be made available after a reasonable requestion following the paths described in the manuscript.

References

[1] Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. BMJ 2020;368:m1036.
[2] Lythgoe MP, Middleton P. Comparison of COVID-19 Vaccine Approvals at the US Food and Drug Administration, European Medicines Agency, and Health Canada. JAMA Netw Open 2021;4:e2114531.
[3] Lankinen KS, Pastila S, Kilpi T, Nohynek H, Makela PH, Olin P. Vaccinovigilance in Europe–need for timeliness, standardization and resources. Bull World Health Organ 2004;82:828–35.
[4] Centers for Disease Control and Prevention. Vaccine Testing and the Approval Process www.cdc.gov/vaccines/basics/test-approve.html (Last accessed August 3, 2022).
[5] European Vaccination Information Portal. Approval of vaccines in the European Union www.vaccination-info.eu/en/vaccine-facts/approval-vaccines-european-union (Last accessed August 2, 2022).
[6] Leroy O, Geels M, Korejwo J, Dodet B, Imbault N, Jungbluth S. Roadmap for the establishment of a European vaccine R&D infrastructure. Vaccine 2014;32:7021–704.
[7] EU-Response investigators group, Diallo A, Troseid M, Simensen VC, Boston A, Demotes J, Olsen IC, Chung F, Paiva JA, Hites M, Ader F, Arribas JR, Baratt-Due A, Melien O, Tacconelli E, Staub T, Greil R, Tsiodras S, Briel M, Esperou H, Mentre F, Eustace J, Saillard J, Delmas C, LeMestre S, Dumousseaux M, Costagliola D, Rottingen JA, Yazdanpanah Y. Accelerating clinical trial implementation in the context of the COVID-19 pandemic: challenges, lessons learned and recommendations from DisCoVeRy and the EU-SolidAct EU response group. *Clin Microbiol Infect* 2021;28:1-5.
[8] Giannuzzi V, Felisi M, Bonifazi D, Devlieger H, Papanikolaou G, Ragab L, et al. Ethical and procedural issues for applying researcher-driven multi-national paediatric clinical trials in and outside the European Union: the challenging experience of the DEEP project. BMC Med Ethics 2021;22:49.
[9] Magnin A, Iversen VC, Calvo G, Cecetkova B, Dale O, Demlova R, et al. European survey on national harmonization in clinical research. Learn Health Syst 2021;5:e10220.
[10] COMBACTE - Combatting antimicrobial resistance www.combacte.com/ (Last accessed August 7, 2022).
[11] ECRIN - European Clinical Research Infrastructure Network www.ecrin.org (Last accessed July 31, 2022).
[12] VACCELERATE-European Corona Vaccine Trial Accelerator Platform www.vaccelerate.eu (Last accessed August 1, 2022).
[13] Salmanton-García J, Stewart FA, Heringer S, Koniordou M, Alvarez-Barco E, Argyropoulos CD, et al. on behalf of the VACCELERATE Consortium. VACCELERATE Volunteer Registry: A European study participant database to facilitate clinical trial enrolment. Vaccine 2022;40:4090–407.
[14] VACCELERATE Site Network https://vaccelerate.eu/site-network/ (Last accessed August 2, 2022).
[15] clinicalsite.org by Healex GmbH https://healex.systems/ (Last accessed August 13, 2022).
[16] Grothe JH, Cornely OA, Salmanton-García J, on behalf of the VACCELERATE Consortium. Monkeypox in Children and Adult Women in Europe: Results from a Flash VACCELERATE Pilot Survey. *Enferm Infecc Microbiol Clin (Engl Ed)* (Accepted).
[17] Grothe JH, Cornely OA, Salmanton-García J, on behalf of the VACCELERATE Consortium. Monkeypox diagnostic and treatment capacity at epidemic onset A VACCELERATE online survey. *J Infect Public Health* 15:1043-46.
[18] Salmanton-García J, Hoenigl M, Gangneux J-P, Segal E, Alastruey-Izquierdo A, Arikan-Akdagli S, Lagrou K, Özenci V, Vena A, Cornely OA. The current state of laboratory mycology and access to antifungal treatment in Europe: A European Confederation of Medical Mycology survey. *Lancet Microbe* 2022;(Accepted).