Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Emerging Manufacturers engagements in the COVID-19 vaccine research, development and supply

Sonia Pagliusi, Stephen Jarrett, Benoit Hayman, Ulrike Kreysa, Sai D. Prasad, Martin Reers, Pham Hong Thai, Ke Wu, Youn Tao Zhang, Yeong Ok Baik, Anand Kumar, Anatoly Evtushenko, Suresh Jadhav, Weining Meng, Do Tuan Dat, Weidan Huang, Samir Desai

PII: S0264-410X(20)30795-7
DOI: https://doi.org/10.1016/j.vaccine.2020.06.022
Reference: JVAC 22060

To appear in: Vaccine

Received Date: 11 May 2020
Revised Date: 4 June 2020
Accepted Date: 8 June 2020

Please cite this article as: S. Pagliusi, S. Jarrett, B. Hayman, U. Kreysa, S.D. Prasad, M. Reers, P. Hong Thai, K. Wu, Y. Tao Zhang, Y. Ok Baik, A. Kumar, A. Evtushenko, S. Jadhav, W. Meng, D. Tuan Dat, W. Huang, S. Desai, Emerging Manufacturers engagements in the COVID-19 vaccine research, development and supply, Vaccine (2020), doi: https://doi.org/10.1016/j.vaccine.2020.06.022

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 The Author(s). Published by Elsevier Ltd.
Title:

Emerging Manufacturers engagements in the COVID -19 vaccine research, development and supply
Title:
Emerging Manufacturers’ engagements in the COVID-19 vaccine research, development and supply

Co-authors:
Sonia Pagliusi*
DCVMN International
Route de Crassier 7
1262 Eysins-Nyon, Switzerland
+41 22 5951393
s.pagliusi@dcvmn.net

Stephen Jarrett
Gracious International
28 Jiafeng Road, Shanghai, 200131 China
Telephone +86 21 52387162
swjarrett@graciousgroup.com

Benoit Hayman
DCVMN International
b.hayman@dcvmn.net

Ulrike Kreysa
GS1
Avenue Louise 326, 1050 Bruxelles, Belgium
ulrike.kreysa@gs1.org
Sai D. Prasad
Bharat Biotech, Hyderabad
Prasadsd@bharatbiotech.com

Martin Reers
Biological E Ltd., Hyderabad
martin.reers@biologicale.com

Pham Hong Thai
BioNet-Asia, Bangkok
hongthai@bionet-asia.com

Ke Wu
Bravovax, Wuhan
ke.wu@bravovax.com

Youn Tao Zhang
China National Biotech Group, Beijing
zhangyuntao@sinopharm.com

Yeong Ok Baik
EuBiologics, Seoul
yobaek@eubiologics.com

Anand Kumar
Indian Immunologicals Ltd., Hyderabad
anandkumar@indimmune.com
Anatoly Evtushenko
St. Petersburg Research Institute of Vaccines and Serums
a.e.evtushenko@spbniivs.ru

Suresh Jadhav
Serum Institute of India, Pune
ssj@seruminstitute.com

Weining Meng
Sinovac Biotech, Beijing
mengwn@sinovac.com

Do Tuan Dat
Vabiotech, Hanoi
dotuandat@vabiotech.com.vn

Weidan Huang
Innovax Biotech, Xiamen
weidan_huang@innovax.cn

Samir Desai
Zydus Cadila, Ahmedabad
samirdesai@zyduscadila.com

(*) corresponding author
Co-authors:

Sonia Pagliusi*, DCVMN

s.pagliusi@dcvmn.net

Stephen Jarrett, DCVMN

swjarrett@graciousgroup.com

Benoit Hayman, DCVMN

b.hayman@dcvmn.net

Ulrike Kreysa, GS1

ulrike.kreysa@gs1.org

Sai D. Prasad, Bharat Biotech

Prasadsd@bharatbiotech.com

Martin Reers, Biological E Ltd.

martin.reers@biologicale.com

Pham Hong Thai, BioNet-Asia

hongthai@bionet-asia.com

Ke Wu, Bravovax

ke.wu@bravovax.com

Youn Tao Zhang, China National Biotech Group
zhangyuntao@sinopharm.com

Yeong Ok Baik, EuBiologics
yobaek@eubiologics.com

Anand Kumar, Indian Immunologicals Ltd.
anandkumar@indimmune.com

Anatoly Evtushenko, St. Petersburg Research Institute of Vaccines and Serums
a.e.evtushenko@spbniivs.ru

Suresh Jadhav, Serum Institute of India
ssj@seruminstitute.com

Weining Meng, Sinovac Biotech
mengwn@sinovac.com

Do Tuan Dat, Vabiotech
dotuandat@vabiotech.com.vn

Weidan Huang, Xiamen Innovax Biotech
weidan_huang@innovax.cn

Samir Desai, Zydus Cadila
samirdesai@zyduscadila.com

(*) corresponding author
Highlights

- Broad research and development is key to achieving an effective safe COVID-19 vaccine
- Currently 19 Network members engaged in research & development of 22 COVID-19 vaccines
- Collectively 37 Network manufacturers supply around 3.5 billion vaccine doses annually
- Existing manufacturing capabilities can accelerate the availability of COVID vaccines
- Deploying available vaccine production capacity, will save time, resources and lives
Abstract

The World Health Organization declared the COVID-19 disease as a pandemic requiring a rapid response. Through online search, direct communication with network members and an internal survey, engagements of developing countries’ vaccine manufacturers’ network members in the research and development of COVID-19 vaccines and their capacities in the manufacturing, fill-finish and distribution of vaccines were assessed.

Currently, 19 network members engaged in research and development of COVID-19 vaccines, using six principal technology platforms. In addition, an internal survey showed that the number of vaccines supplied collectively by 37 members, in 2018-19, was about 3.5 billion doses annually. Almost a third of network members having vaccines prequalified by the World Health Organization comply with international regulations and mechanisms to distribute vaccines across borders. The use of existing manufacturing, fill-finish and distribution capabilities can support an efficient roll-out of vaccines against COVID-19, while maintaining supply security of existing vaccines for on-going immunization programmes.
I. Introduction and background

A new strain of coronavirus not previously identified in humans, the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), emerged in December 2019 [1]. COVID-19 is the name given to the disease associated with the SARS-CoV-2 virus. Given escalating outbreaks in over 100 countries, the World Health Organization declared on 11 March 2020 that the COVID-19 disease can be characterized as a pandemic [2]. Early June, 2020, the total number of cases identified passed 6.5 million with over 380 thousand deaths globally [3].

Coronaviruses are enveloped positive stranded RNA viruses in the order of Nidovirales [4]. Epithelial cells in the respiratory and gastrointestinal tract are the primary target cells of these viruses. COVID-19 is highly contagious which would indicate the need for widespread vaccination, once vaccines are available. The genetic sequence of the novel coronavirus was shared for developing specific diagnostic and other health products including vaccines [5].

The Developing Countries Vaccine Manufacturers Network (DCVMN) is a public-health driven alliance representing vaccine manufacturers from emerging countries engaged in research, development, manufacturing and supply of vaccines for local and international use, aiming to protect all people against known and emerging infectious diseases [6]. DCVMN members have proven manufacturing, formulation, filling, packaging and distribution capabilities to ensure vaccines reach populations round the world in support of the global call to fight the pandemic [7]. This report outlines four key areas where DCVMN-affiliated manufacturers are engaged in vaccine research and development using various technology platforms, and could play a role in large scale manufacturing and supply capabilities, for supporting an efficient roll-out of potential vaccines against COVID-19.

II. Methodology

We conducted an online search, on COVID-19 vaccine research and development activity by DCVMN members, to compile an overview of initial efforts to date, combined with recent survey results on
supply capacity as described in detail elsewhere [6], complemented with some data from 2019. To enable unconflicted responses, individual data regarding number of doses supplied were agreed to remain confidential. Data collected include developments reported through the WHO’s Blueprint updated list [8], information identified from the internet and publicly available sources, reports of scientific meetings and direct communication with DCVMN members. The information is shared in a summarized manner with global health stakeholders to help improve coordination in the COVID-19 response and to achieve the leverage and optimal use of resources and capabilities.

III. Research and Development Efforts and Vaccine Technology Platforms

Of over 125 candidate vaccines from various manufacturers and academic institutions worldwide [8, 9], 19 DCVMN members have rapidly engaged in the research and development of 22 COVID-19 candidate vaccines (Table 1). Four members have candidate vaccines in Phase 1 or 1/2 trials and the others are in the preclinical stage, as of the end of May 2020. Eight of the 19 members’ manufacturers developing COVID vaccines have vaccines prequalified by WHO.

Among the developments, six principal platforms are being pursued worldwide [10]:

1. Live attenuated virus
2. Inactivated virus
3. Nucleic acid: DNA and RNA\(^1\)
4. Replicating viral vectors (e.g. measles)
5. Non-replicating viral vector (e.g. adenoviral vectors and Modified Vaccinia Ankara, MVA)
6. Recombinant protein sub-unit or Virus-Like Particles.

---

\(^1\) DNA=Deoxyribonucleic acid ; RNA= Ribonucleic acid
The feasibility of any of these platforms to use existing manufacturing capacity has to be assessed. Formulation combined with adjuvants may potentially play a role in the immunogenicity and efficacy of candidate vaccines. Interestingly, it has been suggested that immune modulation by Bacille Calmette–Guérin (BCG) could provide protection against COVID-19 [11] and this hypothesis is being tested in randomized clinical trials by at least one DCVMN member. The efficacy of the Recombinant BCG vaccine VPM1002 is in phase 3 study as part of COVID-protection [12].

It is not yet determined what the degree of natural immunity infection elicits, nor what the level of herd immunity, if attainable, might protect people against the viral infection. It is assumed at this stage that vaccination of all populations will be demanded, given the high level of contagion of the virus. It is conjectured that a number of vaccines will be necessary to supply the world’s populations. As yet, there is no determination as to whether any candidate vaccine will be universal or indicated for specific populations, how many doses will be required, nor of the likely container presentations: prefilled single dose syringes, single or multidose vials, nasal spray, micropatches or other delivery devices.

IV. Rapid Scale up and Large Scale Manufacturing

While broad research and development is key to achieving an effective safe vaccine, massive levels of manufacturing will be required to meet the presumed high demand. Speed of transitioning from a proven vaccine to large-scale manufacturing will be essential in order to commence immunization globally as soon as possible. Deploying available facilities, especially viral vaccine production capacity, will likely save time, resources and, importantly, lives, recognizing DCVMN members’ capacities, both those with WHO prequalified vaccines and those certified by national regulatory authorities. [6].

According to an internal survey the total number of doses supplied collectively by 37 DCVMN members was around 3.5 billion in 2018/2019 (Table 2), ranging from 50 thousand to 1.5 billion doses per member company. This amount corresponds in most cases to filling capacity for single dose syringes, single or multidose vials, under routine operations, notably one shift Monday-Friday. If
operations were adjusted to run additional shifts, the capacities could be increased. The survey
assessed supplied doses in 2018-19 only; number of vaccine doses produced, e.g. bulk in stock, or
batches not released, or in storage, were not assessed. Noteworthy, some of the vaccines supplied
included monovalent vaccines such as tetanus, hepatitis B (HepB), Japanese encephalitis, BCG,
rabies, rubella, Haemophilus influenzae type b (Hib), Meningitis A, monovalent Poliovirus, typhoid,
varicella, Enterovirus-71, and Hepatitis E. Other supplied vaccines included combination vaccines
based on two, three, four or five antigenic components, such as Diphtheria-Tetanus-Pertussis (DTP),
Measles-Rubella or Measles-Mumps-Rubella, bivalent-trivalent- and quadrivalent meningitis
vaccines, five-valent rotavirus vaccines, tri- and quadrivalent seasonal influenza vaccines, bivalent
Human Papillomavirus, ten- or thirteen-valent Pneumococcal conjugate, bivalent cholera vaccine,
bivalent poliovirus and trivalent inactivated poliovirus (IPV) vaccines, pentavalent vaccines
(DTPHepBHib) as well as a hexavalent (DTPHepBHib+IPV). Thus, it is suggested that the collective
antigen manufacturing capacity of this group of manufacturers is higher than 3.5 billion doses
annually. In addition, 4 companies did not respond to the survey, and may have additional available
capabilities. Assuming that collectively manufacturers on average were able to dedicate 50% of their
existing capacities to vaccines against COVID-19, manufacturing and filling billions of doses could be
attained in the short term, enabling global access to these new vaccines. Filling a potential COVID-19
vaccine into ten dose vials, as used in large immunization programmes, would imply that with filling
100 million vials, one billion doses could be supplied.

However, the exact available capabilities, for both antigen manufacturing and filling capacity, and the
feasibility and timing of a manufacturing “switch” from currently produced antigens to produce
potential COVID-19 vaccines, need to be carefully assessed in discussions with manufacturers on an
individual basis.
Gavi, the Vaccine Alliance, estimated that the cost of manufacturing hundreds of millions of doses of a single product will range from $50 million dollars for companies with existing facilities and trained personnel, to about $700 million dollars for those starting from scratch [13].

V. Fill-finish and distribution capabilities

To date, DCVMN represents 41 manufacturing member companies across Latin America, Africa, the Middle East and Asia. These companies have established, validated and GMP certified facilities, already providing vaccines to 170 countries. Of these, 13 members have WHO-prequalified vaccines and are familiar with international supply regulations and mechanisms, including international standards, packaging requirements, labelling and regulatory pathways to distribute vaccines safely across borders. Deploying available facilities will likely save time, resources and, importantly, lives, recognizing DCVMN members capabilities, both those with WHO prequalified vaccines and those certified by national regulatory authorities.

The process of filling and finishing vaccines, the last stage in vaccine manufacturing, is where bottlenecks are most likely to occur [13]. Excess capacity is likely to be available at influenza vaccine facilities dedicated to only one hemisphere vaccine. For others, the approach of adding shifts may be able to help to exploit capacity within existing facilities, if two shifts can be managed. Filling capacity for COVID vaccines is being built now, particularly in manufacturers that have a large number of staff and a large footprint.

Notably, 14 member manufacturers with available spare capacity for formulation, fill-finish, labelling, packaging, storage and distribution have voluntarily and publicly declared their technical capabilities [14]. These manufacturers are open to take up the challenges of surge manufacturing or filling, particularly once a potential vaccine against COVID-19 becomes available.

Furthermore, the worldwide unique identification of vaccines will play an important role in creating an efficient supply chain, ensuring vaccines reach those who need them and helping to uniformly
document the vaccination of individuals. Often the supply chain is broken, vaccines are expired or not stored correctly, inventory management is not optimal and traceability is not achievable, thus responsibility towards procurers not fulfilled and vaccines are not reaching the populations. In assessing the programmatic suitability of vaccines for WHO prequalification, the Vaccine Presentation and Packaging Advisory Group (VPPAG) recommended improvements by using barcodes on all vaccine packaging levels used by manufacturers, with the exception of primary packaging [15]. GS1 is a not-for-profit organization\textsuperscript{2} that develops and maintains global standards for business communication, including the barcode, printed on products that allows automatic data capture. The GS1 standards and associated specifications used to encode the Global Trade Item Number (GTIN), lot number and expiry date, and were recommended for the global vaccine supply [16]. Many DCVMN members already comply with the Gavi/UNICEF requirements of adhering to GS1 barcoding traceability standards for international shipping/supply [16]. It will also help to secure the supply chain against substandard and falsified vaccines and provide visibility for all supply chain actors.

VI. Maintaining supply of other essential vaccines

An important concern is that efforts to make vaccines to halt this pandemic should not hamper other vital vaccine production. DCVMN members are engaged in the production or distribution of nearly 50 distinct vaccines with close to 200 products [6]. Ensuring the security of this supply to national and international destinations is central to the mission of DCVMN. The amount of spare capacity available at any time for the formulation or fill-finish of COVID-19 vaccines will depend on the specific situation of each member which is retained by them as confidential information.

\textsuperscript{2} www.gs1.org
Using spare capacity and/or expanding working operations, DCVMN members can support the manufacturing, fill-finish and distribution of COVID-19 vaccines, without jeopardizing the ongoing production of vaccines for national immunization programmes.

VII. Conclusion

DCVMN is collaborating with global health authorities, international organizations and vaccine developers to support the development of vaccines against COVID-19. Not only are several of its members involved in the research and development of vaccines but many have formulation and fill-finish capacities available. In this period of the COVID-19 pandemic, the DCVMN constituency also calls for the attention of governments to make every effort to ensure the routine immunization of children and adults through efficient and timely distribution of available vaccines within the respective countries.

It is to be noted that there are other emerging vaccine manufacturers, with WHO-prequalified vaccines, that are not DCVMN members. Furthermore, there are other emerging vaccine manufacturers not captured in this report, as they are not DCVMN members nor have WHO-prequalified vaccines.

Thus, it is possible to anticipate that the world has the capacity to rapidly manufacture, fill-finish, and supply needed COVID-19 vaccines. Nevertheless, details about the capacity for quality control, supply-chain and delivery capabilities need to be closely assessed. DCVMN serves as a platform to keep a communication channel between member manufacturers and the global immunization community, sharing information in an open and equitable manner, galvanizing international cooperation, enhancing country immunization systems and enabling opportunities for all to understand and contribute to advancing the potential for reaching solutions to the COVID-19 pandemic.
Acknowledgements

We would like to thank the DCVMN manufacturers members for taking time to complete the DCVMN progress survey: AMSON Vaccines & Pharmaceuticals Ltd; Arabio; BCHT; Beijing Minhai Biotechnology Co. Ltd.; PT BioFarma; Biological E. Ltd.; Bio-Manguinhos/Fiocruz; BioNet-Asia Co. Ltd.; Liaoning Chengda Biotechnology; China National Biotech Group; CPL Biologicals Pvt. Ltd.; Eubiologics Co. Ltd.; The Government Pharmaceutical Organization; Green Cross; IMBCAMS: The Institute of Medical Biology, Chinese Academy of Medical Sciences; Incepta Pharmaceuticals Ltd.; Indian Immunologicals Ltd.; LG Chem; Nanolek LLC.; Panacea Biotech Ltd.; POLYVAC; Queen Saovabha Memorial Institute; Serum Institute of India; Sinergium Biotech; Sinovac Biotech Ltd.; SK bioscience; SPbSRIVS; Vabiotech; Walvax Biotechnology Co. Ltd.; Xiamen Innovax Biotech Co. Ltd.; Zhifei Biological Products Ltd.; Zydus Cadila; Biovac Institute; BravoVax Co. Ltd.; Medigen Vaccine Biologics Co.; Pasteur Institute of India; and VINS Bioproducts Ltd. We are to thank the DCVMN Executive Committee for their ongoing support and guidance. This work was partly supported by a grant from the Bill & Melinda Gates Foundation, Grant no. OPP1204376.

Disclaimer

The authors alone are responsible for the views expressed in this article, which do not necessarily represent the views, decisions or policies of any mentioned institutions with which the authors are affiliated. The statements on capacity used here are based on a survey of self-declared qualitative/quantitative data from DCVMN members. The authors are not liable for any data or interpretation thereof.

References
1. World health Organization Timeline – COVID-19. Available at https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19

2. World Health Organization Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

3. COVID-19 Corona virus Pandemic cases, Worldometer. Available at https://www.worldometers.info/coronavirus/

4. Order – Nidovirales. Virus Taxonomy, Ninth Report of the International Committee on Taxonomy of Viruses, 2012, Pages 784-794. Available at https://www.sciencedirect.com/science/article/pii/B9780123846846000665

5. SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2) Sequences. Accessible at https://www.ncbi.nlm.nih.gov/genbank/sars-cov-2-seqs/

6. Hayman B and Pagliusi S. Emerging vaccine manufacturers are innovating for the next decade. Vaccine X 2020. Accessible at https://doi.org/10.1016/j.jvacx.2020.100066

7. Global collaboration to accelerate new COVID-19 health technologies. Available at https://www.who.int/news-room/events/detail/2020/04/24/default-calendar/global-collaboration-to-accelerate-new-covid-19-tools

8. World Health Organization Blueprint - DRAFT landscape of COVID-19 candidate vaccines – 20 April 2020. Available at https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf

9. Than Le T et al. The COVID-19 vaccine development landscape. Nature reviews, 23 May 2020 volume 19: 305-306. Available at https://www.nature.com/articles/d41573-020-00073-5

10. Callaway E. The race for coronavirus vaccines: a graphical guide. Nature 30 April 2020. Volume 580: 576- 577. Available at https://www.nature.com/articles/d41586-020-01221-y

11. MaxPlanck Gesellschaft. Immune boost against the coronavirus. News Release 23-MAR-2020 Available at https://www.eurekalert.org/pub_releases/2020-03/m-iba032320.php
12. O’Neill L and Netea M. BCG-induced trained immunity: can it offer protection against COVID-19? Nature Reviews Immunology 2020, volume 20: 335–337. 
https://www.nature.com/articles/s41577-020-0337-y

13. Miller J and Kuchler H. Drugmakers race to scale up vaccine capacity. Financial Times, April 28 2020. Available at https://www.ft.com/content/87d1170a-78bc-11ea-bd25-7fd923850377

14. DCVMN Technical portal. Available at https://www.dcvmn.org/spip.php?page=partnerships

15. World Health Organization, Vaccine Presentation and Packaging Advisory Group Generic Preferred Product Profile for Vaccines Version 2.1 – Recommendations. 31 March 2015. Available at https://www.who.int/immunization/policy/committees/VPPAG_Generic_PPP_and_Workplan.pdf?ua=1

16. GAVI announcement: vaccine manufacturer GS1 compliance. UNICEF News Note. Available at https://www.unicef.org/supply/stories/gavi-announcement-vaccine-manufacturer-gs1-compliance
Legend to Table 1.

List of DCVMN Member companies currently engaged in COVID-19 vaccine research and development. The data reported on the table include information on manufacturer name and location (first column); WHO Prequalification status of other available vaccines; technology platforms used for COVID-19 vaccine development (second column); the current phase of vaccine development (third column); compliance to global traceability standards for international supply, as provided by GS1, to satisfy GAVI/UNICEF requirements [16]; technical information publicly available; source of information. (*) www.gs1.org ; (***) Biomanguinhos and Butantan are DCVMN members, and collaborate to develop one candidate vaccine.

| DCVMN Member and location | Vaccine technology platform | COVID-19 vaccine development status | Manufacturer using GS1* traceability standards | Technical information publicly available | Information Source |
|---------------------------|-----------------------------|------------------------------------|-----------------------------------------------|---------------------------------------|-------------------|
| Beijing Institute of Biological Products, China National Biotec Group, China | Inactivated virus | Phase 1/2 | Beijing Institute of Biological Products is developing an inactivated vaccine which is in a Phase 1/2 trial. | | https://extranet.who.int/gavi/PQ_Web/ |
| Bharat, India | Non-replicating viral vector | Pre-clinical | YES | Bharat Biotech in collaboration with the University of Wisconsin–Madison and the vaccine company FluGen has begun the development and testing of a vaccine to be delivered intranasally. It will be based on an influenza virus where gene sequences from SARS-CoV-2 are inserted into M2SR vaccine platform (M2-ion channel protein Deficient Single Replication) which has completed Phase II trials in the USA. Bharat will manufacture clinical lots of the vaccine. | | https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines |
| Biological E, India | Recombinant Protein sub-unit | Pre-clinical | YES | Biological E is developing an adjuvanted subunit vaccine comprising the Receptor or Binding Domain (RBD) of SARS-COV-2 spike protein as the antigen candidate. | | https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines |
| Company | Vaccine Type | Stage | Status | Description |
|---------|-------------|-------|--------|-------------|
| EuBiologics, Republic of Korea | Recombinant Protein sub-unit | Pre-clinical | YES | EuBiologics is in a vaccine in consortium with Korean companies and the BSL-3 research institute. It is developing a protein sub-unit vaccine with platform technology of critical antigen and adjuvant formulation technology with TLR4 agonist. EuBiologics is conducting neutralizing antibody test in mice and in vivo proof of principle in Ferret, with adjuvant formulation of each key antigen. |
| Biomanguinhos/Fundaçāo Oswaldo Cruz and Instituto Buntantan, Brazil** | Replicating viral vector | Pre-clinical | | Fundaçāo Oswaldo Cruz and Instituto Buntantan are developing an attenuated influenza expressing an antigenic portion of the Spike protein. |
| Serum Institute of India, India | Live attenuated virus (2 candidates) | Pre-clinical | YES | The Serum Institute of India Pvt. Ltd. (SIIPL) is developing a live attenuated vaccine, in partnership with Codagenix and a measles based viral vectored vaccine, with Themis, both in pre-clinical stage. In addition, SIIPL is also working on VPM1002 as immune enhancer and has started Phase-3 in India. Trials were also initiated in Germany [11] and will start shortly in Canada, Australia and New Zealand. |
| Sinovac, China | Inactivated virus (2 candidates) | Pre-clinical, Phase 1/2 | | Sinovac Biotech, in Beijing, is developing an inactivated vaccine adjuvanted with alum currently in Phase 1/2, and another inactivated vaccine with Dynavax currently in pre-clinical. |
| Zydus Cadila, India | DNA; Replicating viral vector (2 candidates) | Pre-clinical | YES | Zydus Cadila in India is developing two candidate vaccines. The first deals with a DNA vaccine against the major viral membrane protein responsible for the cell entry of the novel coronavirus, expected to enter the preclinical toxicology studies in Q2/2020. Thereafter, Zydus will undertake the clinical development and licensure of this vaccine. This candidate vaccine can be manufactured in biosafety level 1, and be prepared in many facilities to make billions of doses for global use. It can also address antigenic drift or shift of the virus, developing a modified construct in 2-3 weeks. |

Communication from EuBiologics, 6 May 2020

https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines

https://www.pharmaceutical-business-review.com/news/sinovac-biotech-covid-19-vaccine-trial/

https://www.biospectrumindia.com/news/43/15795/zydu$s-to-develop-vaccine-against-covid-19.html
| Manufacturer without WHO prequalified vaccines | Technique | Stage | Description |
|-----------------------------------------------|-----------|-------|-------------|
| Minhai Biotechnology, China                    | Inactivated virus | Pre-clinical | Beijing Minhai Biotechnology is developing an inactivated vaccine, currently in pre-clinical stage. |
| BioNet-Asia, Thailand                          | DNA       | Pre-clinical | BioNet-Asia in Thailand is developing a COVID-19 GENE-based vaccine (COVIGEN) encoding the S (Spike) protein of SARS-CoV-2, and is actively collaborating with different organizations in Thailand and internationally. BioNet’s DNA based vaccine candidate is currently undergoing pre-clinical testing using various delivery systems, and a phase 1/2 trial is planned for Q3 2020. |
| Bravovax, China                                | Non-replicating viral vector (2 candidates) | Pre-clinical | BravoVax, in Wuhan, China, and GeoVax Labs Inc. have signed a Letter of Intent to jointly develop a vaccine. GeoVax’s Modified Vaccinia Ankara (MVA) platform technology, which elicits protective T cell as well as antibody responses, can be combined with the potent immunogenicity of Virus-Like Particles (VLPs). BravoVax will provide testing and manufacturing support, as well as interactions with public health and regulatory authorities. BravoVax also has an in-house adeno-vectored COVID-19 candidate vaccine entering preclinical studies. |
| Indian Immunologicals, India                   | Live attenuated virus | Pre-clinical | YES | Indian Immunologicals Ltd. has entered into a collaboration agreement with Australia’s Griffith University to develop a live attenuated vaccine using the latest codon de-optimization technology, and its existing Vero cell platform technology for mass production of the candidate vaccine. |
| Innovax, China                                 | Recombinant Protein sub-unit | Pre-clinical | Innovax from Xiamen, China, in collaboration with GSK and Xiamen University, is developing a recombinant candidate vaccine based on COVID-19 recombinant
| Institute of Medical Biology, Chinese Academy of Medical Sciences, China | Inactivated virus | Phase 1 | The Institute of Medical Biology is developing an inactivated vaccine currently in Phase 1 |  
|--------------------------|----------------|--------|--------------------------------------------------------------------------------|  
| Medigen Vaccine Biologics Corporation, Taiwan | Recombinant Protein sub-unit | Pre-clinical | Medigen is developing a protein sub-unit vaccine based on spike protein (S-2P protein) + CpG1018 |  
| St. Petersburg Research Institute (SpbNIIVS), Russia | Recombinant Protein sub-unit | Pre-clinical | The Saint-Petersburg Scientific Research Institute of Vaccines and Serums (SpbSRIVS), in Russia, is developing recombinant protein nanoparticles, based on S (spike) protein and other epitopes. |  
| Vabiotech, Vietnam | Recombinant Protein sub-unit | Pre-clinical | Vabiotech in Vietnam, has started developing a vaccine based on the baculovirus expression system with the University of Bristol, UK, and Imperial College, London, within activities of the Future Vaccine Manufacturing Research (FVMR) Hub. |  
| Wuhan Institute Biological Products, China National Biotec Group, China | Inactivated virus | Phase 1/2 | Wuhan Institute of Biological Products, under the China National Biotech Group, is developing an inactivated vaccine, entering Phase 2 trial for age-groups 6 years and above. |  

truncated S (Spike) proteins (XWG-03) currently in pre-clinical stage.
Legend to Table 2.

List of the broad range of vaccine supply capabilities from 37 DCVMN member manufacturers, in 2018-19.

First column shows the various levels of supply capacity from different manufacturers. Second column shows the number of respondents that reported the number of doses supplied in 2018-19. Third column denotes the number of manufacturers with WHO prequalified vaccines within each level of supply. Fourth column shows the number of vaccine doses collectively supplied in 2018-19 by manufacturers within the same level of capacity. Total number of vaccine doses collectively supplied in 2018-19, self-reported by 37 respondents, was 3’456’079’910 doses. Number of doses include all vaccines, if monovalent or multivalent, and also all presentations, if single or multidose vials. Four (4) member manufacturers did not respond to the survey on number of doses supplied.
| Level of capacity in supply of vaccines in 2018/19 (in million doses) | Number of DCVMN members that reported vaccines supplied in 2018/19 | Number of DCVMN members with WHO PQed vaccines per capacity level | Number of doses collectively supplied by members per capacity level in 2018/19 |
|---|---|---|---|
| 0 | 4 | 0 | 0 |
| Up to 1 | 4 | 1 | 1.053.000 |
| 1-10 | 7 | 1 | 36.966.910 |
| 10-20 | 5 | 2 | 81.020.000 |
| 20-50 | 8 | 2 | 217.960.000 |
| 50-100 | 3 | 2 | 231.300.000 |
| 100-200 | 2 | 1 | 267.070.000 |
| More than 200 | 4 | 4 | 2.621.710.000 |
| Total | 37* | 13 | 3.456.079.910 |

(*) 4 member companies did not respond to the survey.
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

All authors are employees of the respective declared organizations and have no other conflict of interest to declare.