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READINESS FOR FUTURE VACCINE DEVELOPMENT AND PRODUCTION IN CAMBODIA

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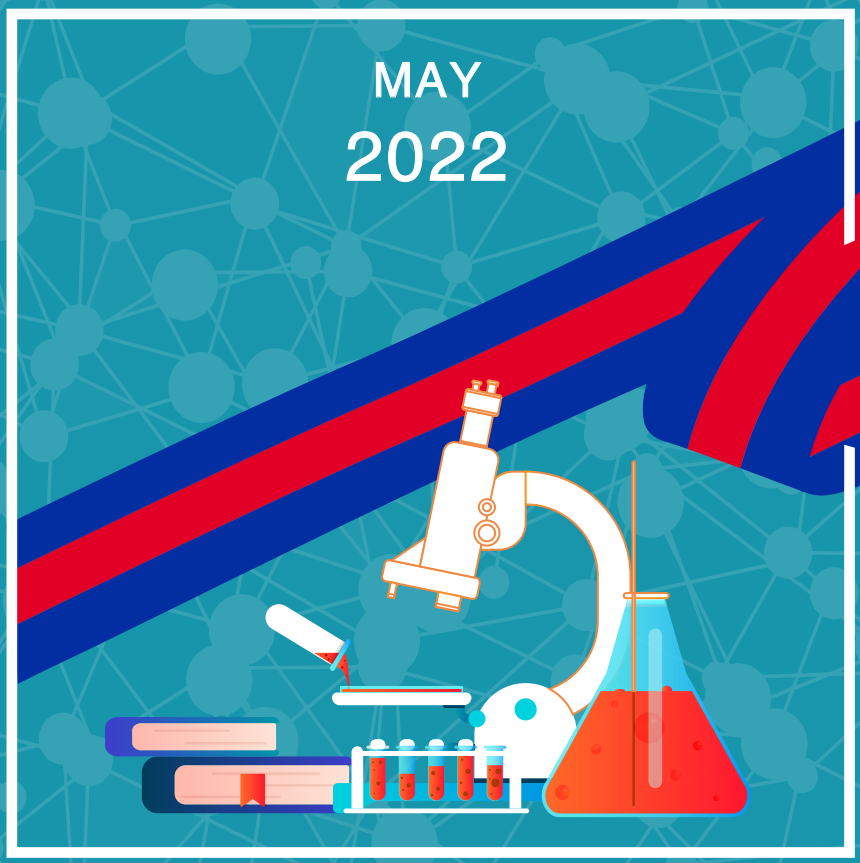

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45 Preah Norodom Boulevard, Sangkat Phsar Thmey III, Khan Daun Penh, Phnom Penh, 120203, Cambodia

អារម្ភកថា

ការរាតត្បាតជំងឺកូវីដ-១៩ បានក្លាយជាកត្តាជាស់ស្មារតីដល់ប្រទេសជាច្រើន ជាពិសេសប្រទេសទាំងឡាយដែលធនធានរបស់ខ្លួននៅមានកម្រិត។ ការទទួលបានវ៉ាក់សាំងគ្រប់គ្រាន់និងស្មើភាពគ្នា បានបង្ហាញជាឧបសគ្គដ៏ចម្បង ក្នុងការប្រយុទ្ធប្រឆាំងទល់នឹងជំងឺ SARS-COV-2 នេះ។

ដោយឈរលើគោលគំនិតសុខភាពសាធារណៈ ព្រះរាជាណាចក្រកម្ពុជាបានទទួលជោគជ័យគួរជាទីមោទនៈក្នុងការទប់ស្កាត់ផលជះអវិជ្ជមាននៃការរាតត្បាតជំងឺកូវីដ-១៩។ ក្រោមការដឹកនាំប្រកបដោយទស្សនវិស័យ និងការទទួលខុសត្រូវខ្ពស់របស់ **សម្តេចអគ្គមហាសេនាបតីតេជោ ហ៊ុន សែន នាយករដ្ឋមន្ត្រីនៃព្រះរាជាណាចក្រកម្ពុជា** សុខភាពសាធារណៈត្រូវបានធានានូវភាពជោគជ័យគួរឱ្យកត់សម្គាល់នៅក្នុងព្រះរាជាណាចក្រកម្ពុជា។ អន្តរាគមន៍តាមវិធានសុខាភិបាលដោយមិនប្រើឱសថព្យាបាល និងផ្តល់នូវការចាក់វ៉ាក់សាំងជូនប្រជាជនដ៏ច្រើន បានផ្តល់ជាកាលានុវត្តន៍ក្នុងការលុបចោលនូវបម្រាមធ្វើដំណើរផ្សេងៗ ដែលធ្វើឱ្យព្រះរាជាណាចក្រកម្ពុជាក្លាយជាប្រទេសឈរនៅលំដាប់កំពូលនៃប្រទេសក្នុងតំបន់អាស៊ានក្នុងការបើកទ្វារទទួលអ្នកដំណើរបរទេស។ ជាមួយគោលនយោបាយនេះ ព្រះរាជាណាចក្រកម្ពុជាបានទទួលយកគោលការណ៍ប្រក្រតីភាពថ្មីក្នុងការរៀនរស់នៅជាមួយវីរុសប្រភេទថ្មីនេះ។

នេះជាពេលវេលាសមស្របក្នុងការស្តារឡើងវិញនូវសេដ្ឋកិច្ចសង្គម ដើម្បីបង្កើតការងារ អាជីវកម្ម និងកំណើនឡើងវិញ។ ក៏ប៉ុន្តែ ព្រះរាជាណាចក្រកម្ពុជាក៏មិនភ្លេចទេថាការរាតត្បាតជំងឺកូវីដ-១៩នេះ មិនមែនជាជំងឺរាតត្បាតចុងក្រោយនោះឡើយ។ យើងនឹងត្រៀមខ្លួនក្នុងការប្រយុទ្ធប្រឆាំងនឹងជំងឺឆ្លងថ្មីៗ និងការរាតត្បាតនាពេលអនាគត។ យុទ្ធបកណ៍ដែលជាគន្លឹះសំខាន់និងចាំបាច់មួយក្នុងការត្រៀមខ្លួនសម្រាប់អនាគត គឺលទ្ធភាពក្នុងការផលិតវ៉ាក់សាំងដោយខ្លួនឯង ដើម្បីទប់ទល់មេរោគដ៏កាចសាហាវទាំងនោះ។

នៅក្នុងកិច្ចប្រជុំលើកទីមួយរបស់ក្រុមប្រឹក្សាជាតិវិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍ ដែលបានរៀបចំឡើងកាលពីថ្ងៃទី០៨ ខែកក្កដា ឆ្នាំ២០២១ មានអនុសាសន៍មួយក្នុងចំណោមអនុសាសន៍សំខាន់ៗផ្សេងទៀតនោះ គឺការសិក្សាអំពីតម្រូវការធនធានបច្ចុប្បន្នដើម្បីជំរុញការការកិច្ចជាតិដ៏ចម្បងនេះ ក្នុងការផលិតវ៉ាក់សាំងសម្រាប់ទប់ស្កាត់ជំងឺរាតត្បាតនាពេលអនាគត។ ដោយយោងតាមទស្សនាទាននិងអនុសាសន៍នេះ ក្រសួងឧស្សាហកម្ម វិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍ បានប្រមូលនិងបង្កើតក្រុមការងារចម្រុះជំនាញរួមមាន វេជ្ជបណ្ឌិត បសុពេទ្យ ឱសថការី ជីវិទូ អ្នកវិទ្យាសាស្ត្រជីវសាស្ត្រ អ្នកវិទ្យាសាស្ត្រកុំព្យូទ័រ និងអ្នកជំនាញបញ្ញាសិប្បនិម្មិត ដើម្បីរៀបចំការសិក្សា ដែលបង្ហាញពីស្ថានភាពសមត្ថភាពទេពកោសល្យនិងហេដ្ឋារចនាសម្ព័ន្ធជាក់ស្តែងបច្ចុប្បន្ន ដើម្បីអាចអភិវឌ្ឍ និងផលិតវ៉ាក់សាំងបាននាពេលអនាគត។

ក្រុមអ្នកជំនាញមកពីក្រសួងឧស្សាហកម្ម វិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍ សាកលវិទ្យាល័យ និងស្ថាប័នស្រាវជ្រាវនានា បានប្រមូលផ្តុំនិងធ្វើសមាហរណកម្មពិពិធចំណេះដឹង ជំនាញឯកទេស និងបទពិសោធន៍របស់ពួកគេដើម្បីផលិតឯកសារដ៏មានតម្លៃនេះឡើង ដែលអាចជាមគ្គទ្ទេសក៍អភិវឌ្ឍវ៉ាក់សាំងសម្រាប់គោលដៅវែងឆ្ងាយ ក្រោមការជួយគាំទ្រដ៏ខ្លាំងក្លាពីដៃគូអភិវឌ្ឍន៍អន្តរជាតិនិងអ្នកជំនាញឯកទេស។ តាមរយៈកិច្ចខិតខំប្រឹងប្រែងនេះ ក្រុមការងារបានបុរេសកម្មក្នុងការចាប់ទំនាក់ទំនងការសិក្សានេះ ជាមួយនិស្សិតវ័យក្មេងបញ្ចប់ការសិក្សាថ្នាក់បណ្ឌិតផ្នែកបច្ចេកវិទ្យាវ៉ាក់សាំង។

ឯកសារនេះ ជាឯកសារទី១ដែលមាននៅក្នុងព្រះរាជាណាចក្រកម្ពុជា ដែលបានត្រួសត្រាយផ្លូវដំបូង ដែលបានប្រមូល និងរៀបចំទិន្នន័យសំខាន់ៗដើម្បីបង្កើតទម្រង់កម្មវិធីផលិតវ៉ាក់សាំងជាតិមួយនាពេលអនាគតដ៏ខ្លីខាងមុខ។ ការណ៍នេះ

ស្របគ្នាជាមួយគំនិតផ្តួចផ្តើមរបស់ **សម្តេចអគ្គមហាសេនាបតីតេជោ នាយករដ្ឋមន្ត្រី** កាលពីថ្ងៃទី១៧ ខែវិច្ឆិកា ឆ្នាំ២០២១ ក្នុងការបង្កើតមជ្ឈមណ្ឌលផលិតវ៉ាក់សាំងកូវីដ។

ខ្ញុំសូមសម្តែងនូវការកោតសរសើរ និងអបអរសាទរយ៉ាងក្រៃលែងចំពោះថ្នាក់ដឹកនាំទាំងអស់នៃក្រសួងឧស្សាហកម្ម វិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍ ជាពិសេសការចូលរួមដឹកនាំរបស់ឯកឧត្តមរដ្ឋលេខាធិការ សាស្ត្រាចារ្យបណ្ឌិត **ឆែម គាតវិទ្ធី** រដ្ឋមន្ត្រីប្រតិភូអមនាយករដ្ឋមន្ត្រី និងក្រុមការងារជំនាញដែលបានខិតខំប្រឹងប្រែងចងក្រង និងរៀបចំឯកសារស្តីពី «**ការត្រៀមខ្លួនសម្រាប់អនាគតនៃការអភិវឌ្ឍនិងផលិតវ៉ាក់សាំងក្នុងព្រះរាជាណាចក្រកម្ពុជា**» នេះ។

ថ្ងៃ សុក្រ ៦ កើត ខែ ផល្គុន ឆ្នាំខាល ចត្វាស័ក ព.ស.២៥៦៥
រាជធានីភ្នំពេញ ថ្ងៃទី ៦ ខែ កុម្ភៈ ឆ្នាំ២០២២

ទេសរដ្ឋមន្ត្រី
រដ្ឋមន្ត្រីក្រសួងឧស្សាហកម្ម វិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍
និងជាប្រធានក្រុមប្រឹក្សាជាតិវិទ្យាសាស្ត្រ បច្ចេកវិទ្យា និងនវានុវត្តន៍

កិត្តិសេដ្ឋាបណ្ឌិត ចម ប្រសិទ្ធ

Foreword

The Covid-19 pandemic had been a wake-up call for many countries, especially for those with limited resources. Adequate and equitable access to vaccines has been identified as the main barrier for the effective fight against SARS-COV-2.

From the perspective of public health, Cambodia has been quite successful in mitigating the impacts of the pandemic on people's health. Visionary and decisive leadership under **Samdech Akka Moha Sena Padei Techo HUN SEN**, Prime Minister of the Kingdom of Cambodia, guaranteed remarkable success in Cambodia. Non-pharmaceutical interventions (NPI) and massive provision of vaccines to the majority of the population gave us the opportunity to remove all NPI restrictions making Cambodia the top country of ASEAN to open its borders to international travelers. With this new policy, Cambodia has accepted the principle that we shall live in symbiosis with the virus.

The time has come for us to rebuild its socio-economic sectors to bring back jobs, business, and growth. Yet Cambodia has not forgotten that this pandemic may not be the last one. We shall be ready to cope with emerging infectious and future pandemics. One of the key tools necessary to prepare for the future is the ability to produce vaccines to combat those deadly germs.

At the first annual meeting of the National Council of Science, Technology and Innovation held on July 8, 2021, one of the major recommendations was to conduct a study of the current resources needed to undertake such a major national task: Producing vaccine to fight future pandemics. Following this vision and recommendation, the Ministry of Industry, Science, Technology and Innovation gathered an interdisciplinary team comprised of physicians, veterinarians, pharmacists, biologists, biomedical scientists, computer scientists, and AI experts to conduct a study that seeks to establish the current status of talent and infrastructures capable of developing and producing vaccines in the future.

Experts from MISTI, universities, and research institutes pool and integrate their diverse knowledge, expertise and experience to produce this valuable report that can guide further development with the potential support from international donors and experts. Through this endeavor, the team has proactively engaged four young Cambodian PhD graduates who have studied vaccine technologies in Korea.

This report, the first of its kind in Cambodia, creates a preliminary roadmap to gather and organize the data necessary to formulate a national vaccine production program in the near future. This coincides with the request made by **Samdech Akka Moha Sena Padei Techo HUN SEN** on November 17, 2021, when he asked China to help Cambodia to establish COVID vaccine production centres.

I would like to warmly appreciate and congratulate all MISTI leaders, especially the leadership of H.E. Prof. Dr. Chhem Kieth Rethy, Minister Delegate Attached to the Prime Minister and Secretary of State at MISTI and his outstanding team for having produced the report on the "Readiness for Future Vaccine Development and Production in Cambodia".

Phnom Penh, 6 May 2022

Senior Minister
Minister of Industry, Science, Technology & Innovation
and Chair of National Council of Science, Technology & Innovation A.C.

Kitti Settha Pandita **CHAM Prasidh**

ខ្លឹមសារសង្ខេប

របាយការណ៍នេះបានបង្ហាញពីប្រព័ន្ធអេកូឡូស៊ីក្នុងការត្រៀមខ្លួន សម្រាប់ការអភិវឌ្ឍនិងការផលិតវ៉ាក់សាំងនៅក្នុងព្រះរាជាណាចក្រកម្ពុជា ដើម្បីជាយុទ្ធសាស្ត្រមួយក្នុងការប្រយុទ្ធប្រឆាំងទល់នឹងជំងឺឆ្លងរាតត្បាតនានាដែលអាចកើតមានឡើងក្នុងពេលអនាគត។ ស្ថិតក្នុងការប្រឈមជាលក្ខណៈសកលក្នុងការទទួលបានវ៉ាក់សាំងមកប្រើប្រាស់ ព្រះរាជាណាចក្រកម្ពុជាចាំបាច់ត្រូវតែគិតគូរ និងត្រៀមលក្ខណៈរួចរាល់ដោយសហការជាមួយដៃគូអភិវឌ្ឍន៍ដែលមានសក្តានុពលដើម្បីផលិតវ៉ាក់សាំងនៅក្នុងប្រទេស។ ឯកសារនេះ រួមបញ្ចូលការពិនិត្យពិចារណា និងការរៀបរាប់អំពីតម្រូវការទូទៅក្នុងការផលិតវ៉ាក់សាំងរបស់ជាតិ។ ជាការពិត ព្រះរាជាណាចក្រកម្ពុជាពុំទាន់មានការដឹកនាំ ឬ ទស្សនវិស័យក្នុងការអភិវឌ្ឍនិងការផលិតវ៉ាក់សាំងនៅឡើយទេ ហើយក៏គ្មានការស្រាវជ្រាវនិងអភិវឌ្ឍន៍ក្នុងវិស័យនេះដែរនាពេលបច្ចុប្បន្ន។ ជាមួយគ្នានេះ ការរៀបចំអង្គភាពណាមួយសម្រាប់បញ្ជត្ត ឬ វាយតម្លៃសុវត្ថិភាពនិងប្រសិទ្ធភាព វ៉ាក់សាំងក៏ពុំទាន់មាននៅឡើយ។

ការផ្ទុះឡើងនូវជំងឺកូវីដ-១៩ ជាការដាស់ស្មារតីប្រទេសទាំងអស់ ជាពិសេសប្រទេសកំពុងអភិវឌ្ឍន៍ឱ្យភ្ញាក់រឭកដឹងពីបញ្ហាប្រឈមរបស់ជាតិក្នុងការទទួលបានវ៉ាក់សាំងមកប្រើប្រាស់។ ឯកសារនេះ នឹងផ្តល់ជាទស្សនវិស័យនិងយុទ្ធសាស្ត្រជាតិ ក្នុងការអភិវឌ្ឍវ៉ាក់សាំងសម្រាប់ការពារការឹកឆាលជាលនៃជំងឺឆ្លងរាតត្បាតផ្សេងៗនាពេលអនាគត។ ឯកសារនេះ រំលេចនូវការរៀបរាប់ទាំងតម្រូវការគុណវុឌ្ឍិនិងទេពកោសល្យផ្នែកវេជ្ជសាស្ត្រ វិទ្យាសាស្ត្រ ព្រមទាំងវិស្វកម្ម និងបរិក្ខាឧបទ្ទេសឧស្សាហកម្ម។ ការរៀបចំឱ្យមានសុខភាពសាធារណៈដ៏ល្អមួយ និងគោលនយោបាយឧស្សាហកម្មនិងក្របខ័ណ្ឌគតិយុត្តសមប្រកប ព្រមទាំងគំរូម៉ូដែលគាំទ្រហិរញ្ញវត្ថុដែលមានបរិយាប័ន្នគឺជាកិច្ចខិតខំប្រឹងប្រែងដ៏ចាំបាច់បំផុត។ ការផ្ទេរបច្ចេកវិទ្យា និងការវិនិយោគផ្ទាល់ពីបរទេស ក៏ជាលក្ខខណ្ឌមិនអាចខ្វះបានផងដែរ។ សរុបមក ការវាយតម្លៃលើប្រព័ន្ធអេកូឡូស៊ីបច្ចុប្បន្ន និងធនធានដែលមានស្រាប់សម្រាប់ការអភិវឌ្ឍវ៉ាក់សាំង គឺជាធាតុចូលដ៏ចម្បង ក្នុងការរៀបចំទស្សនវិស័យនិងផែនការសកម្មភាពច្បាស់លាស់ក្នុងការផលិតវ៉ាក់សាំងនៅព្រះរាជាណាចក្រកម្ពុជា។ ការរៀបចំឱ្យមានសមត្ថភាពផលិតវ៉ាក់សាំងផ្ទាល់ខ្លួនរបស់ព្រះរាជាណាចក្រកម្ពុជា នឹងអាចកាត់បន្ថយ និងប្រយុទ្ធប្រឆាំងទល់នឹងជំងឺឆ្លងរាតត្បាតយ៉ាងមានប្រសិទ្ធភាពនាពេលអនាគត។

Executive Summary

This report explores the readiness ecosystem for vaccine development and production in Cambodia. Because pandemics are likely to occur again in the future, Cambodia needs to be prepared to fight against those emergent infectious diseases. Considering the global challenge of access to vaccine, it is essential for Cambodia to look forward and be ready to eventually produce vaccine locally while collaborating with potential partners. This report reviews the general requirements for a proper national vaccine development program. From the historical perspective there has never been such a program most likely due to the lack of national vision for vaccine production. As a consequence, there is currently no R&D for vaccine production, no agency to regulate or to validate vaccine safety and efficacy.

The Covid-19 pandemic was a rude wake up call for all countries especially for developing ones for which access to vaccines is a serious national challenge. This report offers a vision and strategies for national vaccine development strategy in view to fight future pandemics in Cambodia. It includes the needs for qualified medical, scientific and engineering talents, and industrial facilities. A proper policy and legal frameworks (public health and industrial) as well as an inclusive model for financing is needed. Technology transfer and foreign direct investment is also needed. In sum, a proper evaluation of the current ecosystem and existing resources for vaccine development are essential to establish a clear vision and action plan for vaccine production in Cambodia. A national capacity to produce its own vaccine will allow Cambodia to efficiently mitigate and fight future pandemics to protect the health of its population.

Contributors and Authors

MISTI's officials

Prof. Dr. CHHEM Kieth Rethy	Medical Doctor and Senior Science Policy Maker	Lead
Dr. HUL Seingheng	Science Policy Maker	Member
Dr. KUOK Fidero	Science Policy Maker	Member
Dr. LY Sokny	Scientist	Member
Dr. CHEAT Sophal	Scientist	Member
Dr. UNG Porsry	Engineer	Member
Dr. YUK Sokunsreiroat	Engineer	Member
Dr. POK Samkol	Scientist	Member
Ms. CHENG Kimhaung	Medical Doctor	Member
Ms. LO Naysim	Engineer	Member

Consultants and Authors

Dr. KHIENG Sothy	Scientist	Member
Dr. DUONG Veasna	Scientist	Member
Dr. PUTH Sao	Scientist	Member
Dr. MUTH Boravy	Engineer	Member
Mr. CHUM Pharino	Engineer	Member
Ms. REN Theary	Veterinarian	Member
Mr. KONG Sokom	Veterinarian	Member

Editorial Team

Dr. CHEAT Sophal	Editor in Chief
Dr. HUL Seingheng	Editor
Mr. OEURM Savann	Cover design

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List of Abbreviation

AAHS	Amorphous aluminum hydroxyphosphate sulfate
Ab	Antibody
ADB	Asian Development Bank
Ag	Antigen
AIDS	Acquired Immunodeficiency Syndrome
AMR	Antibiotic microbial resistance
ANA	Antibody neutralizing assay
ASF	American swine fever
B.Sc	Bachelor of Science
BCG	Bacille Calmette-Guérin
BLA	Biological License Application
BVD	Bovine viral diarrhea
CDC	Center for Disease Control and Prevention
CDRI	Cambodia Development Resource Institute
CEO	Chief executive officer
CKB	Cambodia Knowledge Bank
COVID-19	Coronavirus disease 2019

CpG	Cytosine phosphoguanine
CRISPR	Clustered regularly interspaced palindromic repeats
CSF	Classical swine fever
DIR	Director
DNA	Deoxyribonucleic acid
dsDNA	Double stranded deoxyribonucleic acid
DTaP-HepB-IPV	Diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B and inactivated polio vaccine
DTaP-IPV	Diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine
DTaP–IPV/Hib	Diphtheria, tetanus, whooping cough, polio, and Haemophilus influenzae type B
DTP	Diphtheria, Tetanus, and Pertussis
DVE	Duck viral enteritis
ELISA	The enzyme-linked immunosorbent assay
ELISpot	The enzyme-linked immune absorbent spot
ES	Erysipelas salmonellosis
EU	European Union
FACS	Fluorescence-activated cell sorting
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FMD	Food and mouth disease
Gavi	Global Alliance for Vaccines and Immunization
GDAHP	General Directorate of Animal Health and Production
GDP	Gross Domestic Product
Hep A	Hepatitis A
Hep B	Hepatitis B
HepA/Hep B	Hepatitis A and Hepatitis B
HIA	Hemagglutination inhibition assay
HIB	Haemophilus influenzae type B
HPAI	Highly pathogenic avian influenza
HPLC	High-performance liquid chromatography
HPV	Human papillomavirus
HS	hemorrhagic septicemia

IBDV	Infectious bursal disease virus
IPC	Institut Pasteur du Cambodge
IPR	Intellectual property right
JICA	Japan International Cooperation Agency
KOICA	Korea International Cooperation Agency
LDH	Lactate dehydrogenase
LMICs	Low- or middle-income countries
MD	Medical doctor
MEFA	Multi epitope fusion antigen
MMR	Measles-Mumps-Rubella
MoEYS	Ministry of Education, Youth, and Sport
MoH	Ministry of Health
MPL	Monophosphoryl lipid
MR	Measles and Rubella
mRNA	Messenger ribonucleic acid
NAIP-5	NLR family, apoptosis inhibitory protein 5
NGOs	Non-government al organizations
NIP	National Immunization Program
NIST	National Institute of Standard and Technology
NK cells	Natural killer cells
OIE	The World Organization for Animal Health, formerly the Office International des Epizooties
PCR	Polymerase chain reaction
PCV	Pneumococcal conjugate vaccine
PhD	Philosophiae doctor (doctor of philosophy)
PRRS	Porcine reproductive and respiratory syndrome
QA	Quality assurance
QC	Quality control
R&D	Research and Development
RT-PCR	Real time polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
S&E	Scientist and engineer
SDS-PAGE	Sodium dodecyl sulfate-polyacrylamide gel electrophoresis
SIDA	Swedish International Development Cooperation Agency

STEM	Science, Technology, Engineering and Mathematic
TADs	major transboundary animal diseases
TALENs	Transcription activator-like effector nucleases
TB	Tuberculosis
TDaP	Tetanus, diphtheria, and pertussis
TLR	Toll-like receptor
UN	United Nations
UNICEF	The United Nations Children's Fund
VP	Vice-president
WHO	World Health Organization

1. Introduction

1.1. Rational

Microbial diseases have put numerous pressures and threatening to the human health, animal health, and global stability. Diseases derived from bacteria were generally treated by medical drugs such as antibiotics while the outbreak of virus-related diseases have been addressed by the development of vaccines. The speed of disease spreading dose relate to many factors such as demographic trends, high density population, human mobility, transportation service, and inadequate health service. For instance, the recent outbreak of SARS-CoV-2 has given the negative impact on the world economy and social being with the unknown source, high transmission rate and mutation, and its leads to high mortality ever in the elderly and those who have weak immunity system. All countries have taken efforts in emergency responses such as imposing obligation to wear masks, social distancing, travel restrictions, and cities (and whole country) lockdowns. However, the numbers of Covid-19 infection remain very high. The production of vaccine is necessary to combat the outbreak (Excler et al., 2021).

Vaccines are the most successful medical invention to control infectious disease outbreaks derived from viruses and act as a prevention method in the modern therapeutic era. Historically, it has been recorded that the vaccine to prevent the smallpox was accidentally discovered since the ancient time in China in between 1570–1911, in England by Edward Jenner in 1796. The rabies vaccine and attenuated anthrax vaccine was then developed in laboratory by a chemist, Louis Pasteur, during 1885 in French. Later on, the researchers have discovered and developed the various vaccine for controlling the infectious diseases (Excler et al., 2021; Stanley A. Plotkin, 2011). The development of vaccines was involved with the advancement of laboratory equipment to understand the characteristic, virulent gene, their mechanism by microscope, cell culture, sequencing, etc. Researchers were also taking many efforts in animal models trial experiment which is needed for human experiment to validate the efficiency and safety of their vaccine which is time consuming to above 10 years validation (Lombard et al., 2007). In the modern era and in emergency response to the world outbreak of SARS-CoV-2, the development of vaccine was taken time less than 1 year. The challenging in a critical time has brought the speed of new discovery of various vaccines produced by different

techniques such as Pfizer, Moderna, Astra-Zeneca, Sinovac/Sinopharm, Sputnik V, Johnson Johnson (D'Amico et al., 2021; García-Montero et al., 2021). However, the speedy production of vaccines required numbers of raw materials such as nucleic acids, amino acid phenols, acyclic amides, lecithins and sterols. As reported, the global exports of those materials increased by 49 % in the half year of 2020 which equal to US$15.5 billion (World Trade Organization, 2020). In addition to the resource needed, the keys technology and the access to the intellectual property right (IPR) information is also necessary in the production supply chain of the vaccine.

Lacking local production of vaccines, the developing and least-developed nations must spend many million dollars of their national budget to purchase the vaccines from outside. Need to address that most of Cambodia's vaccines have been donated and why cannot Cambodia rely on this in future. Thus, independent local production of vaccine is necessary to combat the current and future outbreak. However, substantial amounts of effort, resource, and time are needed to produce an efficient and safe vaccines for humans (Lombard et al., 2007). This would raise the issue whether the developing and least-developed nations are technologically ready and have adequate resources to locally produce vaccines. So, there is a need to conceptualize the policies to support and invest in research and development on science, technology and innovation, which would be needed to boost the technological readiness.

1.2. Objective

The objective of this report is to determine the landscape and the needs for vaccine development and production in Cambodia in the prospect of future readiness.

2. Vision and Strategy for Vaccine Development

2.1. Vaccine Startup

Within the first 3-5 years, the focus must be on setting up facilities for vaccine research and development (R&D), training of core human resources and experimental production of first vaccines.

2.1.1. Set up Vaccine R&D Facilities

Create R&D laboratories including facilities to be able:

- To perform cell culture

- To produce protein
- To conduct animal experiments
- To perform serological and molecular assays

2.1.2. Training

Prioritize training of core human resource on vaccine development

- Vaccine related training (theory)
- Development of university Master programs to provide theory and practice
- Onsite training at vaccine production facilities
- Produce standard operating procedures

2.1.3. Production of First Vaccine in Cambodia

- List of pathogens with preventable vaccine and other new variants or emerging diseases
- General list of vaccine preventable diseases
- Selection of pathogens for pilot phase
- Acquire funding for laboratory experiment and production
- Set up a national R&D fund for vaccine from Cambodian government and engage local private investment and visible to foreign investment
- Purchase essential equipment, reagents, and consumables to be able to start
- Produce the vaccine, inactivated or attenuated vaccine
- Conduct pre-clinical trial experiment in animals
- Prepare vaccine trial, Phase 1, 2 and 3

2.2. Vaccine Innovation

From the 5th year, R&D have to be focused on new emerging diseases and new technology for development of more advanced vaccine such as mRNA, viral vector, protein, etc.

- More training and bring more expert and talented personnel in the field from abroad (talent grant-in and talent grant-out)
- Improve R&D facilities or laboratories and acquired new equipment to be able to conduct more advanced experiment

- Readiness vaccine for new diseases
- Provide tax incentives

3. Background and Conditions for Vaccine Development

3.1. Overview in humans

Vaccine production approaches continue to be critically important to the global public health and animal health. Scientists are making their best effort for cost effective and safety. Along with antibiotics, vaccines are being known as the most powerful means of combating infectious diseases that mankind has since the discovery of the vaccinia (smallpox) by Edward Jenner in 1790 (Riedel, 2005; Willis, 1997). Particularly, thanks to various vaccines developed since the mid-20th century, mankind was able to escape from the threat of many infectious diseases (Milligan & Barrett, 2015). In 1979, vaccine was used to successfully eradicate smallpox (Fenner et al., 1988; WHO, 1980; Willis, 1997) and it subsequently provides fundamental vaccine development strategy in a series of important vaccine against polio virus (WHO, March 2016), diphtheria, tetanus, and pertussis (DTP) (WHO, 2021), and measles-mumps-rubella (MMR) (CDC, January 2021) worldwide. In addition, vaccine can also be applicable to against noninfectious diseases such as cancer, Alzheimer's disease, diabetes, and type I allergy (Weiss, Scheiblhofer, & Thalhamer, 2014). Also mention vaccines against cancers – Gardasil to prevent HPV for cervical and penile cancers. More importantly, due to the rate of antibiotic microbial resistance (AMR) has been increasing, vaccine has direct and indirect effects to prevent AMR and to improve health and economic prospects (Jansen & Anderson, 2018). From 1994-2013 in US, vaccines prevented 322 million illnesses, 21 million hospitalizations, and 732,000 deaths. Moreover, vaccines saved $295 million direct costs and $1.38 trillion in total societal benefits (Kim, 2021). An effective vaccination program improved the low level of educational attainment, specifically, herd immunity has profound effects to population around the world; vaccinated children also protect adults who live, work, and play with those children (Anekwe, Newell, Tanser, Pillay, & Barnighausen, 2015; D. M. Weinberger, Pitzer, Regev-Yochay, Givon-Lavi, & Dagan, 2019). However, the emergence of conventional infectious and noninfectious diseases strongly demands the development of a new concept vaccine. On the other hands, the aging of the population due to the rapid increase in life expectancy and low vaccine effectiveness in the elderly

population are driving strongly the demand for new vaccines optimized for the relevant population (Haq & McElhaney, 2014; Mangtani et al., 2014).

3.2. Overview in animal/livestock

About 75% of emerging human pathogens are animal origin, veterinary vaccines play a crucial role to public health by controlling of zoonotic disease, food-borne infection, and reduction in the use of veterinary pharmaceuticals (HealthforAnimals, 2015; Rajeshwari, July 2020). Hence, people will not be free in contact with their companion animal without veterinary vaccination. For prominent example, rabies vaccine for domestic animal and wildlife has nearly controlled rabies in humans (CDC, September 23, 2021). Vaccine for bovine tuberculosis (Verma et al., 2014) and Anthrax are being used to control disease in livestock, wildlife, and human (WHO, 2008). In addition, other zoonotic diseases such as brucellosis, leptospirosis, Influenza, Nipah, leishmaniasis, and Japanese encephalitis would not be as highly prevalent without effective vaccine in animals. Apart from giving a significant impact on public health, vaccination of animal is a prominently effective way to promote animal health by preventing and controlling diseases outbreak that can have a devastating effect on animal production. Meanwhile, more than 20% animal product losses in the world are related to animal disease (FAO, 2011). In same way, to improve productivity of the animal that also enable to produce efficient of animal food products and ensure safe and nutritious food for consumers. Thus, a large extent safe and effective vaccine is required in animal farming as currently, more than 100 different veterinary vaccines are commercially available worldwide (HealthforAnimals, 2015). The rinderpest vaccine is an example of a successful animal vaccine deserved to control rinderpest which was the first animal disease eradicated in 2011 (OIE, November 22, 2018). To limit impact of food and mouth disease (FMD) in livestock, moreover, FMD vaccine is given to animal during outbreak and prevention in country where is not free FMD (OIE, 2021) etc. Each year FMD vaccines over two billion doses is used in livestock production (Knight-Jones, Edmond, Gubbins, & Paton, 2014) and it is even larger scale of poultry vaccines.

The effectiveness and importance of vaccines have been reported in recent years, but significant challenge still remain. The world has been experiencing increasing new

diseases harmful to human and animal health, and scientists still have difficulty to prevent or treat particular illness including Ebola, Zika virus and tuberculosis (Kanapathipillai et al., 2014; Marston, Lurie, Borio, & Fauci, 2016; Teppawar et al., 2018). Similarly, these are also encountered in animal diseases such as: Porcine Reproductive and Respiratory Syndrome (PRRS), Bovine Viral Diarrhea (BVD), Salmonella, and Bovine tuberculosis (OIE, 2010). Daunting tasks in vaccine development can arise high rates of antigenic shift, such RNA viruses for example influenza and even coronavirus particularly new variants of SARS-CoV-2 (Andreano et al., 2021; Hope-Simpson, 1992), resulting limitation of cross-protection to heterologous variants by one variant vaccine use. Evidentially, not all vaccine produces sterilizing immunity, as vaccine is derived from pathogen, selected antigens for vaccine development are complicated due to genetic diversity across stains and geographic variability (Andreano et al., 2021). On the other hands, a single manufacture template for vaccine available would not be widely used due to diversity of responsible pathogens. Vaccine developers have been significantly challenged to modify vaccine formulation to ensure efficacy, safety, storage, administration, distribution, and widespread use of vaccine. For example, developing countries frequently lack appropriate facilities and infrastructure for vaccine transportation and storage. According to National Institute of Standard and Technology (NIST), approximately 35% of vaccines lost potency during the shipment, as they were stored at abnormal temperature (Newswire, May 2021). Thus, special care is required for the transportation and storage of the vaccines in order to maintain the efficiency of the vaccines, resulting in additional costs for manufacturing companies and limit the growth of the market.

In addition, most of the existing vaccines were being developed and produced only by countries where there are standardized research facilities and enriched human resources and expertise. Unlike developed countries, developed nations have substantially more challenges such as: 1) governments have limited budget to purchase vaccines, 2) insufficient human resources to manufacture their own vaccines, and 3) research facilities and capacity are inadequate in scientific research and vaccine development etc. Both human and veterinary vaccines would be more expensive and less accessible to low- or middle-income countries (LMICs), resulting in speedy spread of

disease. Although human or animal disease needs little effort to be controlled by vaccination in developed country, the disease still cannot successfully eradicated worldwide due to existing transboundary transmission (Beltran-Alcrudo, Falco, Raizman, & Dietze, 2019; Hassan & Kassem, 2020). Disease can be rapidly spread from place to place through trades and travels as SARS-CoV-2 (Wu et al., 2020). Noticeably, as inherent responsible pathogen causing disease differs based on the geography, therefore formulation of vaccine antigen needs to design preference to region in order to improve an efficacy of vaccine. Therefore, developing country must initiate basic research approaches to establish own vaccine facility to ensure readiness to combat emerging and re-emerging disease.

3.3. Typology of Vaccines

A vaccine is a biological product that can be used to safely induce an immune response conferring protection against infection and disease on subsequence exposure to pathogen. Receiving a vaccine means to induce an innate and adaptive immunity which is the capability of multicellular organisms to resist harmful microorganisms through immunization (Male, Brostoff, Roth, & Roitt, 2012). The innate immunity provides critical mechanisms for the rapid sensing and elimination of pathogens. Many of the cells in the innate immune system (such as dendritic cells, macrophages, mast cells, neutrophils, basophils, eosinophils, and NK cells) produce cytokines or interact with other cells directly in order to activate the adaptive immune system. Furthermore, adaptive immunity has evolved to provide a broader and more finely tuned repertoire of recognition for both self- and nonself-antigens. Adaptive immunity involves a tightly regulated interplay between antigen-presenting cells and T and B lymphocytes, which facilitate pathogen-specific immunologic effector pathways, generation of immunologic memory, and regulation of host immune homeostasis (Bonilla & Oettgen, 2010). Immunization would be an administration of antibody called “a passive immunization” or an administration of antigen called “an active immunization” (Male et al., 2012) (Table 1&2). A passive immunization results when a person has received an administration of antibodies. An antibody, also called immunoglobulin, a protective protein produced by B lymphocyte responses to the presence of a foreign substance, called an antigen. These antibodies recognize and latch onto antigens in order to prevent or fight certain infectious diseases.

However, the protection offered by passive immunization is short-lived, usually lasting only a few weeks or months, but it helps to protect right away. Unlike a passive immunization, an active immunity results when a person's immune system works to produce antibodies and activates immune cells after infection or receiving a vaccine. Particularly, vaccine must contain an antigen that are derived from responsible pathogen. Usually, harmless forms of the immunogenic antigens are used to vaccinate. An antigen is a substance that prompts the generation of antibody and can induce an immune response that provide protection. Moreover, an active immunity requires a process of training immune cells to recognize and counteract foreign bodies (antigens) (Kitasato & Von, January 2018). During the first encounter with an antigen or pathogen, sets of long-lived memory T and B cells are established. In subsequent encounters with the same pathogen, the memory cells are quickly activated to yield a more rapid and robust protective response.

Vaccines are generally classified based on antigens' characteristics. Those antigens can be a live attenuated vaccine (weaken bacteria or virus which will not cause a disease), a killed vaccine (killed organism), a subunit vaccine (the antigenic parts of pathogen such as proteins, peptides, or polysaccharides), or a toxoid-base vaccine (pathogen's toxin) (Male et al., 2012) as shown in Table 3, 4, 5&6. Some vaccines, adjuvant was mixed to enhance the immune responses against the antigen, improving the vaccine's potency in protection. Adjuvant can be chemically or biologically defined molecule which effectively produces a more robust immune response than the antigen alone (Table 7). Based on (CDC, August 2020), particularly, aluminum salts were initially used as adjuvants in the 1930s, 1940s, and 1950s with diphtheria and tetanus vaccines after it was found they strengthened the body's immune response to these vaccines. Moreover, administration of a vaccine should be done via recommended routes: oral, subcutaneous, intramuscular, intradermal, or intranasal etc. and deviation from the recommended route may reduce vaccine efficacy or increase local adverse reactions (CDC, September 8, 2021).

3.3.1. Passive Immunity

As passive immunity, antibodies are generally developed in a laboratory that are specific to pathogenic antigen(s). These antibodies are then administered into the body and can persist in blood for weeks or months before being degraded (Male et al., 2012). In this way, we can develop an immunity to a certain pathogen temporarily. Several antibodies currently in use and those are listed in (Table 1).

Table 1: Passive Immunization

Diseases	Source of antibody	Indication
Diphtheria, tetanus	Human, horse	Prophylaxis, treatment
Varicella-zoster	Human	Treatment in immunodeficiency
Gas gangrene, botulism, snake bite, scorpion sting	Horse	Post-exposure
Rabies	Human	Post-exposure (plus vaccine)
Hepatitis B	Human	Post-exposure
Hapatitis A, measles	Pooled human immunoglobulin	Prophylaxis (travel), post-exposure

3.3.2. Active Immunity

An active immunity can be induced by either naturally via infection or artificially through vaccination. Vaccines are normally developed in laboratories by many methods. Typically, the pathogen is inoculated into hosts, which means that it is changed in some ways so that it does not harm the host as severely as it normally would (Male et al., 2012). In many cases, the person does not show any visible effect when they are vaccinated. In order to reduce the effects of the pathogen, medical researchers usually use some small parts of the pathogen as a vaccine, called subunit vaccines. This way, the body can still produce the antibodies against pathogen, but the body is not hurt in the process. To make subunit vaccines safer and more effective, additionally, scientists developed subunit vaccines in various formulations such as virus-like particle, viral vectored, and nucleic acid vaccines (Pollard & Bijker, 2021) etc. (Table 2).

Table 2: Active Immunization

Types of antigens		Vaccine examples	First introduced
Living organisms	natural	Vaccinia (for smallpox), Vole bacillus (for tuberculosis; historical)	1798 (smallpox)
	attenuated	Polio (Sabin; oral polio vaccine*, measles*, rubella*, yellow fever 17D, varicella-zoster (human herpesvirus 3), BCG (for tuberculosis) *	
Killed organisms	Viruses	Polio (salk)*, rabies, influenza, hepatitis A, typhus, 2019-nCoV (Sinopharm, Sinovac & Bharat Biotech)	1896 (typhoid)
	Bacteria	Pertussis*, typhoid, cholera, plague	
Subunit	Purified protein, recombinant protein, polysaccharide, peptide	Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
	Virus-like particle	Human papillomavirus Hepatitis B (yeast derived) * 2019-nCoV (NovaVax)	1986 (hepatitis B)
	Outer membrane vesicle	Group B meningococcal	Group B meningococcal
	Protein–polysaccharide conjugate	Haemophilus influenzae type B, pneumococcal, meningococcal, typhoid	1987 (H. influenzae type b)

	Toxin	Tetanus*, diphtheria*	1923 (diphtheria)
	Viral vectored	Ebola, 2019-nCoV (AstraZeneca or Johnson&Johnson or Gamaleya-Sputnik V)	2019 (Ebola) (Pollard & Bijker, 2021)
	Nucleic acid vaccine	SARS-CoV-2 (Pfizer or Moderna)	2020 (SARS-CoV-2) (Pollard & Bijker, 2021)
	Bacterial vectored	Bacteria carries pathogen's gens	Experimental
	Antigen-presenting cell	Cell displays pathogen's antigen on surface	Experimental

* Standard in most countries

3.3.3. Live Attenuated Vaccine

A live attenuated vaccine is a weakened form of a virus or other invaders. Often by forcing the virus to grow in unusual conditions, which makes the genetic code change over time. Within weeks or months, those changes make virus or bacteria harmless enough to use as a vaccine. Most of attenuated vaccines can cause mild symptoms but they activate a strong immune response, only one dose is usually needed, and they can offer lifelong protection (Male et al., 2012). Examples of successful live attenuated vaccines that are currently in use as listed (Table 3).

Table 3: Lived Attenuated Vaccines

Diseases		**Remarks**
Viruses	Polio	Types 2 and 3 may revert, also killed vaccine
	Measles	80% effective
	Mumps	85% effective, two doses are required for long-term protection
	Rubella	Now given to both sexes
	Yellow fever	Stable since 1937

	Varicella-zoster	Mainly in leukemia
	Hepatitis A	Also killed vaccine
Bacteria	tuberculosis	Stable since 1921, also some protection against leprosy

3.3.4. Inactivated (killed) vaccines

Similar to live attenuated vaccine employs the whole organism as vaccine. With these types of vaccine, the virus or bacteria was killed by heat, radiation, or chemicals to break apart both the shell and genetic code. The pieces that remain are inactive but can still active the immune system to create an immune response. However, that response is not as strong as with some other vaccines, so multiple doses might be needed, sometimes called boosters (Male et al., 2012). There are numerous killed vaccines currently in use. Examples of successful killed vaccine are listed (Table 4).

Table 4: Killed (whole organisms) Vaccines

Diseases		**Remarks**
Viruses	Polio	Preferred in Scandinavia, safe in immunocompromised
	Rabies	Can be given post-exposure, with passive antiserum
	Influenza	Strain-specific
	Hepatitis A	Also attenuated vaccine
	2019-nCoV	SinoVac and Sinopharm (China), and Bharat Biotech (India)
Bacteria	Pertussis	Potential to cause brain damage (controversial)
	Typhoid	About 70 protections
	Cholera	Protection dubious, may be combined with toxin subunit
	Plague	Short-term protection only
	Q fever	Good protection

3.3.5. Subunit Vaccines

Subunit vaccines are composed of protein or glycoprotein components of a pathogen that can induce a protective immune response and may be produced by conventional biochemical or recombinant DNA technologies. Recombinant subunit vaccines have distinct advantages over live attenuated and inactivated vaccines since they are efficient in inducing humoral- and cell-mediated immunological responses, and the risks associated with handling the pathogen are eliminated. However, subunit vaccines may be more expensive and may require specific adjuvants (Table 7) to enhance the immune response. Table 5 represents the examples of successful subunit vaccines are currently in use.

Table 5: Subunit Vaccine

Pathogens	Organism	Remarks
Virus	Hepatitis B virus	Surface antigen can be purified from blood of carriers or produced in yeast by recombinant technology
	2019-nCoV	- BioNTech/Pfizer and Moderna: mRNA encoding for the Spike protein is protected in a lipid nanoparticle (like a soap bubble). Once absorbed, the cell expresses the Spike protein resulting in an immune response -Oxford/AstraZeneca, Jonhson&Jonhson, and Gamaleya (Sputnik V): double stranded DNA (dsDNA) encoding for the Spike protein is protected in a safe virus. The infected cell expresses the Spike protein which leads to an immune response -NovaVax: nanoparticles are coated with synthetic Spike proteins with additional element called adjuvant allows to boost the immune response

Bacteria	*Neisseria meningitides*	Capsular polysaccharides or conjugates of group A and C are effective, group B is non-immunogenic
	Streptococcus pneumoniae	84 serotypes, capsular polysaccharide vaccines contain 23 serotypes; conjugates with five or seven bacteria serotypes are tested (Male et al., 2012)
	Haemophilus influenza B	Good, conjugated vaccine now available

3.3.6. Toxin-base Vaccine

Common diseases caused by bacterial toxins are typically immunized against them using toxoid vaccines. Specific examples include vaccinations against tetanus *(Clostridium tetani)*, diphtheria *(Corynebacterium diphtheriae)*, botulism *(Clostridium botulinum)* and whooping cough; pertussis *due to Bordetella pertussis* – though this tends to be bacterial components rather than toxoids, but components are incorporated alongside toxoids of other bacteria (Male et al., 2012).

Table 6: Toxin-base Vaccine

Organisms	Vaccine	Remarks
Clostridium tetani	Inactivated toxin (formalin)	Three doses, alum-precipitated, boost every 10 years
Corynebaterium diphteriae	Inactivated toxin (formalin)	Usually given with tetanus
Vibrio cholera	Toxin, B subunit	Sometimes combined with whole killed organisms
Clostridium perfringens	Inactivated toxin (formalin)	For newborn lambs

3.3.7. Types of Adjuvants

An adjuvant is an agent in vaccine to enhance the immune response against the antigen (vaccine works better). It modulates and stimulates immune responses to produce a stronger protective immune response over the antigen alone, especially in subunit antigens which are less immunogenic compared to live attenuated or killed antigens. Adjuvants play a crucial role for enhancing the immune responses in aging population who has a less efficient immune system (Lim et al., 2015; Uthaman et al., 2021; B. Weinberger, 2018). Basically, adjuvants can be chemically and biologically defined molecules that are stable, biodegradable, and safe. However, some adjuvanted vaccines can cause more local reactions (such as redness, swelling, and pain at the injection site) and more systemic reactions (such as fever, chills and body aches) than non-adjuvanted vaccines.

In all cases, vaccines containing adjuvants are tested for safety and effectiveness in clinical trials before they are licensed for use in the United States, and they are continuously monitored by CDC and FDA once they are approved (CDC, August 2020). Also, there are emerging adjuvants in clinical trials such as bacterial flagellin (flagellin-protein), TLR7&TLR8 ligands, and CpG DNA etc (Pulendran & Ahmed, 2011). Basically, the selection of adjuvant is considerable, however, choice of adjuvant use in veterinary vaccine is less restricted compared to human vaccine.

Several different adjuvants are used in U.S. vaccines and emerging adjuvants in clinical trials.

Table 7: Types of Adjuvants

Adjuvants	Composition/actions	Used combination with vaccines
Aluminum	One or more of the following: amorphous aluminum hydroxyphosphate sulfate (AAHS), aluminum hydroxide, aluminum phosphate, potassium aluminum sulfate (Alum)	Anthrax, DT, DTaP (Daptacel), DTaP (Infanrix), DTaP-IPV (Kinrix), DTaP-IPV (Quadracel), DTaP-HepB-IPV (Pediarix), DTaP –IPV/Hib (Pentacel), Hep A (Havrix), Hep A (Vaqta), Hep B (Engerix-B), Hep B (Recombivax), HepA/Hep B (Twinrix), HIB (PedvaxHIB), HPV (Gardasil 9), Japanese encephalitis (Ixiaro), MenB (Bexsero, Trumenba), Pneumococcal (Prevnar 13), Td (Tenivac), Td (Mass Biologics), Tdap (Adacel), Tdap (Boostrix)
AS04	Monophosphoryl lipid A (MPL) + aluminum salt	Cervari
MF59	Oil in water emulsion composed of squalene	Fluad
$AS01_B$	Monophosphoryl lipid A (MPL) and QS-21, a natural compound extracted from the Chilean soapbark tree, combined in a liposomal formulation	Shingrix
CpG1018	Cytosine phosphoguanine (CpG), a synthetic form of DNA that mimics	Heplisa

	bacterial and viral genetic material	
No adjuvant		ActHIB, chickenpox, live zoster (Zostavax), measles, mumps & rubella (MMR), meningococcal (Menactra, Menveo), rotavirus, seasonal influenza (except Fluad), single antigen polio (IPOL), yellow fever
Emerging adjuvants	-Bacterial flagellin Flagellin-protein fusions, it activates TLR5 and the inflammasome components IPAF and NAIP5 in innate immunity -TLR7 and TLR8 ligands, they are TLR7 ligands in innate immunity - CpG DNA, it triggers innate immunity via TLR9 ligand (Pulendran & Ahmed, 2011)	

3.4. The Status on Existing Vaccine in Cambodia

In Cambodia, the National Immunization Program (NIP) is established since 1986 with partners of WHO, UNICEF and Gavi. According to (NIP, 2016), in Cambodia, vaccine eliminated measles in March 2015 and maternal and neonatal tetanus in June 2015. In

addition, vaccine preserved polio virus free status since 2000 (NIP, 2016). In 2015, 89% of new mothers in Cambodia received tetanus toxoid immunization and in 2014 under-5 child mortality rate was 35/1,000, down from 54/1,000 in 2010 (NIP, 2016). Due to various vaccines have been developed, currently, Cambodian population can access numerous vaccines via NIP or at Institut Pasteur du Cambodge (Table 9-10). Particularly, regarding to COVID-19 pandemic, Cambodia government has been implemented a national vaccination program for COVID-19 vaccine through whole country. Cambodian populations were noticeably vaccinated 88.98% of COVID-19 vaccine among total population. With that population age ≥ 18 years old were vaccinated 101.37% compared with the targeted 10 million populations, 99.02 % of population between ≥ 12-18 years old were vaccinated among the targeted 1,827,348 populations, 101.05% of population between ≥ 06-12 years old were vaccinated among the targeted 1,897,382 populations, and 97.64% of population aged 05 year old were also vaccination among the targeted 304,317 populations from 10 February to 22 December 2021 by Ministry of Health (MoH, December 22, 2021).

Like other countries, Cambodia has been using veterinary vaccine to promote animal health and prevent disease outbreak. General Directorate of Animal Health and Production (GDAHP) has been implementing vaccination programs against various diseases, particularly in livestock including ruminants, pigs, poultries, and pets. Animal vaccines listed in (Table 8) are being used in animal farming at medium and industry size, but vaccines are still poorly used in backyard farming. Government has budget to purchase only some important vaccines for livestock and still cannot supply through the country, resulting limitation of prevent outbreak of infectious diseases. At the OIE organization, we normally received Rabies for pets and other vaccines for cattle and poultry. Beside this, we also obtain some vaccines through donation from outside the country, and mostly are from China. To ensure the accessibility of important vaccines for current and future animal disease control, government is planning to produce own animal vaccine.

3.4.1. Types of Vaccines

Vaccines can be divided into several different types, but ultimately work on the same principle. Each type is designed to teach host's immune system how to fight off certain kinds of germs—and the serious diseases they cause. Here, we classified vaccines use in Cambodia as vaccines for animal and vaccines for human.

3.4.2. Vaccines for Animals

Foot and mouth disease (FMD) is endemic with outbreak typically occurring throughout the year in ruminants particularly cattle and buffalos in Cambodia, causing significant losses to smallholders owning the majority of the national large ruminant population. Cattle production in Cambodia is constrained by major transboundary animal diseases (TADs) including foot-and-mouth disease (FMD) and hemorrhagic septicemia (HS) that mostly outbreak happen by animal movement (Young et al., 2014). FMD vaccination was campaigned at the hotspot border areas: Takeo, Kampot, Kampong Speu and Kandal provinces in Cambodia (OIE, 2018).

In pigs, there are common swine diseases such as ASF, FMD, CSF, PRRS, Cholera, Erysipelas Salmonellosis, Colibacillosis etc. An outbreak of ASF was recently reported in the province of Ratanakiri, bordering Viet Nam, a country that is currently responding to an ASF outbreak within its own pig population (FAO, 2019). GDAHP has developed the national strategy for control swine disease and vaccination program is one of the main pillars among fives including surveillance, animal movement control, public awareness, and regulation/Legislation. All vaccines against pig's disease are purchase from other country. The pig vaccination is covered by the farm owner. Most frequently vaccinate against Classical Swine Fever, FMD, Pasteurellosisand Salmonella and about 70% of backyard pig have been vaccinated by VAHWs All pig has been vaccinated by private veterinarian for commercial farm (GDAHP, October 2018).

In 2004, Cambodia was one of the first countries to experience a large epizootic of highly pathogenic avian influenza (HPAI) among poultry, caused by the influenza A(H5N1) virus. In 2005, the virus caused four confirmed human cases in Cambodia, all of whom died. As of April 6, 2006, two additional human deaths have been recorded, and epizootic outbreaks remain disturbingly frequent. The percentages of poor farmers who

vaccinate their animals with a particular vaccine are Newcastle (66%), Cholera (26%), Fowl Pox (58%) (PIN's, September 2013). Moreover, HPAI surveillance programs in several countries including Vietnam, Thailand, Cambodia, China, and Hong Kong have demonstrated that HPAI/H5N1 is circulating in live bird markets. National Strategy on Highly Pathogenic Avian Influenza (2006-2009) was raised up in the Cambodia National Comprehensive Avian and Human Influenza Plan.

In pets, Background Authorities have pledged to eliminate canine rabies by 2020 in Cambodia, a country with a very high rabies burden. Logistic and financial access to timely and adequate postexposure prophylaxis (PEP) is essential for preventing rabies in humans (Tarantola et al., 2015). Animal rabies vaccination activities used to be done in Cambodia include: (1) Piloted mass dog vaccination program in Phnom Penh, Kandal and Battambang provinces (OIE rabies vaccine); (2) Rabies vaccination in Koh Kong, Prey Veng, Sihanouk Ville and Siem Reap provinces (Merieux and OIE rabies vaccine) (RabiesUpdatesinCambodia, 2018). Besides rabies, pet also be vaccinated with parvovirus and so on by the veterinarian, especially at the clinics and animal hospital in Phnom Penh as well as those in the province.

Table 8: Animal Diseases and Vaccines in Cambodia

Animal	Diseases	Types of antigens
Ruminants	Food-mouth-disease (FMD)	Inactivated vaccine using three virus strains: O, A, Asia1 or trivalent strains
	Haemorrhagic septicaemia	Live attenuated vaccine (*Pasteurella mutocida* serotype B:2)
Pigs	Africa Swine Fever (ASF)	Live attenuated vaccine (ASF virus)
	FMD	As mentioned above
	Classical Swine Fever (CSF)	Live attenuated vaccine (CSFV CC-1 virus)

	Porcine reproductive and respiratory syndromes (PRRS)	Live attenuated vaccine as well as killed vaccine using PCV2 (stains PCV2a, PCV2b, and mPCV2b)
	Cholera	Same vaccine as CSF (Live attenuated vaccine)
	Erysipelas Salmonellosis	Subunit vaccine employing multi epitope fusion antigen (MEFA)
	Colibacillosis	Toxoid and toxoid fusion vaccine (ETEC O149)
Poultry	Newcastle	Live attenuated vaccine (Lasota is commonly used)
	Cholera	Inactivated vaccine, Fowl Cholera – there are 3 serotypes, common use (M9 or PM1 strains)
	Fowl Pox	Live attenuated vaccine (Canarypox virus)
	HPAI/H5N1	Inactivated vaccine (Antigens are combined 16 hemagglution units)
	Avian Influenza	Live attenuated vaccine using 2 types of antigens (low pathogenic influenza: H5N6 & H9N2)
	Duck plague	Live attenuated DVE vaccine
	Infectious Bursal disease (Gumboro)	Live attenuated vaccine using serotype 1 and 2 of IBDV

Pets	Rabies	Inactivated and adjuvant rabies glycoprotein (SAG-2 virus strain)
	Parvovirus	Live attenuated vaccine (canine parvovirus type 2b)

3.4.3. Vaccines for Humans

Through NIP, children with age between 0–18-month-old should have received several vaccines such as: BCG, Hepatitis B, DTP, Hib, Hep B, Poilo, PVC, and MR etc. In addition, Cambodian populations with age between 0–18-year-old can also receive a vaccine as recommendation at Institut Pasteur du Cambodge (IPC). Similarly, if persons with general age want a vaccine such as: Rabies, Yellow fever, and Tetanus etc., they may also access it at IPC as listed in Table 9 (IPC, 2021).

Table 9: Vaccines for Human are Currently in Use in Cambodia

Vaccines	**National Immunization Program for children Aged 0-18 months**	**Recommended immunization for persons aged 0-18 years (IPC)**	**Optional Vaccines available at the IPC in Phnom Penh**
BCG (Tuberculosis)	√	√	
Hepatitis B	√	√	
Diphtheria, Tetanus, Pertussis, Hib, Hep B	√	√	
Polio (oral)	√		
PVC	√		

MR (Measles, Rubella)	√		
Pneumocoque		√	
Rotavirus		√	√
Influenza virus		√	√
Measles, Mumps, Rubella		√	
Japanese Encephalitis		√	
Varicella		√	
Hepatitis A		√	√
Typhim Vi (Typhoid)		√	√
Gardasil (Human Papillomavirus)		√	√
Meningococcus		√	√
Rabies			√
Yellow fever			√
Tetanus			√

3.4.4. Others

Certainly, several COVID-19 vaccines are being used in Cambodia. Some of those vaccines were donated from China, India, Japan, and USA. In addition to donated vaccines, Cambodian government has also purchased some vaccines from China using national budgets. Those COVID-19 vaccines are inactivated and viral vector types.

Table 10: COVID-19 vaccines are currently in use in Cambodia

Vaccine against 2019-nCoV	Types of antigens	Remarks
SinoPharm (China)	Inactivated virus (donation and purchase)	SARS-CoV2 is chemically inactivated with a chemical called beta-propiolactone so it cannot replicate but all the proteins remain intact
SinoVac (China)		
AstraZeneca-Covishield (India)	Viral vector (donation)	dsDNA encoding for the Spike protein is protected in a safe virus. The infected cell expresses the Spike protein which leads to an immune response
AstraZeneca (Japan)		
Johnson&Johnson-Covax (USA)		

3.5. Vaccine Infrastructures-R&D

The primary focus of research will be on the development of vaccine to prepare for pandemic infectious diseases in human and animal. This could be used as a platform to rapid response of occurrence outbreak disease. Research and Development of vaccines generally provides a variety of benefits including helping to improve the public's health, improve animal health by prevention of infectious diseases, resulting to improve livestock production, prevention of a disease in animal means to reduce sickness of human in context of one health, secure research and technological capabilities to help eradicated infectious diseases, and new discovery of vaccine leads to the development of vaccine that are low-cost, easy to administer in resource limited settings, easily produced by manufacturers, and protective against disease of global public health.

Vaccine development is a multidisciplinary science, and it composes of several processes to produce a vaccine. Animal model is generally used in an experimental vaccine to give scientific proof of efficacy of vaccine. Vaccine must be safe and works well before moving forward to a clinical trial. In human study, vaccine may progress

sequentially through phase I (~20 volunteers) to evaluate the safety of vaccine, phase II (~100 volunteers) to determine the optimum dose and schedule for maximum immune responses, phase III (~1,000 to 10,000 volunteers) to provide the pivotal efficacy and safety data that are required for licensure. After phase I/II/III, vaccine (company or research institute) must get approval from Biological License Application (BLA) to Food and Drug Administration (FDA) for licensing (CDC, May 1, 2014). Some vaccines need to pass to phase IV clinical trial for large-scale postmarketing studies to access effectiveness of an intervention by obtaining data on rare adverse events. Despite the universal importance of vaccine, human vaccine is evaluated in vaccine efficacy, whereas veterinary vaccine is used to measure range of vaccine protection (Knight-Jones et al., 2014).

To initiate vaccine research, it is important to have informative validation and verification of a pathogen causing a disease in both animal and human. For this purpose, we need to have a diagnostic laboratory unit covering low, moderate and high-risk pathogens. The diagnostic laboratory should have a capability to identify the existing and new targets of pathogens causing a disease that is potent research for vaccine development. With a line to develop vaccine, we need to have additional facilities and machines as follow:

- Starting with identification of agent caused disease. We can use several methods such as: viral/bacteria biochemical tests, serological tests, and molecular methods for sample isolation, antigen detection, PCR, or real-time PCR etc.
- Studying a vaccine, we may need a molecular genetic laboratory for cloning or characterizing an antigen/adjuvant, a mammalian cell culture system to testing the function or toxicity of an antigen/adjuvant to a host's cell or to studying a host-pathogen interaction etc., and an animal facility to immunizing and validating the immune responses and an effectiveness of vaccine.
- Determination of immune responses in animal model, we may use an antigen capture, molecular and immunological techniques. For that purposes, ELISA, Hemagglutination Inhibition Assay (HIA), antibody neutralizing assay, ELISpot, and FACS etc. are required.

In addition, the R&D vaccine facility should operate under the appropriate biosecurity procedures and practices. For high-risk pathogens like highly pathogenic Avian Influenza (HPAI) or Anthrax that will be used in challenge studies, the facility used for such studies should meet the competent veterinary authority within the country minimum requirements for Containment Group 3 pathogens. So Biosafety level 3-4 is needed for research on infection with high-risk pathogens that may cause a threat to humans and the environment. Moreover, the researchers, scientists, and technicians must be well educated about laboratory safety, laboratory management, and biosafety facilities. For these purposes, we need expertise to facilitate the procedures for vaccine research and development such as: vaccinologist, immunologist, bacteriologist, virologist, medicine, veterinary medicine, veterinary public health, bioengineering and biotechnology, and epidemiologist etc.

3.5.1. Vaccine Science & Technology Laboratories

The primary drivers behind the major vaccine industry's best practices and investment decisions are public health (i.e., medical need for a particular product); potential profitability (i.e., return on investment); and technological feasibility (i.e., access to a technology and its maturity). Resolving high priority public health needs fulfills humanitarian concerns and, in turn, ensures sufficient annual sales to provide a return on investment and potential for long-term profits.

The market life for older vaccines is 15–20 years. Newer vaccines are projected to have a market life of 10–15 years (Black et al., 2020). This is an element in industry's investment strategy and decision-making process. The $300 to $400 million is a cost estimate for development of a vaccine that takes 7-12 years (discovery through licensure) and does not include any associated facility capital investment. Market life is becoming shorter while development schedules remain relatively fixed and development costs increase. This translates into potentially dramatic decreases in return on investment (Department of Defense, 2021).

It is estimated that clinical trials represent 30% - 40% of the total vaccine development cost necessary to capture every possible observation and to be able to address them to the Food and Drug Administration (FDA) in terms of demonstrated safety, potency, and

efficacy. Demonstrating safety and efficacy is considered a critical part of the cost of doing business. It demands extensive quality assurance (QA) and quality control (QC) support as well as rigorous reporting.

Technology drives the early decision to develop a vaccine, forces early emphasis on process development, and defines the manufacturing process (Gomez et al., 2012). As a result, options are tested and evaluated as early as possible. Maximizing product progress is a common industry goal in reducing risks and costs. Due to the underlying complexity of the technical processes, once a decision is made to take a vaccine candidate out of discovery and move forward, industry intensely manages the product stream from discovery through production and licensure and brings its full corporate resources to bear on the project. Risks are reduced to a manageable level prior to making the decision to go forward from the science and technology base (i.e., discovery), and industry will shut a project down if it determines there is a problem. The decision to discontinue is normally based on feasibility — an analysis of technical risk. Such technical risks are mitigated by maintaining a robust scientific and technical program of alternative constructs for products in development. Technology based activities typically receive quarterly reviews while developmental testing activities are more heavily scrutinized. Scientific and technical decisions account for the major impacts on vaccine development and licensure costs and schedules.

3.5.2. Experimental Facilities to Develop Vaccine and Prototype

Experimental facilities should be systemically built and equipped for facilitating various types of vaccine research and development. Since each type of vaccine may need a unique facility and machine and some facilities and machines might be interchangeably used. Here, we present the facilities and machines need for R&D vaccine facility as following:

- Live attenuated vaccines: there are several ways to create weakening infectious organisms, called avirulent organism as vaccine that are unable to cause a disease but still replicate and induce protective immune responses.

→ Culturing antigens: multiple rounds of subculturing virus or bacteria under tissue culture or harsh physical conditions that make pathogens avirulent. Vaccine strain will be screened and confirmed by PCR and sequencing.

→ Genetic manipulation: Gene deletion/insertion methods, it targets gene (s) to reduce virulent from a mother strain by gene editing for example TALENs or CRISPR-Cas9. In this technology, PCR and sequencing are extensively used.

- Inactivated or killed vaccines: Inactivated or killing strategy can vary but generally involve the use of heat, radiation, or chemical treatment (formalin or beta-propiolactone). To purify the inactivated viruses, Ultra-centrifuge is used.
- Subunit vaccines: It is a safest vaccine among types of vaccine. It is basically generated as viral vector-base vaccine, RNA-base vaccine, or protein-base vaccine etc.

  → Viral vector-base vaccine: Usually, the major virulent gene (s) were used to incorporate into a viral vector, a safe virus as a carrier by recombinant DNA technology. For that purpose, PCR and sequencer are crucial and a platform of viral vector is also required.

  → RNA-base vaccine: Functional synthetic mRNA may be obtained by *in vitro* transcription of a cDNA template, typically plasmid DNA (pDNA), using a bacteriophage RNA polymerase (we may purchase a Kit). HLPC is required for additional step in purification of mRNA to enhance protein expression. Final mRNA will be incorporated into a platform of protected-lipid nanoparticle. Exceptionally, to generate lipid nanoparticle additional machines are required.

  → Protein-base vaccine: A recombinant protein is generated via engineered DNA technology. It is expressed and purified by bacteria (*E. coli*) or mammalian cell system. To produce a recombinant protein, we may need PCR, *E. coli* or Eukaryotic cell culture system, centrifuges, sonication, HPLC and affinity chromatography systems.
- Adjuvant: In addition to development of a vaccine antigen, an adjuvant is used as helper to enhance vaccine potency and efficacy via modulating and stimulating the

host's immune responses. It is similar to vaccine antigen production, adjuvants can be nucleic acid, protein, or chemical components. Thus, adjuvant can be generated by using similar machines and protocol as subunit vaccine.

- Vaccine validation: To study a vaccine, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), western blotting (WB), enzyme-linked immunosorbent assay (ELISA), enzyme-linked immunosorbent spot (ELISpot), Fluorescence activated cell sorting (FACS) etc. are required.
- Animal facility: To test a vaccine candidate, we need an approval for animal use and an animal facility maintenance: At the initial stage, we better use murine model instead of small pets. Laboratory for animal facility has contributed to advancement of animal research in a variety of ways:
  - → assisting animal research on infectious diseases and vaccine development.
  - → securing the scientific reliability and accuracy of animal research results that give scientific proof of efficacy of vaccine in animal challenge before moving forward to clinical trial in human.
  - → *in vivo* (animal model) application is essential for vaccine study and machines are additionally required such as: multi-output animal anaesthesia machine, animal cages and racks etc.
- Laboratory animal Act – Animal research facility maintenance and experimental procedures must be carried out strictly keeping the guideline of the Animal Welfare Act legislated by a Ministry. All animal experimental procedures must be done with approval from the Animal Care and Use Committee.

Table 11: Names of the Required Machines/equipment and Their Roles/functions for Vaccine R&D Laboratory

Machines/Equipment (Degree of recommendation)	**Roles/Functions**
4^{o}C refrigerator (+++)	4^{o}C refrigerator is cool storage equipment, basic needs in routine work in laboratory, used to cool experimental reagents, sample or specimen for preservation. Storage of

	nucleic acid and protein antigens. Storage of serum samples for short period of time. Generally, at one A 4°C refrigerator is used in cell culture room, one may be used in general lab, and another one is used at animal room to store animal food or other reagents/materials.
-20°C freezer (+++)	It is freezer to store some experimental reagents, sample, or specimens for longer storage or future use Particularly, -20C freezer used to storage materials in purpose t to stabilize their functions, biological and chemical property It is necessary to have at least two -20°C freezers. Similar to required 4°C-refrigerator, one -20°C freezer is separately used at cell culture room and another one may be used in general lab.
-80°C deep freezer (+++)	It is generally used to stock bacteria and virus strains. Sometimes, mammalian cells can be stored at -80°C temporarily. Some nucleic acid, vaccine antigens, and serum or other type of samples are required to store at -80°C for long-term stability.
-150 °C deep freezer (+)	Banking of mammalian cells in long-term period, -150°C deep freezer is generally required.
Ice maker (+++)	It is a convenient way to produce ice that is useful in experimental works.
Clean bench (+++)	Clean bench is laminar flow work cabinet that provide filtered air across the work surface to decontamination. It is used in purpose to create clean bench to support experimental works. It is general used in cell culture room, animal facility, and biosafety level 1and 2 laboratories.
Heat block (+++)	It varies in functions. It can be used for DNA-technological experiments as well as facilitated in tissues' lysis and vaccines' works etc.

Water bath (++)	Similar to heat block, but water bath is used for heating and melting of media, solutions, samples etc. at temperatures below 100°C. It can also be used to maintain constant temperature that is required in microbiology and virology lab work. Several models and types of water bath are available. It is electrically heated and thermostatically controlled.
Microwave (+++)	In molecular genetic lab, microwave is used to dissolve agarose, make some types of culture media, and to facilitate in lysis of bacteria or virus etc.
Hot plate (+++)	Hot plate is used to heat chemicals and reagents. The hot plate is made of an iron plate, which gets heated by an electric heating element from below. The required degree of heating is obtained by a regulator. To see the purity of vaccine antigen, protein antigen is boiled and run in SDS-PAGE. It is very important for QC of vaccine antigen. Sometimes, water boiler is used to lyse bacteria in DNA-cloning.
Ultrapure water purification system (+++)	Pure and ultra-pure water purification system is a highly efficient water treatment to produce quality of the ultraclean water required completely free of contaminant of DNase, RNase, endotoxin etc. It is a very important component in laboratory.
Autoclave (+++)	Autoclaves operate a high temperature and pressure in order to kill microorganism and spores. It is the nucleus of a microbiology laboratory. It is used to decontaminant certain biological waste, instruments, and sterilize liquid substances such as media and saline (diluents) solutions.
Hot air oven (++)	It is used for sterilization of glassware's, such as test tubes, pipettes, and petri dishes. Such dry sterilization is done only for glassware's.

Dried oven (+++)	It serves a variety of tasks including evaporation, sterilization, temperature testing. For preparation of certain reagents, the glassware's, after proper cleaning and rinsing with distilled water, are required to be dried. Setting temperature is important for temperature sensitive experiments. .
Vortex mixer (+++)	This equipment is used for mixing liquids kept in a test tube. It has one or more cup-like depressions at the top to receive the bottom of the test tube. The machine is electrically powered. When actuated, the machine moves the bottom of the test tube in a gyratory motion, thereby affecting a thorough mixing of the solution.
Rotator (+)	Main function for substance mixing application for molecular biology, biochemistry. This equipment is required for various experiments such as: removal of endotoxin from vaccine antigen, lysis of bacteria, and sometimes it will be also used in protein purification etc.
Balances (+++)	Balance is needed to measure weight or mass of substance chemicals, samples, media etc. that give high degree of accuracy.
UV chamber (+++)	This equipment is used for analyzing fluorescent materials, spots in thin layer chromatography, etc. Specifically, it is used to visual DNA and protein. The equipment has two lamps for long- and short wavelength UV radiation. Since UV radiation is genotoxic (mutagenic) its exposure to skins and eyes must be avoided. A viewport with colored glass is provided for safety.
pH meter (+++)	pH meter is an electrical instrument used for measuring hydrogen ion concentration of solutions and mixtures. In microbiology lab, it is used for maintaining pH of the medium and diluents. The pH meter must be standardized

	with buffer solutions before operation. Since the instrument is very sensitive, it must not be used for stirring and it must not be dipped in hot or very cold solutions. The electrodes must always be kept immersed in suitable solutions. Read the manual carefully before using the instrument.
NanoDrop (+++)	It facilitates in DNA-technology to measuring DNA/RNA concentration and quality as well as protein concentration.
Spectrophotometry (+++)	It is an instrument for measuring the differences in colour intensities of solutions. In microbiology lab, it is used for direct counting of bacteria in suspension as well as for other purposes like measuring protein antigen concentration.
Microplate luminometer (+++)	It is a very important machine for functional study of vaccine or adjuvant via an experimental system of luminescence. It is used to evaluate the cytotoxicity via LDH released or transfected cell expressing luminescence system etc.
Agarose-gel electrophoresis (+++)	It is the standard lab procedure for separating DNA molecule by size (length in base pairs) for visualization and purification of DNA quality. It is widely used in molecular genetic laboratory. But is rather old fashioned now with the decreased costs of gentotyping by sequencer.
SDS-PAGE (+++)	It is an electrophoresis method to allow protein separation by mass. It evaluates the purity and estimate the molecular weight of protein. Furthermore, it is also used in western blotting for vaccine validation.
Multi-shaker (+++)	It is used in western blotting assay to evaluate the antibody and vaccine. It is also used in staining or de-staining SDS-PAGE gel.
Microbiological Incubator (+++)	This an insulated, electrically heated cabinet meant for providing microorganisms with optimum temperature for growth. The cabinet is insulated and thermostatically controlled. For routine purposes, the temperature is

	maintained at 28-30°C for bacteria, about 25°C for molds, and 35-37°C for mesophilic bacteria.
Shaking incubator (+++)	It is used in bacterial culture to provide optimum temperature and shaking condition.
Shaking incubator (HB-201SL) (++)	Similar to an above shaking incubator, it is used in bacterial culture to provide optimum temperature and shaking condition. However, it is used for large-scale culture (0.5L, 1L, or 2L in a single flask).
CO_2 incubator (+++)	Important equipment for mammalian cells culture. It is really need in vaccine technology for example: *in vitro* study of vaccine via neutralization assay, hemagglutination inhibition assay, and other pathogen-host interaction studies.
Capillary Sequencer (+++)	Used to read the nucleotide sequences. It is crucial to in DNA technology.
High performance liquid chromatography (HPLC) (+++)	Use for separate, identify and quantitate compound in liquid sample. It used to purify vaccine antigens or increase the purity of DNA or RNA in complex of compounds dissolved in solvents.
Eppendorf centrifuge 5424R (+++)	Important and frequently use in flow centrifugation samples. It is used for harvest bacteria or cells pallet from aqueous solution. Setting temperature and strong force will be used for multiple functions.
Eppendorf centrifuge 5810R (+++)	Similar to Eppendorf centrifuge 5424R, but it is used for 15 ml and 50 ml tubes. It is very important for general uses to harvest bacteria or cells with 10- or 15-ml volume. It should be separately installed in cell room and general experiment.
High-Speed refrigerated Centrifuge (++)	It is one of the most important machines facilitating in vaccine laboratory. It is used to harvest bacteria, cells, or cell-free supernatant in large-scale culture (up to 500ml in

	a single tube). It is important for subunit vaccines or live/killed bacterial vaccines.
Ultra-centrifuge (++)	It is used to purify virus or other proteins (outer membrane proteins). It is important for viral live/inactivated vaccine.
Sonicator (+++)	It is used to rupture cells using high frequency waves. It is very important for purification of vaccine proteins from prokaryotic cells for example *E. coli* cells.
Polymerase chain reaction (PCR) (+++)	It is crucial for general uses molecular works of microorganisms, particularly DNA editing.
Perform quantitative polymerase chain reaction (q-PCR) (+++)	It is a very important equipment facilitates in molecular diagnostics. It is used to quantify amount of nucleic acid in various biological samples using florescent dyes or probes. It used in a variety application including pathogen detection, gene expression, miRNA, and noncoding RNA etc.
ELISA plate reader (+++)	It is used to measure concentration or absorbance by wavelength. It is important to do performance of ELISAs, fluorescence detection assay. Particularly, in vaccine study is really need for immunology study of testing vaccine efficacy. ELISA is used to detect and titrate the antibody production in serum or other types of samples.
ELISpot reader (++)	ELISpot assay is used to study antibody or cytokine production. It is important to know whether vaccine induces cell-mediated immune responses via cytokine ELISpot.
Flow cytometry machine (FACS) (++)	It is a modern technology to study a specific immune cell population. A specific cell type can be identified by a combinational antibody stained.
Microscopy (florescence, confocal, and electron)	It is an instrument for observing microscopic items such as cells, crystals and cell organelles. It has the dual function of magnification and resolution. For routine microbiological

(+++)	works, bright field compound microscope with oil immersion objective is adequate.
Animal house (+++)	Animal facility must be well equipped. Plastic cages are used to maintain the animals with a panel rack. This system must be connected to a proper air circulation system.
Multi-output animal anaesthesia machine (+++)	It facilities in animal experiment. It is used anesthetize animals for immunization, collect serum, or scarification.

3.5.3. Vaccine Manpower and Expertise

Overview of Human Resource Involve in Vaccine Development

Vaccine development required careful work from trained professionals from various sectors including health professionals, private sector as manufacturers, engineers, academia, government agencies, media, and individuals and communities (*Producing Prevention: How Vaccines Are Developed | Online Public Health*, n.d.). Details of each role and range of expertise are summarized in **table 12.**

Table 12: Summary of Human Resource in Vaccine Development: Expertise and Roles

	Range of Expertise	**Roles**
Health professionals	Advanced degrees in biology, chemistry, epidemiology, medicine, and a variety of other health fields play a crucial role in identifying and vetting vaccines. Those leading the research in vaccine development typically have "a doctorate degree in cellular and molecular biology, biochemistry, or microbiology";	These professionals also require help with an array of research functions that can be conducted by people who have bachelor's or master's degrees in those subject areas.

Manufacturers and private industry	Management teams are multidisciplinary, typically led by a scientist with in-depth expertise and experience, and many establish written agreement or “contract” with each of the project teams executing the different components of the overall process.	Private institutions such as pharmaceutical companies are the source of funding for developing and testing a vaccine. Risk taker of as the cost for developing and testing a vaccine are expensive processes with great potential of liability. With great reward as a return of investment.
Government agency	Overall organization consists of leadership preferable to a PhD or MD candidate. Each center is led by a PhD or MD in respect to the center role and expertise.	Federal agencies such as the FDA (for the United State of America) must serve as the check and balance for any vaccine that will be made available to the general public. (*FDA Overview Organization Chart - Text Version | FDA*, n.d.). Each MD and PhD of each center works with policy experts to create sound policies to ensure safety of vaccine development process.
Academia	Strong fundamental research background and academics on fundamentals of nature in the field of Science or B.Sc Degree in Biology, Chemistry, Biotechnology, Cellular Biology or Microbiology. With a master's degree background in cellular biology or biotechnology. A PhD with at least 5 years’ experience of relevant postdoctoral experience (Kanika, 2020).	Researchers’ community that provides potential help other stakeholders understand what can be learned about numerous aspects of the vaccination development process. They also advocated for evidence-based immunization practices, reflect on socio economic implications for a vaccine for an at-risk

		community or synthesize past research.
Media	Reputable multimedia expertise personnel in the industries (The Role of Media and the Internet on Vaccine Adverse Event Reporting: A Case Study of Human Papillomavirus Vaccination, 2014).	Increasing public awareness of the profile of a certain disease or condition that required a vaccine. They also report the details of a vaccine's progress, challenges or dangers and provide an important public service. However, the media can exacerbate unfounded fears around certain diseases or catalyses unrealistic expectations for the timing of a vaccine's availability.
Individual and communities		Playing a crucial role in determining the safety and effectiveness of a vaccine. Participating in trails or serving as end user for an approved drug, understanding the real-world implication for a vaccine come down to this group.

Management of Vaccine Development

Decision making (responsibility, authority, and accountability) is vested by corporate executives in the management team overseeing execution of the process; that is, industry delegates decision making to the management team collocated with the discovery and development project teams. A generic industry model presented in **figure 1**. The management teams are multidisciplinary, typically led by a scientist with in-depth expertise and experience, and many establish written agreement or "contract" with each of the project teams executing the different components of the overall process. Industry emphasis on individual performance and accountability is reflected in comparison reviews

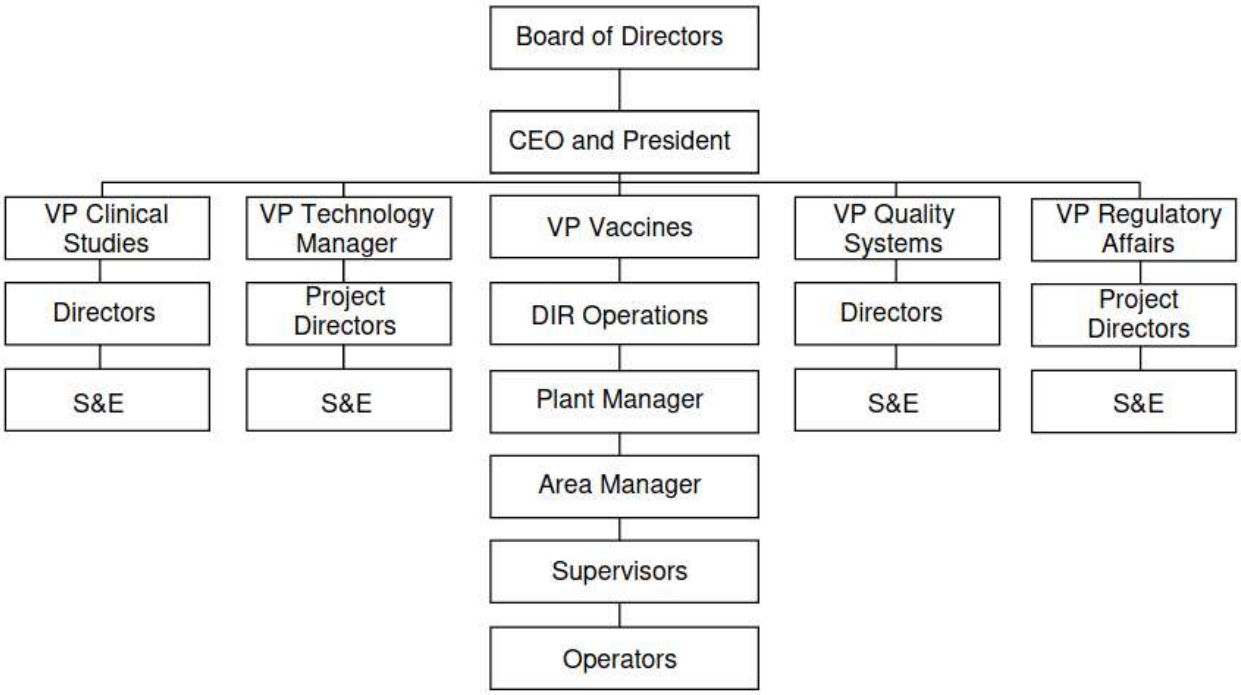

Figure 1. *Generic industry organization model of managing vaccine (Report on Biological Warfare Defense Vaccine Research & Development Programs, 2001)*

that commonly incorporate consideration of both team and individual performance and accomplishment.

The management philosophy and approach used in industry, as stated below, gives the management team and project teams maximum flexibility (right people, skills and resources during and any time on the process) and accountability for success:

- Goal: quality product
- Scientific expertise at every level
- Problem focuses for continuing development with rapid assessment and decision
- Mitigate risk at every level
- Commitment to development and production follow a successful discovery phase
- Empowered and accountable management team

4. Vaccine National Ecosystem

4.1. Policy and Legal Framework

The governance of all pharmaceuticals in the Kingdom of Cambodia is enacted in the law on the management of pharmaceuticals, adopted by the National Assembly of the Kingdom of Cambodia on May 9th, 1996, during the 6th plenary session of the 1st legislation, and promulgated in the Royal Kram No. CS/RKM/0696/02 on June 17th, 1996. As it is detailed in Article 2 of this Royal Kram No. CS/RKM/0696/02, the pharmaceuticals refer to one or many kinds of substances which are primarily from chemicals, bio-products, microbes, and plants combined, and include vaccines. In fact, this Royal Kram also emphasizes that only Cambodian pharmacist(s) accredited by the Ministry of Health is permitted to manufacture, import, and export vaccines in Cambodia (see Article 4 of the Royal Kram No. CS/RKM/0696/02) while the technical procedures and conditions for manufacturing and functioning of the pharmaceutical manufacturing establishments shall be determined by Sub-decree (See Article 7). On November 8th, 2007, the amendment of the law on management of pharmaceuticals was adopted by the National Assembly during the 7th session of the third legislature, and approved by the Senate on December 6th, 2007, during the 4th senate plenary meeting of the 2nd legislature, in Royal Kram No. NS/RPhM/1207/037. In this amendment, the definition of a counterfeit pharmaceutical including vaccines is specified as a medication in which there exist inactive ingredients or inappropriate quantities of active ingredients. This counterfeit products include also those may not contain enough active ingredients as stated on the label; or, all product have the packaging, design, identification similar to or the same as the original products and probably be produced or packaged without licensing from the Ministry of Health (see Article 2-New). Moreover, the Article 4-New of this Royal Kram No. NS/RPhM/1207/037, extends the right of both genders of Cambodia nationality or foreigner to run a pharmaceutical (including vaccines) manufacturing establishment, importing or exporting establishment and trade of vaccines in Cambodia.

4.2. Funding (Budget/ R&D funding)

Global health funding must provide support for new product development by connecting public health and innovation to consider R&D funding as an essential aspect of the global effort to reduce infectious disease, as well as child and maternal mortality

rates. Moreover, the sustainable development goals will not be achieved without R&D for new health equipment and facilities1.

WHO is a manifestation of the advantages of cooperation and collaboration, and it consistently leads member states in ways that uphold its mission to advance the highest standard of health for people around the world? As an illustration, WHO has advocated for global financial solidarity by establishing the Covid-19 Solidarity Response Fund in April 2020 and the external independent WHO Foundation in May 2020. Because of the Covid-19 pandemic, **EU funding** also has supported European companies to develop the new generation of vaccines, through successive EU research and innovation program's grants, as well as loans provided via the European Investment Bank2. The global fund has started to developed vaccines and medicine to cure global diseases and issues. Clear evidence has shown threw the funds for diseases R&D such as AIDS, Malaria, and Tuberculosis (TB) which are responsible for the death of over 5 million people a year worldwide (WHO, 2000), with over 70 per cent of these deaths occurring in Africa alone (EU, 2000). The economic and social repercussions that entire countries and continents experience because of these pandemics are tremendous. UN (2001) estimated that AIDS alone will cause South Africa's GDP to fall by 17 per cent by 2010 - this without considering falling worker's productivity, declining savings and investment, rising business costs, and decreasing life expectancy. Similar patterns are also envisaged for Malaria and TB (WHO & UNICEF, 2002)3. Even though those diseases have been harassed across one country or continent, but the fund for R&D for health equipment, vaccine, and medicine has been contributed globally to secure the global health, social and economic.

Recently, to strengthen the fight against Covid-19 pandemics, team Europe and other partners such as the United States, the World Bank Group, and regional donors are the initial funding and expertise to accelerate the construction of the new production plant,

1 Theolis Costa Barbosa Bessa (2017). R&D in Vaccines Targeting Neglected Diseases: An Exploratory Case Study Considering Funding for Preventive Tuberculosis Vaccine Development from 2007 to 2014. Hindawi BioMed Research International (Vol. 2017, Article ID 4765719). https://doi.org/10.1155/2017/4765719

2 Mariya Gabriel. (2021). EU research and innovation supporting vaccine development for COVID-19. European Union. https://doi:10.2777/0170

3 The Brookings Institution. Improving the Financing of Health R&D for Developing Countries: A Menu of Innovative Policy Options. www.brookings.edu/global/health

increase access to affordable vaccines, and enable vaccine production to rapidly respond to new pandemics*4*. This is showing the global socioeconomic issue and intervention.

Cambodia is a developing country and plans to have populations living in the upper middle-income country in 2030 and high-income country in 2050. The Royal government of Cambodia has given attention to enabling environment for R&D, attraction of outsources, open innovation to reach her goal. Cambodia's socioeconomic future is also affected by the cause of the Covid-19 pandemic, and Cambodia depends completely on the vaccine imported from abroad because Cambodia hasn't started to conduct research and produce the vaccine or other related material. Thus, it is a lesson learnt for Cambodia to initiate building human resources by contacting the resource in-country and out-sources who are staying abroad, prepare strategic research policy to accelerate vaccine development. In this regard, support, and consultation from shareholders as technical, training, financial, and monitoring are needed.

National and international collaboration is the key success of this strategic plan. All relevant stakeholders and key actors must be engaged in the process and implementation. Moreover, the technology and knowledge transfer from international collaborators and partners are indeed important and gain the time to discover what has been done.

4.3. National Collaboration (Triple helix)

Having successfully trial vaccine production in Cambodia, Government will work closely with the relevant centers to enable the processing and also provide funding supporting, human resource, and infrastructures with technical equipment which call triple helix. ***Samdech Akka Moha Sena Padei Techo*** **HUN Sen** mentions that the Kingdom of Cambodia will be able to produce vaccine for our own use and also help other countries in the future.

In this last 20 years, Triple Helix is recognized as conceptual framework which brings together knowledge, consensus, collaboration, and innovation of three social important actors: Academia- Government - Private Sector and provide better cradle for

4 European Commission - Press release (2021). Republic of Senegal and Team Europe agree to build a manufacturing plant to produce vaccines against COVID-19 and other endemic diseases.

social and economic development [5]. In this framework, the government needs to create a convenient, encouraging, transparent and honest general and entrepreneurial business framework, which will encourage individuals, businesses, and universities to continually improve their efficiency, productivity and performance in R&D and Innovation as manner to improve vaccines and other sector' technology and innovation process.

4.4. International Collaboration-Science Diplomacy

4.4.1. International Technical Assistance

To establish vaccine production center in Cambodia, International scientific collaboration is one of the key successes of this strategic plan. International scientific collaboration is the ways to increase knowledge, exchange skill and data, enhance professional advancement with less expense on communication, facilities and mobility. The Kingdom of Cambodia requests to all relevant stakeholders, partners, and key actors to support the technical vaccine processing such as raw materials, supplies, manufacturing capacity/complex, specialized and intensive bioprocess and implementation. Due to Covid-19 pandemic, global vaccination efforts face this challenge by initiative the complex manufacturing with specialized and intensive bioprocess. The manufacturer needs to identify their own potential manufacturing partners, specific considerations of vaccine in mind, highly technical in nature, single step or stage of the overall manufacturing process[6]. Some effective strategies to advance and improve technical assistance are [7]: 1. Promoting collaboration between international and local technical assistance, 2. Create independent scientific expert in formal governmental advisory boards and 3. Increasing the number of diplomats with an intermediate to advanced background in or knowledge of science at embassies and diplomatic mission abroad.

[5] Etzkowitz, H., Leydesdorff, L. (2000): The Dynamics of Innovation: From National Systems and "Mode 2" to a Triple Helix of University-Industry-Government Relations.

Research Policy, (29), 2: pp. 109-123;

[6] Richard Moscicki, M.D. PhRMA (2021). How industry collaboration and partnerships are supporting COVID-19 vaccine manufacturing.

[7]

4.4.2. Technology Transfer

Technology transfer requires a proactive approach that combines engaging research, promoting technology, and encouraging potential industrial partners to use the technology. Successful transfer and development of the technology helps promote the research institution and its commercial partners. The university obtains recognition and gain reputation for their research and innovation potential. The industry partners can also reduce the cost and time in research and development by licensing technology from university. The knowledge of technology transfer from international collaborators and partners are also important. Vaccine production is the most important key measure to prevent the spread of Covid-19 for the government's strategic policy. ***Samdech Akka Moha Sena Padei Techo*** **HUN Sen** requests license from China to produce Covid-19 vaccines. To challenge the delivery distance and time management, the purchase or provide the authorization of producing the vaccine is the opportunity to build the vaccine startup in Cambodia to reduce the tragedy of deaths and prevent the virus revolution[8].

5. Challenges for Vaccine Development & Production

5.1. Past Experiences in Vaccine Development

Vaccination represents a significant advancement in the prevention of infectious diseases. Vaccination works by simulating a pathogen's natural interaction with the human immune system to induce protection against it. Following subsequent exposure to an infectious agent, the vaccine reduces the risk of complications and mortality.

The challenging months of 2020 have highlighted the important problems connected with the development and formulation of effective therapies and, eventually, a vaccine during epidemics and pandemics (Nascimento Junior et al., 2020). The development of a new form of respiratory coronavirus (severe acute respiratory syndrome, SARS, CoV, or 2019 novel CoV) and it's spread in the current pandemic are reminiscent of the last two CoV experiences, namely SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (Nascimento Junior et al., 2020; Tu YF et al., 2020). However, after the pandemic was under control, the investigation of effective vaccines for SARS-

[8] Yim Sreylin. KhmerTimes (2021). PM requests licence from China to produce C-19 vaccines.

CoV or MERS-CoV was halted or canceled (Modiarrad et al., 2016; Wang et al., 2015). Critical studies of pandemic preparedness following the H1N1 pandemic that highlighted the inadequacy to provide enough vaccinations where they were needed, when they were needed, had not been applied before the outbreak of SARS-CoV2 (Fineberg, 2009). This has induced a delay in the identification and formulation of candidate vaccines for SARS-CoV2, necessitating an extraordinary effort on the part of both the public (academic and government) and private (industrial) sectors to accelerate vaccine development (Sempowski et al., 2020).

The vaccine development process can be time-consuming, involving several processes and regulatory inspections. Each of these processes may be divided into the following stages: preclinical, clinical, and post-licensure. These milestones are incorporated into the process to make sure the final approved product's safety and immunogenicity/efficacy (Leroux-Roels et al., 2011). As new vaccines come into the market, the issues are progressively being addressed; nonetheless, the scientific and financial concerns remain significant. The following are the main priorities for resolving outstanding challenges and barriers to successful vaccine development (Oyston and Robinson, 2012):

- Inadequate preclinical data and a lack of precise information on protective correlates of immunity lead to clinical trial product failure.
- Inadequate information about potential vaccine recipients' infectious exposures.
- Vaccine formulations must be constantly updated due to antigenic variation.
- Due to the high costs of vaccine development, potentially useful products are abandoned prematurely.
- Inadequate access to vaccines, particularly those used to combat diseases, in developing countries.

Therefore, improving the existing vaccines and finding new vaccines, it is important to understand the immunological principles of vaccination. There are still major challenges, especially concerning target pathogens for future vaccine candidates and the acceptance of the vaccines.

5.2. Challenges Vaccine Development

Vaccine development and production in Cambodia has several obstacles, which will be discussed in this section. Human resources, infrastructure/facilities, financing, and government policy are the four major difficulties for vaccine development and manufacture in Cambodia.

5.2.1. Human Resources in STEM field

Cambodia Knowledge Bank (CKB) is one of the great importance factors, although Cambodia has built the human capital in the last decade with high quality education system, where some students have been trained oversee with various expertise through scholarships. However, there is not data indicating students pursue the area of vaccine development or other related field which raise concern on the capability of Cambodia to develop its own vaccine to prevent novel disease. To add up in education system, enrollment of students in Science, Technology, Engineering and Mathematic (STEM) education is quite low compared to the other field (JICA 2016) which indicate the low interest of student towards the STEM education and development with the country. The causes for the poor interest in STEM courses include:

i) A misunderstanding of the job that will be available after graduation
ii) Parental, self-interest, society influencing and peer pressure
iii) Cultural impact in terms of employment biases.

Another factor to consider is that there is no evidence or data to suggest that Cambodian colleges offer majors in the subject of vaccine development.

As it has been known that vaccine development is a uniquely set of challenges that includes multiple phases ranging from target selection and validation to vaccine assessment and manufacture. These stages need the collaboration of specialists from several fields and might take years to complete (Penny 2020). As a result, Cambodia requires a large and prospective expert in different sectors of vaccine development and manufacture to assure the country's adequate human resources.

5.2.2. Infrastructure and Research Facilities

- **Lack of teaching and research facilities**: In terms of knowledge-based development, Cambodia is still making modest progress in comparison to its

surrounding countries. Due to a lack of resources and facilities, education in Cambodia is primarily done in the classroom, with a little practical exercise/experiment to fully learn and to adopt the new ideas, which preventing them from reaching their full potential in terms of knowledge and experience. On the other hand, due to the high investment costs and specialized manpower necessary, research facilities are restricted and limited. To the best of our knowledge, there is just one testing lab, which is primarily used by research institutes and universities. Currently, there are no large-scale detection, production laboratory and facilities to facilitate the vaccine in Cambodia yet.

- **Lack of building a strategy plan to attract the scientific talent**: To attract the young/talented scientists/engineers (Cambodian), it is required to provide them with secured financial support to encourage them in their fields of interest for performing scientific research and development within our countries.

5.2.3. Technical Assistance and Funding

- **Technical assistance**: It is relatively novel for Cambodia to produce its own vaccine, as it has not done so previously. Vaccine development necessitates the use of a variety of techniques and skills. The support team is unimportant for the commencement of vaccine development and manufacturing since it might include administration, management, and accountants. However, expertise in the creation and manufacture of the vaccine itself are limited, as vaccines contain a small portion of the disease-causing organism, which necessitates the use of a specialist. As a result, a safety and operating handbook, clinical-trial examination, analytical procedures, as well as technical support, are necessary.
- **Funding within University**: A study with 15 universities in Cambodia showed that there is little data on Cambodia's funding of research and experimental development and almost all universities do not have a clear research policy/agenda with supporting institutional mechanisms to promote the research quality and quantity (CDRI 2010). Furthermore, many people associate research with student research, which is jeopardized if instructors are not involved in

research or scientific discovery. It is also noted that the number of students pursuing Ph.D. degrees in Cambodian colleges is low (CDRI 2010).

- **Funding from partnership for university**: Most universities in Cambodia have many potential partner universities oversea that can provide many scholarships various areas/fields to potential and outstanding students to pursue higher level of education. However, the scholarship can be provided if the partner university has the similar majors/courses which give a challenge for university to provide scholarship related to field of vaccine development.
- **Lack of fund for scientific research:** Cambodia has enjoyed economic growth through the investments and growth of industry; however, the funding for research and development is still low with 0.12% of GDP compared with 0.53%, 1%, 2.19% and 3.3% of GDP for Vietnam, Thailand, China, and Sweden (World Bank 2021); thus, researchers require/rely on competitive grant from donors to conduct the research. On the other hand, the government relies on the development partners (DPs) to support the research development that come from World Bank, ADB, JICA, KOICA, SIDA, etc. DPs designed the support which aligns with policies that would implement so that fund for research project is limited.
- **Lack of fund for acquiring technology and equipment**: It is unquestionable that to develop and produce vaccine, the technology, tools, research equipment to equip in the laboratory are necessary.

5.2.4. Government Policy and National Research Development

- **Lack of national research agenda**: Research agenda is a tool/road map/guideline to guide, and this initiative will help scientist to identify national priority research projects that will generate the successful research projects as well as produce clear/precise framework. To produce it; literature review, stakeholder consultation, focus group discussion and key informant interview are required to achieve a full picture of research topics.
- **Lack of policy as enabling environment to build research development:** Although Cambodia designed policies to promote research development such as 1) Policy on Research Development in the Education Sector (2010), 2) Sub-Decree on Appointing Professors in the Field of Health (2010) and 3) Master Plan

for Research Development in the Education Sector (2011); however, the policies and strategies did not have precise technical and financial policies as the engine to boost the research field (Cambodianess 2020).

- **Patent protection** is required to protect the scientific discoveries, although the government of Cambodia has set up the mechanism, but the examination rely on the external expert to evaluate the results, thus this should be a challenge for researchers to feel comfort with their efforts. On the other hand, patent protection is time consuming to get the license to protect new discoveries. (Oyston and Robinson 2012) pointed out that there is lengthy time required to take a product for the development and regulatory approval.

5.3. Road Ahead

To conclude the challenge vaccine development and manufacturing, four considering ideas as following are to consider.

5.3.1. STEM Education to Increase Human Resources

To help Cambodian students, understand the significance of STEM educations, the Cambodian government, particularly the MoEYS (Ministry of Education, Youth, and Sport), must highlight/enhance/clear vision on education roadmaps and strategy plans to encourage policymakers to comprehend the importance of STEM education in order to increase human capital and also ensure a relevant job market for whose graduate from the field of STEM and vaccine development.

5.3.2. Research Capability and Funding

To increase research capabilities, universities should seek partnership for funding, provide scholarship for outstanding student to purse high level of education as well as establish their research fund strategy plans. So that professors/lecturer can attract and recruit outstanding students and other researchers to do scientific research on related field of vaccine as well as other fields of interest related to STEM major.

5.3.3. Establish Research Facility Both University and National Level

There is now only one testing laboratory in Cambodia, as noted before. A greater number of research institutions at both university and national levels should be explored in Cambodia to study/analyze/evaluate the existing accessible diseases and create an

effective vaccine. There are laboratories in most universities for lecturers/professors and students to perform experiments in their respective disciplines, and vaccine research is no exception. Financing and human resources are needed to establish strong foundation new research facility that focuses on vaccine development and manufacture and other related areas.

5.3.4. Rewards, Letter of Recognition in Scientific Discovery

Scientists/engineers should be admired for new discoveries, publications, and patents and should be rewarded by their institute as well as the government to improve research capability and development in the country.

6. Policy Options

The important report provides for the first time the significant direction for local actors to place critical attention for Cambodia to fight the current and future pandemic. The investment law recently promulgated on 25 October 2021 lists health sector to one of the eighteen investment priority. A resilience ecosystem must be in place to ensure a self-reliance capacity to combat the future health crisis. The report points some policy options which could be essential for the Kingdom.

- Establishment of public private partnership mechanism for local production of vaccines and drugs with sufficient supporting ecosystem viewing the priority of technology transfer
- Creation of talent pool standing with foundation of collaboration and R & D investment
- Collective efforts for investment in public health in education sector
- Building infrastructures in place including norms and standards
- Making sustainable financing mechanisms for readiness in flighting unpredictable crisis of deceases
- Establishing ecosystem to mobilize investment in public health, particularly vaccines and drugs production

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