JURNAL FARMASI SAINS DAN KOMUNITAS, November 2021, 65-77 Vol. 18 No. 2
p-ISSN 1693-5683; e-ISSN 2527-7146
doi: https://doi.org/10.24071/jpsc.003459

STUDY OF CORONAVIRUS DISEASE 2019 (COVID-19) VACCINATION IN INDONESIA: A LITERATURE REVIEW

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Received June 17, 2021; Accepted October 4, 2021

ABSTRACT

Research and development of the COVID-19 vaccine give hope to all people to stop the COVID-19 pandemic in the world. This literature review explores the safety and efficacy of the COVID-19 vaccine used in Indonesia and discusses Indonesia's current vaccination process. The primary databases for the reviewed articles were PubMed and Mendeley. Others are official websites, such as World Health Organization (WHO); COVID-19 and National Economic Recovery Committee in Indonesia (KPCPEN); the National Agency of Drug and Food Control (NA-DFC–in Bahasa Indonesia: BPOM) of the Republic of Indonesia; the US Food and Drug Administration (FDA), ClinicalTrials.gov, COVID-19 vaccine Tracker, the Indonesian regulations, and guidelines regarding COVID-19. The inclusion criteria of the searched articles were those published from December 2019 to April 30, 2021, and those which discussed vaccines' types, efficacy, and safety. Acceptance of the COVID-19 vaccination is quite high (65%). Refusal was related to vaccine safety (30%); effectiveness (22%); distrust of vaccines (13%); fear of side effects (12%); and religious reasons (8%). The COVID-19 vaccines planned by the Indonesia Government have gone through clinical trials phases I to III. The Coronavac vaccine efficacy showed seroconversion that occurred was 92.4% to 97.4%, and no severe side effects have been reported. The ChAdOx1 nCoV-19 efficacy was 66.7% to 76.0%, and none of the tested participants was hospitalized, serious side effects were very small (0.9% to 1.1%). The mRNA-1273 efficacy was 94.1%, and its reactogenicity was mild to moderate. The BNT162b2 efficacy was ≥ 92%, and no severe or specific safety concerns have occurred. The efficacy of the BBIBP-CorV vaccine has not been established. Ongoing phase I, II, and III clinical trials will provide more information on safety and immunogenicity for the BBIBP-CorV. Three of the six vaccines have obtained EUA from BPOM and approval from the Indonesian Ulema Council (MUI). A health promotion program about the safety, efficacy, and the 'halal' of the COVID-19 vaccine; acceleration and ensuring access to the COVID-19 vaccination program are urgent to end this pandemic immediately.

Keywords: COVID-19; Indonesia; vaccines; vaccinations

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a contagious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The disease began to emerge in December 2019 in China. On March 2, 2020, the President of the Republic of Indonesia announced the first case of COVID-19. The World Health Organization (WHO) announced COVID-19 as a global pandemic on March 11, 2020 (World Health Organization, 2020).

Currently, there is no specific drug that can cure COVID-19. Therefore, the development of vaccines seems the most appropriate strategy at this time. Vaccination aims to reduce transmission of COVID-19, reduce morbidity and mortality, achieve herd immunity, and preserve people to remain

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productive socially and economically. Herd immunity can only be formed if the vaccination coverage is high and evenly distributed throughout the region. In addition, from an economic point of view, vaccination seems more cost-effective compared to therapy. Therefore, stakeholders must ensure the success of the COVID-19 vaccination program. This literature review aims to explore the safety and efficacy of the COVID-19 vaccine used in Indonesia, and discusses Indonesia's current vaccination process.

METHODS

This is a literature review. The primary databases for searching the article were PubMed, and Mendeley with the keywords "COVID-19" OR "SARS CoV-2" AND "Vaccine" AND "Efficacy" AND "Safety" OR "Indonesia" OR “Sinovac” OR “ChAdOx1” OR “mRNA-1273” OR “BNT162b2” OR “BBIBP-CorV”. The articles obtained from the main database are filtered based on their abstracts. The inclusion criteria of the reviewed articles are those which were published from December 2019 to April 30, 2021, and those which discussed the COVID-19 vaccines’ efficacy and safety. Furthermore, articles related to the safety and efficacy of the vaccines taken are six types of vaccines contained in the Regulation of the Minister of Health of the Republic of Indonesia No. HK.01.07/MENKES/9860/2020 concerning Determination of the Types of COVID-19 Vaccines. Research on vaccines given to patients with other diseases (co-morbid) was excluded from the articles used. The search results from PubMed and Mendeley obtained 19 articles used in this literature review.

Other references are official websites, such as World Health Organization (WHO); COVID-19 and National Economic Recovery Committee in Indonesia (KPCPEN); the National Agency of Drug and Food Control (NA-DFC, in Bahasa Indonesia: BPOM) of the Republic of Indonesia; Food and Drug Administration, the official website of ClinicalTrials.gov, the official website of COVID-19 Vaccine Tracker, as well as Indonesian regulations and guidelines regarding COVID-19.

RESULTS AND DISCUSSION

Acceptance of the COVID-19 vaccine among Indonesians

Several studies on the acceptance of the COVID-19 vaccination among Indonesians have been conducted. A cross-sectional study conducted in July 2020 concluded that 93.3% of the 1359 respondents wanted to be vaccinated if the vaccine used was proven to be 95% effective. On the other hand, if the effectiveness is proven to be only 50%, the vaccination acceptance rate will decrease to 67.0% (Machindra Kudale *et al*., 2020).

A survey conducted on September 19, 2020 to 115,000 respondents from 34 provinces by the World Health Organization, the Ministry of Health of the Republic of Indonesia, the United Nations Children's Fund (UNICEF), and the Indonesian Technical Advisory Group on Immunizationshow that about 65% of respondents would likely to accept the COVID-19 vaccination when it is provided by the Government, while 8% of them refused. However, as many as 27% expressed doubts about the Government's plans regarding the COVID-19 vaccination program. The most common reasons for refusal of the COVID-19 vaccine were related to vaccine safety (30%); effectiveness (22%); distrust of vaccines (13%); fear of side effects (12%); and religious reasons (8%) (Indonesian Ministry of Health *et al*., 2020).

Types of vaccines, safety, and efficacy of the COVID-19 vaccine used in Indonesia

Vaccines are biological products containing antigens in the form of live attenuated or inactivated microorganisms, toxoid, or recombinant proteins (Kementerian Kesehatan Republik Indonesia, 2020). The types of COVID-19 vaccines are 1) Live-attenuated or inactivated virus; 2) Nucleic acids, i.e., modified DNA and modified RNA; 3) Protein-based types, i.e., virus-like particle and protein subunits; 4) Vector-based, i.e., replicating viral and non-replicating viral (Mellet and Pepper, 2021).

The safety or risk of the vaccine must be justified to get EUA. Safety data are from the phase I and II tests that focus on serious adverse events, adverse events of particular interest (side effects of special concern), and severe incidents of COVID-19 in each test group need to be collected. The EUA permit also requires phase III clinical trial data to provide sufficient information to assess the risk-benefit profile of the vaccine, including side effects; severe cases of COVID-19 disease among study subjects; and cases of COVID-19 that occurred two months after the complete vaccination regimen was administered (Food and Drug Administration, 2021). These guidelines from the FDA are used by other countries to approve the use of the COVID-19 vaccine in their country.

The development of vaccine candidates around the world currently reaches 107 vaccines, 302 clinical trials, and 14 vaccines that have been approved by countries around the world. The 14 vaccine names and companies are Anhui Zhifei Longcom: RBD-Dimer (ZF2001), Bharat Biotech: Covaxin (BBV152), CanSino: Ad5-nCoV (Convidecia), Chumakov Center: KoviVac, FBRI: EpiVacCorona, Gamaleya: Sputnik V (Gam-COVID-Vac), Janssen (Johnson & Johnson): Ad26.COV2.S (Ad26COVS1, JNJ-78436735), Moderna: mRNA-1273, Oxford/AstraZeneca: AZD1222 (Vaxzevria), Pfizer/BioNTech: BNT162b2, Serum Institute of India: Covishield, Sinopharm (Beijing): BBIBP-CorV, Sinopharm (Wuhan): Inactivated (Vero Cells), and Sinovac: CoronaVac ("COVID19 Vaccine Tracker," 2021).

In Indonesia, the Directorate General of Disease Control and Environmental Health of the Ministry of Health of the Republic of Indonesia has established the Indonesian Technical Advisory Group on Immunization (ITAGI) as a committee that provides periodic monitoring reports and scientific assessment of new vaccines before a new vaccine was determined to be used in Indonesia (Kementerian Kesehatan RI, 2010). On December 3, 2020, the Indonesian Ministry of Health had determined the types of COVID-19 vaccines that can be used in Indonesia, namely: vaccines produced by PT. Bio Farma Indonesia (Persero), AstraZeneca, China National Pharmaceutical Group Corporation (Sinopharm), Moderna, Pfizer Inc., and BioNTech, and Sinovac Biotech Ltd. The Minister of Health can make changes to the types of COVID-19 vaccines based on recommendations from ITAGI and considerations from the COVID-19 and National Economic Recovery Committee. The use of vaccines can only be done after obtaining a distribution permit or an emergency use authorization from the National Agency of Drug and Food Control (NA-DFC) of the Republic of Indonesia (Kementerian Kesehatan Republik Indonesia, 2020). The vaccine was produced by PT. Bio Farma Indonesia (Persero) has not yet had sufficient research data to be included in this literature review. The other five vaccines are the products of AstraZeneca, Moderna, Pfizer Inc., and BioNTech, Sinovac Biotech Ltd., and China National Pharmaceutical Group Corporation (Sinopharm), which will be discussed in the following sections.

Coronavac

Coronavac is a vaccine produced by Sinovac which contains an inactivated coronavirus. Coronavac has completed three phase I clinical trials, four phase II clinical trials, and seven phase III clinical trials and has been approved for use in 22 countries, including in Indonesia ("COVID19 Vaccine Tracker," 2021).

The Coronavac vaccine has arrived in phase III clinical trials and has begun to be implemented in Brazil and Indonesia. Before the phase III clinical trials, the Chinese Government approved the Sinovac Emergency Use Authorization (EUA) in July 2020. Phase I and II clinical trials involving healthy volunteers aged 18 to 59 years and have been completed. The Sinovac vaccine is given in two dosage regimens (day 0 and day 28th). The phase I clinical trial involved 143 participants. The phase II clinical trial involved 600 participants aged 18 to 59 years who were randomly divided into three groups with a 2:2:1 ratio receiving two intramuscular injec-

tion that is, the group that received an injection of 3 μg per 0.5 mL of Coronavac, the group that received an injection of 6 μg per 0.5 mL of Coronavac, and the group that received the placebo injection; either on day 0 and day 14th or day 0 and day 28th (Poland *et al*., 2020).

The test results showed that in the dose group given the second dose on day 14th, the seroconversion that occurred was 92.4%. In the dose group given the second dose on day 28th, the seroconversion rate was 97.4%. Participants aged 18 to 39 years produced significantly higher seroconversion than participants aged 40 to 59. Seroconversion in participants given the second dose on day 28th was more significant than in those given the second dose on day 14th. No severe side effects have been reported (Poland *et al*., 2020). Considering safety, immunogenicity, and production capacity, a 3 μg dose of Coronavac is the recommended dose for assessing its efficacy in future phase III clinical trials (Wu *et al*., 2021).

One of phase III clinical trials of this vaccine in Indonesia is officially registered at ClinicalTrials.gov with identifier number: NCT04508075. This phase III clinical trial was conducted using an observer-blind, randomized, placebo-controlled study involving 1620 participants in individuals aged 18 to 59 years (U.S. National Library of Medicine, 2020). As of this writing, the results of the seven clinical trials in phase III of the Coronavac vaccine have not been reported by the developers of this vaccine.

ChAdOx1 nCoV-19 (AZD1222)

The vaccine developed by AstraZeneca in collaboration with Oxford University is named ChAdOx1 nCoV-19 or AZD1222, also known as the COVID-19 Vaccine AstraZeneca. This type of vaccine is classified as a vector-based viral type that uses the Chimpanzee adenovirus viral vector. The ChAdOx1 nCoV-19 Vaccine (AZD1222) has passed seven phase I clinical trials, 11 phases II clinical trials, and six phase III clinical trials, and its use has been approved in 91 countries, one of which is Indonesia ("COVID19 Vaccine Tracker," 2021).

From the clinical trials mentioned above, four randomized trials were summarized, and conclusions were drawn about the efficacy and safety of this vaccine. The four clinical trials are phase I and II clinical trials in the UK officially registered at ClinicalTrials.gov with identifier number: NCT04324606 (Barrett, J.R., Belij-Rammerstorfer, S., Dold, 2021; Ewer, K.J., Barrett, J.R., Belij-Rammerstorfer, 2021; The Oxford COVID Vaccine Trial Group, 2020); Phase I and II clinical trials conducted in South Africa are officially registered at ClinicalTrials.gov with identifier number: NCT04444674 (The Oxford COVID Vaccine Trial Group, 2021a); Phase II and III clinical trials conducted in the UK and Northern Ireland are officially registered at ClinicalTrials.gov with identifier number: NCT04400838 (The Oxford COVID Vaccine Trial Group, 2021b); Phase II and III clinical trials conducted in Brazil isofficially registered at ClinicalTrials.gov with identifier number: ISRCTN89951424 (The Oxford COVID Vaccine Trial Group, 2021a).

The summary results of these four studies were that the overall vaccine efficacy more than 14 days after the second dose was 66.7%, while the vaccine efficacy after administration of the second dose of vaccine from day 22nd to day 90th was 76.0%. None of the participants in the test group who were vaccinated against ChAdOx1 nCoV-19 was hospitalized with COVID-19 after an initial 21-day period of being given this vaccine. A total of 108 (0.9%) of the 12,282 participants in the ChAdOx1 nCoV-19 group and 127 (1.1%) of 11,962 participants in the control group experienced serious side effects. Seven deaths were considered not related to vaccination (two in the ChAdOx1 nCov-19 group and five in the control group), one death related to COVID-19 in one participant in the control group (The Oxford COVID Vaccine Trial Group, 2021a).

mRNA-1273

The mRNA-1273 vaccine, which is classified as an m-RNA (modified-Ribonucleic Acid) vaccine, was developed by Moderna with the Vaccine Research Center at the National Institute of Allergy and Infectious

Diseases (NIAID) in the United States. The mRNA-1273 vaccine has passed three phase I clinical trials, five phase II clinical trials, and six phase III clinical trials, and has been approved for use in 46 countries ("COVID19 Vaccine Tracker," 2021).

From the clinical trials above, one clinical trial stated the efficacy and safety of the mRNA-1273 vaccine is a clinical trial officially registered at ClinicalTrials.gov with identifier number: NCT04470427. This phase III clinical trial was conducted using a randomized, stratified, observer-blinded, placebo-controlled trial involving 30,420 participants in individuals aged ≥ 18 years. The mRNA-1273 vaccine was given 100 µg, given intramuscularly two times (0.5 mL each) at a distance of 28 days to each participant in the mRNA-1273 vaccine group and the placebo group with a ratio of 1:1 participant. This study showed that the vaccine efficacy was 94.1% and mild to moderate reactogenicity occurred in the mRNA-1273 vaccine recipient group (Baden *et al*., 2020).

Vaccination-related side effects were most common in both groups, i.e.,fatigue in 1.5% of the mRNA-1273 vaccine group; and headache occurred in 0.9% of the placebo group and 1.4% of the mRNA-1273 vaccine group. The frequency of grade 3 adverse events occurred in 1.3% of the placebo group and 1.5% of the group receiving the mRNA-1273 vaccine, as was the frequency of adverse events treated medically by 9.7% of the placebo group and 9.0% of the placebo group. The group received the mRNA-1273 vaccine, and serious adverse events occurred in 0.6% of both groups (Baden *et al*., 2020).

BNT162b2

The BNT162b2 vaccine, which is classified as an m-RNA (modified-Ribonucleic Acid) vaccine, was developed by Pfizer Inc. and BioNTech. The BNT162b2 vaccine has passed three phase I clinical trials, eight phase II clinical trials, and six phase III clinical trials, and its use has been approved in 82 countries ("COVID19 Vaccine Tracker," 2021). The dose of the BNT162b2 vaccine was given 30 µg 0.3 mL twice, three weeks apart.

This vaccine is recommended for individuals aged ≥ 16 years. According to the US Department of Health and Human Services Centres for Disease Control and Prevention report, the efficacy of this vaccine of ≥ 92% was consistently observed across age, sex, race, and ethnicity categories, including patients who had been infected with SARS-CoV-2. The primary evidence for the efficacy of this vaccine is one randomized, double-blind, placebo-controlled clinical trial involving 43,998 participants, ranging in age from 16 to 91 years. The study is officially registered at ClinicalTrials.gov with identifier number: NCT04368728 (Oliver, S.E., Gargano, J.W., Scobie, H., 2021).

From these clinical trials, symptoms of reactogenicity or local injection site symptoms, or systemic reactions for seven days after vaccination were frequent and primarily mild to moderate. Systemic side effects were reported more frequently after the second dose than after the first dose and were generally more frequent and severe in people aged 18 to 55 years than in those over 55 years. Systemic side effects have a mean onset of one to two days after vaccine reception and resolve within one day. Among vaccine recipients, 8.8% reported a rate of adverse reactions ≥ 3. The most common symptoms were fatigue (4.2%), headache (2.4%), muscle aches (1.8%), chills (1.7%), and injection site pain (1.4%). Generally, adverse reaction rates ≥ 3 were more frequently reported after the second dose than after the first dose and were more common in younger participants. Serious side effects occurred in an equal proportion of vaccine recipients (0.6%) and placebo (0.5%). No severe or specific safety concerns have occurred during the use of this vaccine (Oliver, S.E., Gargano, J.W., Scobie, H., 2021).

BBIBP-CorV

Sinopharm and Beijing Institute of Biological Products developing the BBIBP-CorV vaccine. This vaccine contains an inactivated coronavirus and has passed one-

phase I clinical trial, one phase II clinical trial, and four phase III clinical trials, and its use has been approved in 40 countries ("COVID19 Vaccine Tracker," 2021).

In pre-clinical trials, the BBIBP-CorV vaccine has proven effective in preventing disease against SARS-CoV-2 in Rhesus macaques monkey test animals (Wang *et al*., 2020). The phase I and II clinical trial showed that BBIBP-CorV was safe and tolerated at all dosage levels and in both age groups, namely the 18 to 59 year age group and the ≥ 60 year age group. All participants showed a humoral response to the vaccine after 42 days. Two doses of this vaccine, namely a dose of 4 μg on day 0 and day 21st, as well as on day 0 and day 28th, achieve neutralizing antibody titers that are higher than a single dose of 8 μg or a dose of 4 μg on day 0 and day 14th. No severe side effects were reported within 28 days post-vaccination for all groups (Doroftei *et al*., 2021). The efficacy of the BBIBP-CorV vaccine has not been established. Ongoing phase I and II clinical trials and ongoing phase III clinical trials will provide more information on safety and immunogenicity, dosage, and schedule for the BBIBP-CorV vaccination (Xia *et al*., 2020).

Information regarding the COVID-19 vaccine clinical trial identifier number used by Indonesia is in Table 1.

Table 1. The COVID-19 vaccine planned by Indonesia and the clinical trial number for each COVID-19 vaccine as of April 18, 2021 ("COVID19 Vaccine Tracker" 2021)

Vaccine Type	Vaccine Name	Development Company	Phase I Clinical Trials	Phase II clinical trials	Phase III clinical trials	The number of countries that have approved its use
Inactivated viruses	BBIBP-CorV	Sinopharm & BeijingInstitute of Biological Products	ChiCTR2000032459	ChiCTR2000032459	NCT04510207 ChiCTR2000034780 NCT04612972 NCT04560881 BIBP2020003AR	35
Inactivated viruses	CoronaVac	Sinovac	NCT04352608 NCT04383574 NCT04551547	NCT04352608 NCT04383574 NCT04551547 PHRR210210-003308	NCT04651790 NCT04456595 NCT04508075 669 / UN6.KEP / EC / 2020 NCT04582344 NCT04617483 PHRR210210-003308 NCT04800133	22
mRNA	mRNA-1273	Moderna	NCT04813796 NCT04785144 NCT04839315 NCT04283461	NCT04649151 NCT04748471 NCT04761822 NCT04405076 NCT04796896	NCT04649151 NCT04470427 NCT04796896 NCT04811664 NCT04805125 NCT04806113	46
mRNA	BNT162b2	Pfizer & BioNTech	EUCTR2020-001038-36 NCT04380701 NCT04839315 NCT04816643 NCT04588480	EUCTR2020-001038-36 NCT04380701 NCT04368728 NCT04761822 NCT04824638 NCT04754594 NCT04649021 ISRCTN69254139 NCT04588480	NCT04368728 NCT04805125 NCT04816669 NCT04713553 NCT04754594 NCT04800133	83

Non-replicating virus vector	AZD1222	AstraZeneca & Oxford University	NCT04760730 NCT04684446 NCT04816019 PACTR202005681895696 PACTR202006922165132 NCT04444674 NCT04568031 EUCTR2020-001072-15 NCT04324606	CTRI / 2020/08/027170 NCT04686773 NCT04760730 NCT04684446 ISRCTN69254139 ISRCTN15638344 EUCTR2020-001228-32 NCT04400838 PACTR202005681895696 PACTR202006922165132 NCT04444674 NCT04568031 EUCTR2020-001072-15 NCT04324606	CTRI / 2020/08/027170 NCT04800133 ISRCTN89951424 NCT04536051 NCT04516746 EUCTR2020-001228-32 NCT04400838 NCT04540393	92

The COVID-19 vaccination process in Indonesia

The COVID-19 Vaccination in Indonesia is conducted in 4 stages, namely:

1. The first stage of the COVID-19 vaccination targets health workers, assistant health workers, support staff, and students who are currently undergoing education of medical professionals who work in Health Service Facilities. The estimated number of people in stage I is 1,400,000. Implementation time is from January to April 2021.
2. The targets for the COVID-19 vaccination phase II are:
    a. Public service officers, namely the Indonesian National Army and National Police of the Republic of Indonesia, legal officers, and other public service officers, including officers at airports/ports/stations/terminals, banks, state electricity companies, and regional drinking water companies, as well as other officers involved directly in providing services to the community. The estimated number of people in this group is 17,400,000.
    b. Elderly group (≥ 60 years). The estimated number of people in this group is 21,500,000. Implementation time is scheduled in January-April 2021.
3. The target of COVID-19 vaccination phase III is vulnerable people from geospatial, social, and economic aspects, which covers 63,900,000 estimated people. Implementation time is scheduled in April 2021-March 2022.
4. The target of vaccination phase IV is the community and businessman using a cluster approach following the availability of vaccines. The estimated number of people in this group is 77,400,000. Implementation time is scheduled in April 2021-March 2022 (Direktur Jenderal Pencegahan dan Penanggulangan Penyakit Kemenkes RI, 2020; Nadia, 2020).

Epidemic prevention can be achieved if vaccine efficacy is at least 60%, 70%, or 80% if vaccine coverage is given to 100%, 75%, or 60% of the population, respectively (Bartsch *et al*., 2020; Mehrotra *et al*., 2021). The total population of Indonesia in 2020 who are more than 18 years old is 188,700,000 people, so that after deducting the people who suffer from comorbid diseases, pregnant women, older adults, and people who are exposed to COVID-19 are 7,200,000 people, the target population is 181,500,000 people. Based on these data and considering the vaccine's efficacy rate, so far, no one has reached 80%, and the addition of the vaccine wastage rate by 15%, the Indonesian Government needs 426,800,000 doses of vaccine to form herd immunity in Indonesia (Nadia, 2020).

Until now, the COVID-19 vaccine that has received the Emergency Use Authorization (EUA) from the National Agency of Drug and Food Control (NA-DFC) of the Republic of Indonesia is the Coronavac brand produced by Sinovac Life Sciences Co., LTD, China, with the number EUA2057300143A1 and the brand ChAdOx1 nCoV-19 (AZD1222) produced by AstraZeneca, UK with number EUA2158100143A1 (Badan Pengawas Obat dan Makanan Republik Indonesia, 2021; Badan Pengawasan Obat dan Makanan, 2021).

In addition, NA-DFC has also provided EUA to vaccines produced by PT. Bio Farma, Indonesia, with registration number EUA2102907543A1. This vaccine is named the COVID-19 vaccine. The COVID-19 vaccine must be registered for EUA, even though its content and efficacy, and safety profile are the same as the CoronaVac Vaccine produced by Sinovac, Beijing, which previously received EUA from the NA-DFC. There are differences in production sites, different packages from a single dose to multiple doses, so according to the regulations,

it must be registered to get EUA (Badan Pengawas Obat dan Makanan, 2021).

The Indonesian Ulema Council (MUI) stated that COVID-19 Vaccine Products from Sinovac Life Sciences Co. Ltd. China and Pt. Bio Farma (Persero) are "halal" and can be used for Muslims under credible and competent expert supervision (Majelis Ulama Indonesia, 2021a). On the other hand, the AstraZeneca COVID-19 vaccine produced by AstraZeneca at SK Bioscience Co. Ltd., South Korea, is "haram" because, in the production process, it uses trypsin from pigs. However, its use is currently permissible ("*mubah"*) because of a condition of emergency ("*syar'iy")*. However, there is a statement from the expert about the risks of not getting the COVID-19 vaccination immediately; while, the availability of "halal" vaccines is not sufficient for the implementation of the COVID-19 vaccination to realize herd immunity. In this case, the Government does not have many choices given to the limited vaccines available (Majelis Ulama Indonesia, 2021b).

The implementation of the COVID-19 vaccination in Indonesia was first given to the President of the Republic of Indonesia, Joko Widodo, on January 13, 2021. After the vaccination process, COVID-19 cases in Indonesia decreased day by day. The increase in the number of daily cases on January 30, 2021, was 14,518 confirmed cases of COVID-19, and after that, the daily cases of confirmed COVID-19 patients did not exceed this number. The vaccine doses have been given to the public in Indonesia until April 26, 2021, totalling 19,230,446 doses.

To accelerate COVID-19 vaccination in Indonesia, the Government asks stakeholders to cover costs of vaccination for their employees, called the "Gotong Royong" Vaccination. The type of COVID-19 vaccine for the "Gotong Royong" Vaccination must be different from the ones used for the regular Vaccination Program (Kementerian Kesehatan Republik Indonesia, 2021).

People who have been designated as target recipients of the COVID-19 vaccine must take the COVID-19 vaccination. Those who do not participate in the COVID-19 vaccination can be given administrative sanctions in the form of postponement or termination of social security or social assistance provision, postponement or termination of government administration services, and fines (Presiden Republik Indonesia, 2021).

DISCUSSION

Accelerated clinical trials of the COVID-19 vaccine need to be carried out with a high level of accuracy. On the one hand, it is a race against time and on the other hand, the safety and efficacy of vaccines when used in humans must be ensured. The more clinical trials in different countries, the more accurate evidence of safety and efficacy will be. Therefore, participation from various countries is highly expected to prove the safety and efficacy of the COVID-19 vaccine, including Indonesia. If vaccine efficacy is at least 60%, 70%, or 80% so vaccine coverage shouldbe given to 100%, 75%, or 60% of the population, respectively, to achieve epidemic prevention (Bartsch *et al*., 2020; Mehrotra *et al*., 2021). The higher the vaccine efficacy, the lower the vaccine coverage needed. The COVID-19 vaccine used in Indonesia needs clinical trials involving the Indonesian people to obtain data related to efficacy and safety from each of the COVID-19 vaccines. If the clinical trials' results on the COVID-19 vaccines' efficacy are high, the Indonesians who need to be vaccinated against COVID-19 can be reduced.

The total coverage of the COVID-19 vaccination announced by the Indonesian Government is 426,800,000 doses of vaccines (Nadia, 2020). The Indonesian government needs to ensure the continuity of the availability of the COVID-19 vaccine to achieve the vaccination coverage target to obtain herd immunity in Indonesia. Moreover, the halal factor is an important factor considering that the majority of Indonesian people are Muslim. Non-halal COVID-19 vaccines need to get approval from the MUI when this vaccine is to be used in Indonesia.

Based on the information presented in this literature review, people should not hesitate to receive any COVID-19 vaccine because the results of clinical trials have supported its efficacy and safety. Moreover, the acceleration of vaccination to achieve herd immunity is urgently needed to stop the spread of COVID-19.

CONCLUSION

The sanction for people who refuse the COVID-19 vaccine is not the only way to increase acceptance of the COVID-19 vaccination. Promotive programs could be better than a punishment or sanction. Therefore, it is urgent to inform people regarding the safety, efficacy, and the 'halal' of the COVID-19 vaccine to increase the acceptance of the COVID-19 vaccination. Furthermore, ensuring access to COVID-19 vaccines and accelerating the vaccination program are urgently required.

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