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Review Article

## Developing Halal Vaccine Production in Indonesia: Challenges and Future Opportunities

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### Abstract

When the Covid19 pandemic occurred, Indonesia was the largest country in Southeast Asia with the most positive confirmed victims and the highest death rate. The consequences of the government's efforts to prevent the government from ordering vaccines reached 450 million doses for 187 million people in order to achieve individual immunity and herd immunity. As a country with the largest Muslim population in the world, the halal status of vaccines is very important. Of the six types of vaccines in Indonesia, namely; only the Sinovac vaccine received halal status, while other vaccines such as AstraZeneca, Pfizer, Moderna, Sinofarm were ultimately still used for emergency reasons due to insufficient halal vaccines. In the future, Muslim countries need to continue to develop alternative technologies and materials to ensure that the vaccines given are halal. Use of cell lines to produce vaccines such as Vero (Monkey), MDCK (Dog), BHK21 (Hamster), HEK (Human), PER (Human). The medium used for cell growth (upstream process) also contains Human Blood (HuS), Horse Blood (HS), Cow Blood (FBS). Likewise, the use of Pig and Animal Trypsin that is not slaughtered in a halal way, as well as the use of stabilizers in vaccine formulations such as Human or bovine (cow) Serum, Porcine or Cow Gelatin, Ethanol are critical points for fatwa institutions such as not passing the halal category. The use of alternative materials in vaccine production such as insect cells, yeast, fungi, non-animal medium and vegetable stabilizers has the opportunity to replace mainstream materials. The independence of halal vaccine production provides an opportunity to increase national resilience.

## 1. INTRODUCTION

The impact of the COVID-19 virus on the world at the beginning of 2020 brought many changes in the new world order. Indonesia as the country with the largest Muslim population in the world [1] is one of the countries that has had a fairly serious impact not only in the economic sector, but also in the social and psychological sectors [2]. In the economic sector, during the pandemic, the Indonesian economy was minus 5.3% in the 2020-2021. The state also prepared a budget of 937.4 trillion for covid-19 prevention (including the Regional Budget/APBD) [3]. Social Impact with increasing poverty rates and decreasing community participation in public activities due to micro and macro scale restrictions [4]. Even The Covid-19 pandemic has led to the worst economic downturn in the last 50 years [3].

Covid-19 entered Indonesia for the first time on March 2, 2020 when it was discovered that 2 people were confirmed positive for Covid-19 due to contracting a Japanese foreigner. Next, in just 37 days (9 April 2022) COVID-19 has spread to 34 provinces on the island of Java (DKI Jakarta, West Java, Central Java) as the provinces most exposed to the virus [5]. Since then, the recording of cases has become more massive, until November 2, 2022, Indonesia has penetrated the number of infected humans as many as 6.5 million people and the recovery rate has reached 6.3 million people [6] and the death rate is 158,807 people [7]. This figure is the largest in Southeast Asia [8]

To tackle the Covid-19 pandemic situation, vaccination program is considered very important and urgent because it is considered capable of growing individual and collective (herd immunity) (9). However, vaccines cause polemic especially in Muslim world itself because apart from being expensive, it is also related to the status of its use in the medication, whether it is halal or not. In Islam, the well-being of the Muslim Ummah, healthy body, mind and spirit is so emphasized and should be protected, vaccinations which have been shown to be very effective in preventing

disease, are allowed in Islamic law based on *Istihsan* principles (10) as well research finding fatwa about vaccination which found that vaccination (not only covid19 vaccine) is permissible in Islam where is supported by various Islamic legal maxims; it is in line with the preservation of the *Maqasid al-Shariah* on 'the maintenance of life' (*hifz al-nafs*) (11).

The need for such a large vaccine has become a separate problem for state finances, where Indonesian Finance Minister Sri Mulyani, at the end of 2020, stated that Indonesia had spent a budget of IDR 637.3 billion on buying the initial stage of the coronavirus (COVID-19) vaccine [12]. The problem does not stop with the procurement of vaccines, the next problem is that most of the vaccines imported by the Indonesian government have not been certified halal. Indonesia has the largest Muslim adherents in the world and religion is an important aspect of daily life, which is a serious concern for the Ulama (Islamic Scholar) and Umaroh (Government) as well as the community [13]. Vaccines that generally involve various sources of material from animals, pigs or their derivatives, or blood [14], all of those materials are prohibited or forbidden to be consumed by Muslims, this is a concern for the majority muslims of Indonesia. In Islamic teachings, guidelines for consuming halal are contained in several verses of the Qur'an as follows;

*"Indeed, Allah only forbids you **carion, blood, pork, and animals that (when slaughtered) are called (names) other than Allah.** However, whoever is forced (to eat) while he does not want it and does not (also) exceed the limit, then there is no sin for him. Verily Allah is Forgiving, Most Merciful."* (Surat al-Baqarah [2]: 173).

*"will not find in the revelation that was revealed to me anything that is forbidden for those who want to eat it, except if the food is **carion, flowing blood, or pork, because verily they are dirty, or animals slaughtered in the name of other than Allah.** Whoever is forced (to eat) while he does not want it and does not (also) transgress, then indeed your Lord is*

Forgiving, Most Merciful." (Surat al-An'am [6]: 145)

The Phrase: “*fa maniḍturra gaira bāgiw wa lā 'ādin fa lā iśma 'alaiḥ*” based on *al muyassar tafseer* meaning that **And among Allah's bounties and conveniences for you is that He makes all the forbidden foods lawful in an emergency. So whoever is squeezed by an emergency condition to eat something from it, without wanting to commit injustice in consuming more than what is needed, and does not exceed the limits of Allah in what has been made lawful for him, then there is no sin on him in that action. Verily, Allah is Forgiving of His servants, and Most Merciful towards them.** Al Aşyqar said to interpret that ayah as follow: **فَمَنْ اضْطُرَّ**. (But whoever is forced to (eat) Namely those who are in a situation that requires them to eat these forbidden foods because they are hungry or do not have something to eat or because **they are forced and afraid of getting the danger from that Coercion**It means that the change of situation and condition will change the law status of “haram” substance.

As a country with a Muslim majority population, the government has serious concerns regarding the halal status of vaccines. Not only approval from the Food and Drug Supervisory Agency (BPPOM), vaccines also should get halal status from the Indonesian Ulama Council based Article 1 Number 10 of Law Number 33 of 2014 concerning Guarantees for Halal Products states: *"Halal certification is an acknowledgment of the halalness of a product issued by BPJPH based on a written halal fatwa issued by the MUI* In the context of vaccine safety, the head of BPOM of the Republic of Indonesia stated that the vaccine is allowed to be given in an emergency situation, and this has been in line with Emergency Use Authorization (EUA) of COVID-19 vaccine and the World Health Organization (WHO) [15]. It is not enough that the government through the fatwa institution encourages the Indonesian Ulema Council to determine the halal status of the vaccine with five criteria. First, vaccine

ingredients must not contain ingredients from animals that are not halal or are slaughtered in a manner that is not in accordance with sharia. Second, it does not contain *najis*, such as carrion, blood, dogs, pigs, and everything that come from genital and rectum. Third, the vaccine must be safe for consumption, non-toxic, non-intoxicating, and not harmful to health. Fourth, the equipment must not be contaminated. Fifth, the vaccine does not contain human body parts [16].

MUI has issued fatwas for 5 types of vaccines, namely Sinovac, Sinovac is the first type of vaccine that received approval from MUI. This vaccine uses Vero Cells from African green cells to quantify the virus, but provides assurance that human and animal tissues are not found in the final product, including guaranteeing not to use trypsin from pigs or animal product in its production process [17,18]. Next is Astrazeneca, this vaccine is produced by the University of Oxford UK, using a viral vector platform where the cell line used is human embryonic kidney (HEK 293, descended from tissue taken from a 1973 abortion in the Netherlands. Based on MUI Fatwa no. 14 of 2021, the vaccine this type of status is haram, because it uses trypsin from pigs. However, MUI allows it to be used for emergency reasons [19]. AstraZeneca Vaccine Company also confirmed that no pork and animal product was found in the final product of astrazeneca [20]. As for the types of Sinofarm, Moderna and Pfizer vaccines, until now, MUI has not been able to issue a fatwa that is completely clear because, however, MUI has declared it Haram as Haram since there was an allegation that they used porcine trypsin during manufacturing or contain animal products. But vaccination is permissible by Islamic laws because there is an urgent need to vaccinate immediately and sufficient clean and Halal product is not available [21]. Actually, the use of cow, horse and human serum in vaccine production is commonly used, of course, the MUI decision is based on strong reasons as in

the hadith of the prophet, the hadith of the prophet:

Allah has sent down disease and medicine, and made a cure for every disease; So, seek treatment and do not seek treatment with things that are unlawful.” (Narrated by Abu Dawud from Abu Darda).”

”Allah does not send down a disease except to send down (also) the cure.” (Narrated by Al-Bukhari from Abu Hurairah).

”The Messenger of Allah was asked about a rat that fell into the cheese. He replied: ”If the cheese is hard (solid), throw the mouse and the cheese around it, and eat (the rest of) the cheese; but if the cheese is liquid, then do not eat it” (Narrated by Ahmad from Abu Hurairah)

”If there are two kulah of water, then it doesn't contain any impurities.” (Narrated by Abu Dawud, at-Tirmidhi, an-Nasai, Ibn Majah from Abdullah Ibn Umar. This hadith is considered authentic by Ibn Huzaimah, al-Hakim, and Ibn Hibban).

Likewise there are *qaidah fiqh* schemed by Ibrahim (22) as based argumentation allowing consumption of non halal product in emergency situation;



Figure 1. Compilation of Qaidah Fiqhiyyah About “Darurat” Condition

The *Qaidah Fiqhiyyah* above are squeezed from various ayat from the Koran as; Al-Baqarah: 173, Al-An’am: 145, Al-A’raf: 55 and Al-Qassash 77) as well Abu Sa’id al-Khudri reported: The Messenger of Allah, peace and blessings be upon him, said,

لَا صَرْرَ وَلَا ضِرَارَ

“Do not cause harm or return harm” (al-Sunan al-Kubrā lil-Bayhaqī 11384)

Thus, so that the pros and cons of halal vaccines do not continue to occur, it becomes a collective obligation (*fardhu kifayah*) for the Islamic world, especially the government to seek vaccines that are truly halal for several reasons; 1. It is impossible for the state to continue to spend trillions of funds on vaccine purchases which can drain the country's foreign exchange, 2. The reason for the emergency use of non-halal vaccines must be found a solution, if the emergency (*dharurat*) is

gone, they must move to pure halal vaccines, 3. Provide security and satisfaction guarantees for the Muslim community to get vaccines that are truly halal so that there is no reason to refuse vaccines for the safety of mankind. Therefore, a study is needed on; 1. Analysis of vaccine consumption in Indonesia, 2 Identification of haram or unclean ingredients in the vaccine manufacturing process, 3. Propose the alternative fully halal materials to substitute the “non halal materials” in recent vaccine production.

## 2. METHODS

Literature study about Consumption of vaccines based on type and capacity, identification of non-halal materials in the vaccine production was carried out. The process of producing vaccines that have been released to the public including official press releases from vaccine producing companies. The study also focusing on determining halal and haram based on the Indonesian Ulama Council (MUI)’s Standard, as well as determining alternative materials and production scheme how to substitute non-halal materials by using Halal Critical Point Vaccine Production.

## 3. RESULTS and DISCUSSION

### a. Received Vaccines : The Type and Quantity

Various government policies to stem the pandemic have been carried out, including macro and micro-scale restrictions, social distancing [23] and prevention through vaccination [24]. The need for vaccines in Indonesia is very large, as many as 450 million doses with a target of more than 187 million populations and has reached 80% vaccination coverage in early 2022 [25] and has a value of trillions of rupiah. As of December 31, 2021, the Government of Indonesia has received eight vaccine brands with no less than 429.2 million doses consisting of the CoronaVac, Covid Bio, Astra Zeneca, Sinopharm, Moderna, Pfizer, Janssen and Novavax vaccines. The coverage of this vaccination has reached 79.4% for the first dose and 54.68% for the second dose. This has exceeded the WHO target of 40% of the population being fully vaccinated by the end of 2021[24,25]. Of the 450 million doses of vaccine needed, Sinovac-Coronavac dominates 66%, followed by Pfizer, Novavac, AstraZeneca, Moderna, Sinopharm and Janssen (Table 1).

**Table 1.** List of Covid19 Vaccines used in Indonesia

Vaccine Type	First Release	Initial number of releases (million doses)	Target 2021 (million doses)	Total Percentage	Market price (Per Dose in USD)
Sinovac-CoronaVac	December 6, 2021	1.2	283	66.2%	13-17
Covid-19 Biopharma	February 19, 2021	7.8	-	-	
Astra Zeneca	March 12, 2021	1.1	20	4.7%	3-5.25
Sinopharm	May 1, 2021	0.5	5.7	1.3%	15-40
Moderna	10 July 2021	3	18.3	4.3%	15-34.5
Pfizer	August 19, 2021	1.5	50	11.7%	6.75-19.5
Janssen	11 September 2021	0.5	0.3	0.1%	8.5-10
Novavax	27 November 2021	0.135	50	11.7%	3

Source: Tempo and Ministry of Health Republic of Indonesia [25, 26]

### b. Steps in Common Vaccine Production

Vaccine content may contain inactivated pathogens, or inactivated microbial components or also bacterial fragments or cell structures to form antigens. In general,

vaccines can be divided into 5 categories; Live-attenuated vaccine, inactivated vaccine, Recombinant vaccine, Toxoid and Conjugate polysaccharide-protein vaccine [15, 27].

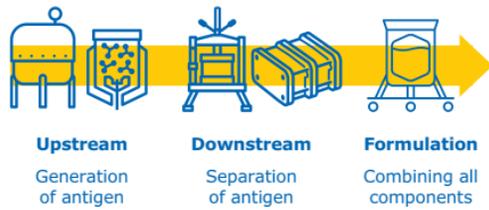


Figure 2. Main stages of vaccine production [27]

Although the type of antigen used varies between different vaccine types, the vaccine manufacturing process, in general, has similar principles for all types, see figure 2 [27]. It is divided into 3 main stages, namely; upstream, downstream and formulation. In the Upstream Stage, antigens are generated by taking them from the pathogen itself or from recombinant proteins, there are three types of antigens commonly used to make vaccines to induce the immune system, namely viruses grown in primary cells (e.g. chicken embryos) or continuous cell lines (e.g., chicken embryos) for example, Vero, MDCK, BHK21, HEK, PER, SF9 and others). Next, if the antigen is in the

form of bacteria, it can be grown in a fermenter. The recombinant protein is produced by bacteria, yeast, or cell culture. While in the downstream process is done so that the antigen is separated from the impurity. This is to improve product safety and vaccine stability [27]. The antigen is released from the substrate (eg, lysed cells) if necessary and isolated from the bulk environment. Depending on the characteristics of the antigen and impurities, purification technologies may be used: chromatography, ultrafiltration, precipitation, enzyme digestion, or other processes. And the final stage (third stage) is the Formulation of All components which is the final product vaccine designed to maximize stability while creating a format that allows efficient distribution and the preferred clinical delivery method. Formulated vaccines may include adjuvants to enhance immune response, stabilizers to extend shelf life, and/or preservatives ensuring that multidose vials can be administered.

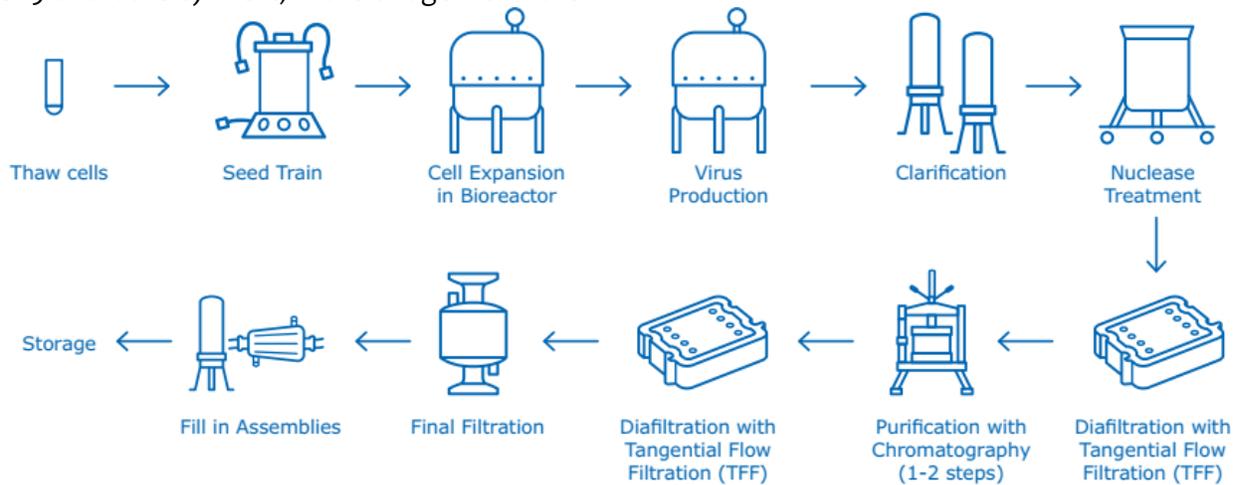


Figure 3. Generic cell-based viral vaccine production process [27]

As Diseases the viruses also evolve [28]. From various vaccine production processes, cell-based viral vaccine production (figure 3) based on mammalian and avian cells is currently preferred because of its high yield and immunogenicity compared to insect or bacterial cell-based cells [29]. The problem is that the cells used in vaccine production if they

come from animals will cause halal problems, as well as serum in cell growth media, enzymes and ingredients as stabilizers (Table 2). The process involves some unavoidable unclean items. Although vaccine companies have announced that the final product does not contain any animal ingredients, this is a matter of debate among scholars.

### c. Identification of non-halal ingredients in vaccine production

The use of animal cells for vaccine production has a very important position. Viruses to be propagated must go through a growth and replication phase in the host cell. Likewise, the cultured cells will only be able to grow with a suitable medium and generally use mammalian serum as the main component of the growth medium. Vero cell, extracted from an African green monkey is used by the vaccine company China National Biotec Group (CNBG) for the Sinopharm and Sinovac-Coronavac (Sinovac) vaccine brands. While T-REx-293 cells, a derivative of the human embryonic kidney (HEK 293) cell line, descended from tissue taken from a 1973 abortion in the Netherlands from an undisclosed source were used by Oxford University and AstraZeneca for the production of Vaxzevria or AstraZeneca/AZD1222. Meanwhile, the PER.C6G TetR cell line, derived from human embryonic retinal cells, obtained in 1985 from fetal retina tissue, was used in vaccine production. Janssen/Ad26.COV 2.S by Johnson & Johnson company [23]. Likewise, trypsin and gelatin are widely used in health products and medicines including vaccines [30, 31].

All those Host Cell line, Serum, Enzyme and Stabilizer mentioned above are included in the non-halal category based on Islamic sharia [17, 33].

**Table 2.** Non-Halal Materials for Vaccine Production Stages

Material Type	Non-halal Material	Process Stage
Host Cells for Virus Production	Vero (Monkey), MDCK (Dog), BHK21 (Hamster), HEK (Human), PER (Human)	Upstream
Common Serum	Human Blood (HuS), Horse Blood (HS), Cow Blood (FBS)	Upstream
Enzyme (Protease)	Trypsin Pigs and Animals that are not slaughtered in a halal way	Formulation
Stabilizer	Stabilizers; Human or bovine (cow) Serum, Porcine or Cow Gelatin, Ethanol	Formulation

Based on the results of the literature study conducted, the following are the types of vaccines used in Indonesia based on information from the ministry of health: and analysis of fatwas from MUI (Table 3).

### d. Indonesian Ulama Council (MUI) Fatwa to Current Halal Status of Vaccine in Indonesia

With all the limitations and the urgent need for materials, the MUI finally issued a fatwa regarding the permissibility of using non-halal vaccines because the availability of truly halal vaccines is very limited. MUI also made a statement that the types of vaccines from Astrazeneca and Pfizer N Biotech were known to be unlawful but allowed to be used for emergency reasons. Among the rules used by Islamic scholars are; al-qur'an hadith and qaidah fiqh which reads; Emergencies make what is forbidden to be lawful [1,15,19].

**Table 3.** Vaccine Halal Status in Indonesia

Vaccine Name	Producer	Platforms	Cell Line used	MUI Fatwa	Reference
Sinovac-Coronavac	(Sinovac)	Inactivated	Vero cell, extracted from an African green monkey	Halal	MUI Fatwa No. 02 of 2021 [18]
BIBP(China National Biotec Group)	(CNBG), Sinopharm)	Inactivated	Vero cell, extracted from an African green monkey	Haram-permittable	Sinofarm Halal Status [35]
Vaxzevria or AstraZeneca/AZD1222 vaccine	(Oxford University and AstraZeneca)	Viral VectorEach	T-REx-293 cells, a derivative of the human embryonic kidney (HEK 293) cell line	Haram-permittable	MUI Fatwa No. 14 of 2021 [19,35]
Janssen/Ad26.COV 2.S	(Johnson & Johnson)	Viral VectorEach	PER.C6G TetR cell line, derived from human	not yet Halal/Haram	EUA (Emergency Use Authorization) from the

Comirnaty BNT162b2	or (Pfizer-BioNTech)	Each mRNA	embryonic retinal cells	certified by MUI	B POM 7 September 2021 [36]
Spikevax mRNA-1273 vaccine	or (modern)	Each mRNA	None (cell-free in vitro transcription process from DNA templates)	Haram-permissible	Pfizer Halal Status [34, 37]
				not yet Halal/Haram certified by MUI	can be used as long as there is not enough halal vaccine [34, 37]

The Indonesian Ulema Council (MUI) emphasized that non-halal Covid-19 vaccines may be used as long as there are no other alternatives or the availability of halal vaccines is not sufficient to realize herd immunity. This was conveyed by the Chairman of the MUI for Fatwa, KH Asrorun Niam Sholeh at the Fatwa press conference No. 8 of 2022 regarding the Red and White Vaccine developed by PT Biotis Pharmaceutiscals in collaboration with Airlangga University (Unair) Surabaya, Thursday (10/2/2022). "However, if the availability of halal vaccines is sufficient to

achieve herd immunity. So, it is no longer allowed to use non-halal vaccines" [34].

From the table above, it is known that the halal status of the vaccine is only for the Sinovac vaccine, while others are not halal, but may be used temporarily due to the limited supply of halal vaccines. Furthermore, a comparison of the results of the MUI decision regarding 2 types of vaccines, namely Sinovac and AstraZeneca, it was found that both had different statuses due to the following reasons (Table 4).

**Table 4.** Comparison of Sinovac and AstraZeneca . Vaccine Fatwa Products

Process	Non Halal Materials involved in vaccine production	Reason	Halal Status	Reffrenece
Sinovac	<ol style="list-style-type: none"> <li>Vero Cell, This cell is obtained from the kidney cells of the African Green Monkey (African Green Monkey).</li> <li>FBS (bovine blood serum) for cell growth culture</li> </ol>	<ol style="list-style-type: none"> <li>does not utilize (intifa') pigs or materials contaminated with pigs and their derivatives.</li> <li>do not use parts of the human body (juz' minal insan).</li> <li>in contact with mutawassithah unclean goods, so that it is considered mutanajjis, but purification has been carried out which has fulfilled the provisions of purification according to syar'i (tathhir syar'i).</li> <li>using production facilities that are sacred and only used for covid-19 vaccine products.</li> </ol>	Halal	Fatwa Indonesian Ulema Council Number: 02 of 2021
Astrazeneca	<ol style="list-style-type: none"> <li>Adenovirus from Chimpanzees</li> <li>Host cells are derived from HEK239 (Human Epithelial Kidney Cell)</li> <li>FBS (Fetal Bovine Serum)</li> <li>Trypsin from Pig Pancreas</li> </ol>	<ol style="list-style-type: none"> <li>Haram because it uses tripsi from Pig</li> <li>May be used for reasons; urgent needs and needs, not enough halal vaccines, there is a security guarantee from the government, there is no other choice</li> <li>If an emergency is lost, eating is forbidden to use</li> <li>The government must strive for halal vaccines as much as possible</li> </ol>	Haram-Permitted to Use	Fatwa Indonesian Ulema Council Number: 14 of 2021

From the explanation in the table above, it is known that according to MUI, the use of cell line and medium with serum from blood is not a problem as long as the ingredients that are haram and unclean are not found at the end of the product, known as *istihalah*. A natural process in which the material undergoes a transformation into another form so that its status changes, both changing its physical,

chemical and characteristics [33, 38]. Unlike the case with Sinovac (not using any pork ingredients), AstraZeneca uses Trypsin from pigs, for this reason the MUI through fatwa no. 14 of 2021 stipulates that the vaccine is haram but may be used temporarily due to an emergency. Even though the MUI has determined that the Sinovac vaccine is halal, the use of vero cells from African Green

Monkey (African Green Monkey) and FBS (bovine blood serum) for cell growth culture in the process is still being questioned by some scholars.

**e. Alternative Strategy and Materials for Vaccine Production**

The inability to provide truly halal vaccines is a challenge for industry and the Islamic world to provide alternative solutions. That is by replacing the ingredients that are haram with ingredients that are truly halal. If not, then it will forever be a very plausible reason

vaccines that are not really halal will be rejected by some people in Muslim-majority countries [39]. From the literature review above, it can be understood that the critical points of halal are contained in 3 main processes (Figure4). Namely the selection of the cell line, medium and vaccine formulation. Of the 3 processes, more attention must be given to efforts to obtain a halal cell line, medium and the addition of preservation, adjuvant, and surfactant. Therefore studies related to these materials need to be continuously developed and optimized.

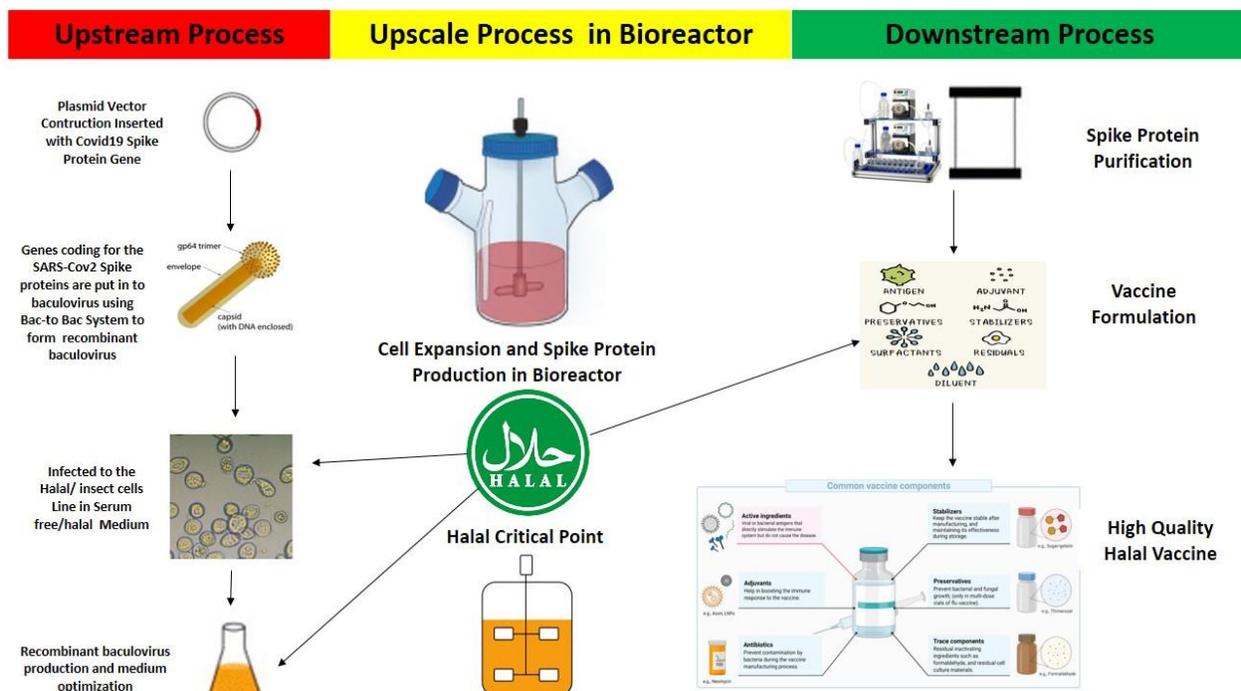


Figure 4. Halal Critical Point Proposed for Halal Vaccine Production

Among the materials that can be used as an alternative to the main ingredients for vaccines are (Table 5) Animal cell lines can be replaced with cell lines obtained by slaughtering according to animal laws that are halal to eat. It is also possible to use insect cell cultures [40] or Duck or Chicken Cell [41], even though animals are tolerated as halal. Meanwhile, blood serum from cows, horses or humans can be replaced with media without containing serum that has been widely

developed [42, 43]. Trypsin could be changed by Accutase [43, 44] and gelatin can also be substituted [41, 46] or developed from halal animals slaughtered according to sharia and stabilizers which can also be found along with the development of animal tissue culture technology

**Table 5.** Non-Halal Materials and Alternatives

Non-halal Material	Function in the process	Potential Substitute Material	Source
Animal cell line	Host cell, a place for virus propagation	Slaughtered halal animal cell, Insect Cell	40,41
Animal Serum (Bovine or Equine)	host cell growth medium	Serum free media	42,43
Pork Trypsin	cell detachmen t	Slaughtered bovine, Goat trypsin or Accutase	44,45
Gelatin	stabilizer	Slaughtered Cattle Bone, Cytopore, Cytolin	41,46

From the table above, we can understand that to produce a vaccine that is truly halal (Halal 100%), we must at least pay attention to the important ingredients used. Where the usual material has been used as main materials. Such as the type of cell used for culturing (cell line) (41), medium that still uses animals whose halal status is unclear (42, 43), trypsin enzymes (44, 45) and gelatin (41, 46) as stabilizers. So that research related to the discovery of alternative cell lines, media without serum, herbal trypsin and gelatin from halal ingredients needs to be carried out by Islamic countries and researchers who are experts and have the concern and obligation to solve halal- vaccine problems

#### 4. CONCLUSION

Efforts to develop vaccines that are truly halal are of course not easy and fast. It takes patience, persistence and continuous continuity as well as cooperation from all parties, both researchers, government and industry players. However, in the future, the halal market and public awareness about the importance of a true halal vaccine will certainly continue to increase, especially at this time the Muslim awareness of halal products is increasing by time as well as as quantity the fastest growing population in the world. Government budgets of hundreds and even thousands of trillions can be reduced by

developing new strategy to produce the halal vaccine. So that they are more efficient in the future, have export opportunities, and maintain national security in the health and economy aspect. The key of problem solution is the substitution of non halal to halal material in the vaccine production, from upstream to downstream processes, mainly the substitution of Animal Cell Line, Animal Serum, Trypsin (Enzyme) and gelatin (as stabilizer ingredients).

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