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ROLE OF WORLD HEALTH ORGANIZATION IN TECHNOLOGY TRANSFER AND CLINICAL EVALUATION OF VACCINE

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The Human body is prone to the infection and disorders of various diseases. A disease is an abnormal condition that affects the structure or function of part or whole of the body and is usually associated with specific signs and symptoms.[1] A disease may be caused due to coming in contact with an infectious pathogen or it may be a bodily disorder. In earlier times, the life span of humans remained short due to unavailability of treatment for diseases and disorders. But medical science has changed the course of society and played a vital role in securing human health. Among the treatment methods, the extremely useful and potent substance in curing a disease is vaccine. The vaccines are the substances that are most difficult to invent for any institution/organization or for any pharma company but if a vaccine is invented for a particular disease, the lives of millions can be saved by it. The use of vaccines against an infectious disease as a means to prevent the infection caused by the microbe may stop the biological tragedies like epidemics and pandemics. The continuous immunization programs against a particular disease may lead to its eradication. In order to recover the expenses caused during the invention of the vaccine, the inventor causes their vaccines to be patented which ultimately create obstruction in technology transfer of vaccines. Patented vaccines bring fortune to the inventing agency in the form of exclusive rights like licensing. Every licensing agreement to manufacture the vaccine may not come with the technology transfer of that vaccine leading to increase in the price of vaccine and hindrance caused in the access to vaccine. For every vaccine that is invented, clinical evaluations are required to be conducted in accordance with the guidelines and regulations prescribed by the WHO expert committee on biological standardization.

Keyword: Licensing, Immunization, Technology transfer, Vaccine, Microorganism

INTRODUCTION

WHO is a specialized international agency, recognised under Article 57 of the UN Charter, working in the field of health. With the objective as to "attainment by all peoples of the highest possible level of health", WHO acts as the health ministry of the world. WHO recognises "right to health" as the fundamental rights of every human being. Apart from WHO on health, the Universal Declaration of Human Rights (UDHR) stepped further and prescribes for the right to a "standard of living adequately for the health and well being"[2]. The

[1] Definition of disease on the website of national cancer institute, USA available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/disease, (Last viewed at 17-03-2023)

[2] UDHR under Article 25(1) "Everyone has the right to a standard of living adequately for the health and well being of himself and of his family, including food, clothing, housing and medical care and necessary social services".

right to health, ICESCR recognises, as the highest attainable standard of physical and mental health.[3] It doesn't matter in which document the right to health has been defined but it will always be the facts that the right to health, wherever defined, shall remain an inclusive right. In adherence to aforesaid international documents, member states are duty bound to protect their citizens in the best interest of securing human health.

The emergence of new infectious diseases and their transmission has become a crisis of international importance. New infectious diseases are emerging (e.g. COVID-19) and old known infectious diseases are re-emerging (e.g. polio virus). The emergence and re-emergence of infectious diseases are the outcome of natural factors or due to human factors. Naturally microorganisms multiply and under favourable geographical conditions evolve themselves into an infectious disease. Whereas human factors like population growth, green gas effect, deforestation and climate change are the leading cause for the emergence of new infectious diseases. The population growth of humans has resulted in the deforestation of forests landscape in order to develop more agricultural land to sustain the food demand of increased population. This deforestation had resulted in the entry of humans close to the early forested area thereby bringing the human close to the area once resided by the infected wild animals. The burning of fossil fuel has resulted in the increase of the atmospheric temperature causing the animals to migrate from their natural habit to the places suitable for survival. Humans and animals are together surviving on this planet Earth and humans are domesticating them for their efficient working skills and massive muscle power. A large part of human civilization relies on animals for their meat as the main course of diet. But this proximity of humans with animals has been one of the factors of zoonosis. An event where infectious disease that evolves inside the animal is transmitted to humans is called zoonosis. The recent COVID-19 pandemic is also presumed to be the result of zoonosis caused by bats.

Every vaccine that is invented to cure any microbial infection is the result of huge investment made by vaccine developers in the field of research and innovation. Every new vaccine is a technological marvel and is the outcome of long term scientific exploration. Thus the vaccine developers are found to be very particular about the protection of their intellectual properties. As per WIPO, from January 2020 to September 2022 total 7,758 patents were filed related to COVID-19 technologies where 1,298 patents are filed relating to vaccine development.[4] Thus patent of vaccines becomes one of the major issues in the technology transfer of vaccines. Although the patent does not cover reverse engineering but patent grants the vaccine developers the exclusive right relating to their intellectual properties. Thus the patent grants exclusive rights to the vaccine developer which may include selective licensing or the use of the vaccine to the exclusion of any other agency. Vaccine developers are also very cautious for the technology transfer as they do not wish to transfer technology to low income countries or to countries lagging in capacity building. Even if a vaccine developer agrees for licensing, the licensing agreement does not end in technology transfer and mere manufacturing rights are granted. And the biggest issue with technology transfer and patent rights is that the entire scenario is completely separated from the functioning of WHO thereby the organisation, despite being working in the field of health, is clueless about the number of technology transfer of vaccines, the drivers and the barriers associated with technology transfer.

The invention of vaccines and getting it prepared for safe use in public are two extremely different processes. It does not matter which substrate is used for vaccine invention/manufacture but what matters is the clinical evaluation of the vaccine. Vaccines brought to market without clinical evaluation can cause serious effects to persons taking them; even causing death. The vaccine trial on humans without his informed consent is a human right issue. Clinical evaluation of vaccines is a long process which involves multiple stages and includes involvement of animals and human volunteers. A vaccine which is properly evaluated and licensed by the National regulatory authorities (NRA) undergoes inspection of WHO prequalification programme. The WHO Prequalification programme inspects and review the novel vaccine and on being satisfied recognise it to be useful in the nations immunization programme. WHO works to control and eradicate the disease and thereby saves the lives of millions every year. The immunization programmes of WHO have ultimately reduced the impact of polio virus, otherwise half of the population of the world have been disabled. As per WHO, Smallpox is the first disease that is eradicated from this earth

[3] ICESCR under Article 12(1) "The state parties to the present covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health

[4] Exploring COVID-19 vaccine patent, WIPO: https://www.wipo.int/web/patent-analytics/exploring-covid-19-vaccine-patents (Last visited dated 14-04-2024)

VACCINATION AS POTENT TREATMENT

Vaccines are the immunity boosters that were introduced in the human body to develop the natural resistance/immunity against the disease so that when the body comes in contact with actual infection, the body of an individual can protect itself. This technique of introducing material under the skin to produce immunity against a particular disease became universally known as vaccination, A word derived from the latin word for the cow (vacca), in Jenner's Honour).[5] Vaccines are the most potent means to cure a disease whether of communicable or non communicable nature. The vaccines like COVIDSHIELD which was prepared within two years time was so potent that it had reduced the number of deaths caused by covid-19 and also immunized the people to tolerate other variants of the covid-19 as well.

The website of Jenner Institute mentions, "Jenner was born in Berkeley, Gloucestershire on 17th May 1749. In May 1796 a dairymaid, Sarah Welmes, consulted Jenner about a rash on her hand, He diagnosed cowpox rather than small and had confirmed that one of her cows, a Gloucester cow named blossom, had recently developed cowpox. Jenner took this opportunity and started testing on disease. Jenner chose James Phipps, eight year old son of his gardeners, to fit for the experiment. On May 14, Jenner made a few scratches on one of James' arms and rubbed into them material taken from one of the pockets from Sarah's hand. Within a few days, James became ill with the cowpox but was well again a week later. From the infection to Sarah and James, Jenner derived that cowpox could pass from human to human and from human to animals.The second step was to test and check whether cowpox protects James from smallpox. On 1st July Jenner variolated the james but he did not develop smallpox. Jenner conducted the experiment with many other people and in 1798 published his experimental research on the book named "an inquiry in the causes and effect of the Variolae Vaccine; A disease discovered in some of the western countries of England, particularly Gloucestershire, and known by the name of the cowpox'."[6]

SDG 3 "Good Health and Well Being" targeted to end the epidemic like AIDS, tuberculosis etc. and other communicable diseases by 2030. Although before COVID-19 pandemic till 2019, WHO identified that the leading cause of death globally, in ordinary course, is non communicable disease.[7] Thus WHO emphasizes on the vaccination target and disease eradication. Vaccination is an important step in which through vaccines immunity is developed in a human body prior to the actual infection. Vaccines developed for "human use" may be made using the categories of technologies mentioned as follows -

- Microorganisms inactivated by chemical/physical means that retain adequate immunogenic properties.[8]
- Living microorganism that are avirulent to human or have been selected for their attenuation whilst retaining immunogenic properties[9]
- Antigen extracted from organism, secreted by them[10]
- Antigen produced by recombinant DNA technology[11]

CLINICAL EVALUATION OF VACCINES AND WHO

Every drug/vaccine, before it is supplied in the market for public use, needs to undergo ethical clinical evaluations for gathering scientific data. Vaccines developers are required to conduct the clinical evaluations to gather scientific data about the vaccine safety to obtain license from national regulatory authorities (NRA) for supplying the end product in the market for the public use. The vaccine supplied in the market without clinical evaluation may be unsafe for the public and a single defective batch of vaccine can cause unprecedented health issues to the person taking it.

[5] About Edward Jenner, UK, available at https://www.jenner.ac.uk/about/edward-jenner, (Visited dated 17-03-2024)
[6] https://www.jenner.ac.uk/about/edward-jenner, (Visited dated 17-03-2024)
[7] https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death, Dated 29-02-2024
[8] 52nd report of WHO expert committee on biological standardization, Annexure 1, page 48, available at https://www.who.int/publications/i/item/9241209240, last visited date 18-03-2024
[9] ibid
[10] ibid
[11] ibid

One of the most technical works associated with the vaccine is the clinical evaluation of vaccines. It is significant to note that the clinical evaluations of vaccines need to be done in a standardized manner and it is more important to note that the vaccine trial shall involve good practices. A trial of a vaccine on a human being without the informed consent is a matter of human right violation which cannot be allowed to happen. Good practices, therefore, are an inherent part of clinical trials. Every clinical trial is conducted to collect scientific data about vaccines but this data collection may be insufficient or inappropriate when it comes to the supply of vaccines in the global markets. Thus WHO plays a vital role in providing assistance to the nation in standardisation of clinical trial. WHO through its expert committee on biological standardisation works in the direction of standardisation of clinical trials. As a committee established by WHO, ECBS provides recommendations and guidelines for the manufacturing, licensing and control of blood products and related in vitro diagnostic tests, biotechnology products and vaccines along with the establishment of WHO biological reference materials.[12] Thus ECBS, in its fifty second report, provided an outline of the scientific data which need to be collected at every stage of clinical evaluation of vaccines.[13] This fifty second report under annexure-1 specifically mentions that the guidelines are being provided at the request of the nationals regulatory authorities for their assistance in clinical evaluation[14]. The ECBS divided the clinical evaluation of vaccines into three stages: Developmental, Licensure and Post licensure.

DEVELOPMENTAL STAGE

The developmental stage consists of two parts -

1. Preclinical research and development
2. Clinical research and development

Preclinical research and development

The preclinical testing was conducted on the animals. The reason for using animals for vaccine testing is the responsiveness of animals toward medication. The preclinical research is a laboratory based testing conducted using either in vitro or in vivo method. The data collected from preclinical testing possess the scientific records showing the reasonable ground for continuing the vaccine development, hence the data of preclinical testing suggest the grounds for furtherance of vaccine development.

Clinical Research and Development

After the completion of the preclinical research, the vaccine researcher submits the scientific data of preclinical vaccine trials on animals to the national regulatory agency (NRA) seeking permission for the continuation of clinical trial of the vaccine. This stage involves controlled trial of a proposed vaccine on the human volunteers. The clinical trial (also called clinical research and development stage) is divided into three phases - Phase 1, Phase 2, Phase 3.

Phase 1 studies are primarily focused on the determination of clinical tolerance and safety of vaccines. Phase 1 studies are usually the studies in which the volunteer is well informed of the drug/vaccine administered and this study is not arranged with placebo control groups. Placebo is an inactive compound that exactly looks like the original drug that is to be administered in a volunteer. Thus the placebo control test group is not set up in the stage and the volunteers were administered with a new vaccine to check the vaccine toleration and safety of the vaccine.

Phase 2 provides for the determination of the immune response of the volunteers body against the active component(s) of the new vaccines and check the safety profile of the vaccine.[15] This immune response is

[12]WHO expert committee on biological standardisation: https://www.who.int/groups/expert-committee-on-biological-standardization#:~:text=The%20WHO%20Expert%20Committee%20on,with%20the%20establishment%20of%20WHO, (Last visited Dated 14-04-2024

[13] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 36, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)

[14] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 36-37, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)

[15] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 71, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)

determined on the various variables associated with the human body such as age, ethnicity, gender, pre-existing antibodies.[16] This phase requires involvement of a larger number of volunteers in the clinical evaluation and the relevant factors that are studied with reference to vaccine are immunogenicity, safety profile of vaccine, doses of vaccine, interval between two doses, number of vaccines to be administered and route of vaccine administration and the duration of the immunity etc.[17]

Phase 3 studies are primarily focused on the determination of data on vaccine efficacy and safety.[18] This phase demands a much larger number of volunteers for the purpose of clinical trials and the data is collected from the immunized population as well as from the vaccine failure persons at regular intervals.[19] This collection of data is done again and again to check the vaccine efficacy and safety

LICENSURE STAGE

A vaccine that is being developed after completing its clinical evaluation needs to get authorization by the National Regulatory Authority (NRA) of that country. The vaccine after authorization from the National Regulatory Authority reaches the WHO Prequalification programme, through dossier, to check whether the vaccine is safe to be used in nations immunization programme.

POST LICENSURE STAGE

This stage is also known as phase 4. After licensing from national regulatory authorities, when the vaccine is brought into the public use a routine surveillance is done for monitoring the vaccine for its efficacy, safety and quality referred to as postmarketing surveillance.[20] The purpose as prescribed by WHO is to study the performance of a vaccine in the large target population under conditions of routine use, to detect adverse reactions and to monitor efficacy and effectiveness.[21]

TECHNOLOGY TRANSFER OF VACCINE AND WHO

Technology transfer is the sharing of knowledge from those who own know-how to those who do not[22]. Thus technology transfer means transfer of knowledge from those countries which are good at invention to those who are not good at invention. Ordinarily, vaccines are developed after a huge monetary investment in the field of technology and innovation. Thus, developed countries with larger economic pockets are more prone to vaccine innovation. But innovation of vaccines and its accessibility in one part of the world does not end the health crisis and vaccine scarcity in other parts. Therefore, technology transfer is necessary for access to vaccines, cost affordability and for the consequential improvement in health. One such big issue faced by WHO with respect to technology transfer is the failure to have any regulatory mechanism/body which could keep a record of the number of vaccine technologies already transferred, who the "transferer was" and who the "recipients was" and what are the driving factors and what are the barrier in the technology transfer.[23] To resolve this problem, WHO has undertaken a project in partnership with "United Nations Conference on Trade and Development" and "International Centre for Trade and Sustainable Development" and "European Union".[24]

Vaccines are the most potent products to cure a disease. It may take several years to even several decades for the invention of a vaccine to cure a particular disease, and even more time to reach the market for

[16] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 71, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)
[17] ibid
[18] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 73, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)
[19] ibid
[20] 52nd report of WHO expert committee on biological standards, TRS 924, Annexure 1, Page 85, Dated 1-01-2002: https://www.who.int/publications/i/item/9241209240 (last visited on 13-04-2024)
[21] ibid
[22] Increasing access to vaccine through technology transfer and local production, Page 9, Dated 01-july-2011: https://www.who.int/publications/i/item/9789241502368, (Last visited on 28-02-2024
[23] Increasing access to vaccine through technology transfer and local production, page 9, Dated 1 july 2011: https://www.who.int/publications/i/item/9789241502368 (Last visited 14-04-2024)
[24] ibid

public use. The biggest problem with respect to vaccine accessibility and affordability is the investment incurred by the vaccine developer and the intellectual property rights. Usually, the vaccine developer gets their vaccine patented (under patent cooperation treaty) authorising the developer with a bundle of exclusive rights. When vaccines were invented by any entity, it was the entity that incurs the investment and ultimately decides the amount at which vaccines will be sold. Patent of vaccine and associated technologies assures the vaccine developer with the guarantee to the protection of their product from unwanted exploitation and to recover the cost that was incurred by the developer in the innovation of a new product. Patent of vaccine may bring fortune to the patentee. The patentee (i.e. vaccine developer) may license its patented vaccine at such terms and conditions which it may deem necessary in its interest. Vaccine developers may also share the marketing rights with interested persons at the conditions that suit the vaccine developer. As pointed out by WHO in its project, there are two identified models of technology transfer are -

1. The trend for technology transfer from industrialised countries to emerging and developing countries to be in the form of joint venture[25]
2. The trend for technology transfer is facilitated by the public sector to use centralised technology transfer hubs or platforms where a technology is established and multiple recipients can receive training.[26]

Prior to 1990, technology transfer of vaccines was in the hands of the government because the government companies and national health institutions were leading the vaccine market but this position changed with the decline in the government manufacturing capacity globally. Thus there is a rise of the private sector in inventing and manufacturing the vaccine. Thus many alliances also work in manufacturing and are beneficiaries of technology transfer of vaccines. Developing countries vaccine manufacturers network (DCVMN) is a public health driven alliance of vaccine manufacturers from developing countries that aims to make a consistent supply of good quality vaccines.[27] DCVMN members have been the recipient of huge technology transfers in the last few decades. Few are as follows-

- Measles, mumps and rubella vaccine from the institute of immunology, Zagreb[28]
- Hib vaccine from NVI[29]
- Meningitis A vaccine with PATH, WHO[30]
- COVID-19 vaccine through astrazeneca and Oxford University[31]

It is necessary to understand that vaccine invention and bulk manufacturing of vaccines are two different things. A large number of countries are good at vaccine innovation but they lack the capacity to manufacture vaccines in quantity to vaccinate the entire planet whereas on the other hand some are good at bulk manufacturing although they are not good at vaccine invention. The problem before the world is the profit deriving mentality of the organisation innovating the vaccine. The organisation and government who are “know how” usually don't agree to transfer technology to countries “do not know”.

CONCLUSION

WHO strongly presents itself at the international forum as the specialised agency of UN working in the field of health. The constitution of WHO binds the organisation with a broad spectrum of function allowing the presence of WHO in every circumstance associated with health. From naming the pathogenic disease till its eradication, WHO finds its authority over every aspect of health. WHO does not interfere in the local activities of any state until requested by the state to do so. Inference, WHO works as the recommendatory body. Although WHO does not find much authority when it comes to technology transfer of vaccines because

[25] Increasing access to vaccine through technology transfer and local production, page 16, Dated 1 july 2011: https://www.who.int/publications/i/item/9789241502368 (Last visited 14-04-2024)
[26] ibid
[27] Increasing access to vaccine through technology transfer and local production, Page 20, Dated 1 july 2011: https://www.who.int/publications/i/item/9789241502368, (Last visited 28-02-2024)
[28] Increasing access to vaccine through technology transfer and local production, Page 21, Dated 1 july 2011: https://www.who.int/publications/i/item/9789241502368, (Last visited 28-02-2024)
[29] ibid
[30] ibid
[31] ibid

licensing and patenting are the functions of patentee and WTO respectively. But since 2011 WHO had initiated a project in collaboration with the United Nations Centre for Trade and Sustainable Development and United Nations Conference on Trade and Development. This project aims at keeping the record of technology transfer, who the donor was, who the recipient was, what are the drivers and barriers in technology transfer.

Further, it can be seen that the World health organisation through its expert committee on biological standardization plays an eminent role in standardisation of clinical evaluation of vaccines. Vaccine developers need to get their product through a standardised clinical evaluation involving good practices set out by the WHO's Expert committee on biological standardisation (ECBS). Clinical evaluations were conducted clearly obeying the guidelines of WHO collecting standardised scientific data at every stage of trial. All clinical evaluations must be conducted in a standardised manner as set out by WHO and the results of clinical evaluation were used by national regulatory authorities for licensing the vaccines for marketing. Thus WHO's standardised guidelines keep a check on the clinical evaluation of vaccines assuring that the vaccines that are supplied in the market are safe for public use at large.

In the end it may be concluded that the WHO plays a great role in the welfare of humanity throughout the globe by taking steps to eradicate the various diseases causing alarm in the society