Fog over Covid-19 Vaccines in India
All-India Peoples Science Network (AIPSN) Position Paper
16 Dec 2020

Many new developments have come about in recent weeks regarding Vaccines against Covid19 both internationally and in India. These have raised some optimism, but also several concerns about vaccine politics, undue commercial influence and other extraneous factors playing out around the world and, specifically, in India. This Position Paper focuses chiefly on India, within the global context, whereas international dimensions have been dealt with in a separate Statement and the Indian response to EUA for vaccines was highlighted in another Statement.

AIPSN calls for a science-based, equitable and rigorously conceived nation-wide policy in India for development, manufacture and deployment of vaccines in a free, universal vaccination strategy against Covid-19 as discussed below.

1. Context and Status

Accelerated development and deployment of a safe and effective vaccine is crucial to combat the rampaging Covid-19 pandemic to protect individuals and enable full and safe re-opening of the economy and society. Access to free vaccination is essential for people's right to life and health, since the disease has a significant burden of preventable morbidity or serious illness and mortality or deaths. Though the proportion of infected persons who get serious disease is low, in absolute numbers the number of persons who are at risk is unacceptably high. Free vaccination is also necessary since it is low-income working people who have paid the maximum social costs of the lock-down and disruption of the economy, and because vaccine development has mostly been done with public funds. At the same time, a nationwide vaccination programme is a challenge and raises crucial questions including with regard to the preparedness of the public health system in India to deliver this without compromising other essential health services.

Internationally, some leading vaccine candidates have, in recent weeks, declared high levels of efficacy or effectiveness based on preliminary results from on-going Phase-3 clinical trials. US-German Pfizer-BioNTech and US-based Moderna have both declared efficacy of above 90% for their two-dose vaccines and applied for Emergency Use Authorization (EUA) in the US and Conditional Marketing Agreement (CMA) in EU. Both these vaccines are relatively expensive (at around USD 40 (Pfizer) and USD 70 (Moderna) for two doses) and, importantly, require very low temperature cold chains, adding to the costs and delivery challenges for India and other developing countries. At the time of writing, Pfizer has obtained a global first EUA in the UK and subsequently in Bahrain, Canada, and US.

UK-based Oxford University-Astra Zeneca, which is partnering with the world's largest vaccine manufacture Pune-based Serum Institute of India (SII), for mass production of its vaccine, has claimed average 70% efficacy across different modes and 90% efficacy at specific dosages. This double-dose vaccine is expected to be relatively inexpensive at around USD 6 and, significantly, can be stored at ordinary refrigerator temperatures, making delivery easier in India and other developing countries. SII has publicly claimed that it would be supplying around 300 million doses for India by mid-2021.

Russia's RDIF-Gamaleya Institute too has declared effectiveness of over 90% for its "experimental" Sputnik-V vaccine. The powdered version requires storage at refrigerator-like temperatures, while the liquid version has to be at -18 deg C. The vaccine is expected to cost about USD 20 for 2 doses. This vaccine is undergoing Phase-3 trials in different countries including India and is to be manufactured by Hetero Biopharma in Hyderabad.

China's Sinovac is being deployed widely in China and also in Brazil, and is gearing up for global supply when regulatory approvals are obtained, with a price tag internationally of around USD 60 for two doses and also requiring only refrigerator-like temperatures. Again at the time of writing, another China-origin vaccine from Sinopharm has been declared by the UAE as having 86% efficacy in Phase-3 trials in that country where it had been given EUA in September for front-line workers, but data from the trials are still not public.

These developments represent a significant achievement for science and medical research, because these promising results, however limited and preliminary have been attained in less than a year from the outbreak of the Covid-19 disease compared to the normally expected several years for vaccine development.

However, detailed data related to all these vaccine trials have not yet been published or peer-reviewed, which would bring out additional and important information such as effectiveness in different age-groups and segments of the population, prevention or reduction of severe illness and deaths, prevention of transmission, duration of immunity or protection etc. These properties may vary for different vaccines and may influence choices for deployment. Other vaccine candidates too are at various stages of clinical trials, and may similarly also obtain EUA over the next 3-6 months.

Therefore, questions have already been raised about how scientific, rigorous or transparent these EUAs have been. Both "vaccine nationalism" and commercial interests are known to be deeply involved, apart from panic response by governments in the face of failures to control the pandemic, as evidenced by pronouncements of government spokespersons in many countries including in India. The sharp rise of concerned company values in stock markets could also be contributing to the haste in these announcements.

In India, several indigenously developed vaccine candidates have also come to the forefront in recent weeks. Leading candidates are from ICMR/NIV-Bharat Biotech in Hyderabad, Zydus Cadilla in Ahmadabad and Gennova in Pune. There are already undergoing, or soon to start, Phase-3 trials and are expected to become available in early to mid-2021. Some other promising indigenous candidates are a few months behind. The Gennova vaccine, co-developed with HDT Biotech of the US and supported through seed funding by Department of Biotechnology (DBT), which has also supported indigenous development of some other vaccines, has recently received approval to start Phase-1 and 2 clinical human trials in India. This vaccine is of particular importance for future scientific and medical research in India since it is the first indigenous development of an mRNA (messenger RNA) vaccine, using a technology that may also be very useful for new-generation pharmaceuticals for treatment of infectious diseases and cancers.

After the Prime Minister's recent visits to and meetings with several of these companies to encourage them in their efforts, he is reported to have also instructed the regulatory agencies to facilitate the expedited approvals process. It is important that data from clinical trials for all these candidates are scientifically assessed without "vaccine nationalism," pressure from political or commercial interests, cronyism or favoritism and also meet high standards of efficacy and safety, especially since high efficacy percentages have been announced by leading international candidates.

2. Need for transparent, science-based trials and approvals

In this context, extraneous considerations do appear to be creating untoward interference in scientific processes involved in vaccine trials, assessments and expedited or emergency approvals with implications for deployment as well. There are indications, covered in the media and supported by several experts, that ongoing clinical trials for vaccine candidates are "designed to succeed" in several ways.

It may be recalled that the Director General, Indian Council for Medical Research (ICMR) had, earlier this year, written to all hospitals where clinical trials were underway demanding that they expedite results by 15th August this year, clearly to enable a grand announcement from the Red Fort. Fortunately, a massive outcry by scientists, medical professionals and civil society organizations brought about a retreat from this blatant attempt at pressurization. However, the danger remains in many ways.

Thresholds for efficacy or effectiveness (i.e. the percentage of infections the vaccine prevents), different aspects of efficacy as discussed earlier, as well as the sample size required for grant of EUA, may be lowered to enable vaccine candidates to more easily pass the test. While anxiety to roll-out an indigenous vaccine quickly through EUA is understandable for several

reasons, it is crucial that clinical trials and assessments of results are, and continue to be, conducted transparently by scientific-medical Data Review Boards independent of political and bureaucratic influence, and results be made public and, when completed Phase-3 trials, be published and subject to peer review. This is essential to build global and domestic public confidence in Indian-origin vaccines.

In this context, it is a matter of considerable satisfaction that the Subject Expert Committee (SEC) of the Central Drugs Standards Control Organization (DSCCO), at its meeting on 9th December 2020, has kept pending its consideration on the applications for Emergency Use Authorization (EUA) of Covid-19 Vaccines by SII and Bharat Biotech, and has asked for additional information. The regulatory agency Drugs Controller General of India (DGCI) was to have decided on grant of EUA based on SEC's recommendations. The SEC has, at least for now, rightly asserted its responsibility for scientific assessment of Covid vaccine candidates independent of political, bureaucratic or commercial interests.

The SEC decision has come against the background of considerable pressure from different levels of government, such as several recent public statements by the Health Secretary, Dr.V.K.Paul of Niti Aayog heading the National Task Force on Covid-19, and by DG ICMR. These officials pushed for a quick grant of EUA for these and other applicants, rather than respecting due process and scientific evaluation of data relating to safety and efficacy.

Urgency for approval and deployment of vaccines is no doubt important, but not at the cost of safety or potential impact in tackling the pandemic. More robust data would be available soon, providing opportunity to "hasten slowly". Self-reliance and encouraging indigenous research and manufacturing industry too are important, but sloppy or unscientific decision-making relating to public health will only damage the reputation of Indian science and regulatory processes, far outweighing any brownie points gained by rolling-out vaccination a few weeks early. Problematic EUA approval may also add to existing vaccine skepticism or hesitancy among the public.

The SEC and DCGI should therefore fearlessly conduct a thorough scientific assessment of available early data from Phase-3 trials in India or abroad, resisting pressure from different quarters. SEC/DCGI should also release the data based on which any recommendation is made so as to enhance transparency and secure the confidence of the scientific and medical community in India and internationally. This is especially crucial if India is to contribute to the global fight against the Covid-19 pandemic through its indigenously developed and manufactured vaccines. While granting EUA, it is also important to set up extensive surveillance of the vaccination programme, and to continue with rigorous Phase-III trials and peer review and publication of its data.

It must be also understood that, at this stage of development of different vaccines, it is not clear whether each vaccine is efficient at preventing infection, as distinct from preventing serious disease or mortality. It is also important to know whether infection can spread from persons administered specific vaccines, and the duration for which each vaccine protects persons. These specificities need to be taken into account for decisions on deployment. These unknowns at the present stage and the need to find answers them underline the necessity for continuation of clinical trials involving the larger numbers of enrolled volunteers, extensive post-vaccination surveillance and, importantly, continuing with all other public health measures of disease prevention and epidemic management.

The reputation of India's science, vaccine manufacturing industry and regulatory institutions depends heavily on such unbiased, rigorous and science-based assessments, since India could potentially emerge, now or in the future, as a major exporter of low-cost indigenously developed vaccines especially to other developing countries.

3. Free and Transparent Vaccine deployment strategy

Ruling parties in different States are making promises of free vaccines to all, especially in the run-up to State elections. The nation needs a science-based and nationwide policy on vaccine deployment to be implemented by States with additional measures if desired, keeping in mind, the phased availability of different vaccines. The National Task Force on Covid-19 headed by Dr.V.K.Paul of Niti Aayog recently announced a prioritization roadmap proposing to initially vaccinate health care workers, other frontline workers, security personnel and those above 50 years of age and persons with co-morbidities, amounting to an estimated 300 million persons, starting perhaps in March 2021.

A clear, well reasoned and long term vaccination roadmap is required, especially keeping in mind the different indigenous vaccines set to obtain regulatory approval in the near future. The policy needs to more definitively identify those included in the category of "frontline workers," how senior citizens and those with co-morbidities would be enumerated, address phase-wise coverage of the rest of the population especially children and young adults not mentioned so far but whose immunization against Covid is necessary for early and much-needed resumption of safe and regular in-person education. It is also important to specify which categories of the population, such as infants or the elderly, would be immunized using which vaccine, depending on the efficacy characteristics of available vaccines.

The Prime Minister in his televised address to the nation on October 20 assured that the government seeks to ensure "delivery of the vaccine to every citizen." However, the Health Secretary in the presence of DG ICMR stated

categorically that the government has never committed to universal vaccination which was in fact not necessary since the need is only to break the chain of transmission and obtain 'herd immunity,' and therefore the government may not vaccinate the entire population. It would, however, be extremely difficult to decide which sections to leave out of the vaccination programme and explain such a decision, since this would raise serious apprehensions of discrimination or injustice on different grounds.

Further, although achieving a threshold level of herd immunity (loosely estimated at 60% of the population) could prevent epidemic spread, the disease would still remain endemic in the country especially in population sub-groups, with significant numbers developing the disease and more limited outbreaks continuing in different parts of the country. Similar phenomena are seen in diseases like measles and diphtheria. The more skewed the demographic characteristics of the persons immunized, the less would be the braking effect of herd immunity.

In the Indian context, equity as a value and principle demands that those least able to practice social distancing, because of working and living conditions, need it most. All things considered universal vaccination may be the best option to prevent arbitrariness, real or perceived discrimination and emergence of a black market, besides enabling more robust and sustainable disease control.

A danger is that many Vaccine manufacturers in India and other corporate interests are already lobbying for the Government to allow delivery of vaccines by the private health sector at market prices to those who can afford to pay, as was done in Covid Tests and Hospital charges. Such a vaccine deployment strategy would, however, completely undermine equity and divert precious vaccine doses to privileged paying sections away from the vast poor underprivileged masses, and would also distort government procurement and equitable vaccination.

It is therefore essential that the Government of India announces a clear and transparent vaccination programme including a categorical and binding commitment to a programme of free universal vaccination with a fair and transparent policy of phase-wise prioritization for different segments of the population so as to ensure access to most vulnerable segments and marginalized sections.

4. Obstacles to domestic manufacturing and deployment

There is much confusion regarding the Indian government's participation in COVAX, the newly created global institution under the Global Vaccine Initiative (GAVI) and WHO. COVAX is funded by donor countries, corporate philanthropy notably the Gates Foundation and Wellcome Trust, as well as the 10% down payment from self-funded participating countries. COVAX has provided financing to different vaccine

developers and manufacturers in exchange for a proportion of vaccines produced, all through confidential agreements. COVAX also has agreements with participating countries to provide upto 20% of their vaccine requirement, for the duration of the agreement period which is now only till end-2021, with special arrangements for lower income countries. On the other hand, rich countries with 13% of the world's population have already purchased over 50% of the world's scheduled vaccine production and many other such bilateral agreements have been signed.

In this context, several Indian vaccine manufacturers who have agreements to manufacture leading vaccines developed elsewhere, would be bound by confidential agreements made with COVAX and also with their corporate partners as regards prices and supply schedules. Voluntary licenses granted by vaccine developers to Indian manufacturers prevent the latter from transferring the technology to other Indian companies or from exporting to countries not covered by COVAX. It would therefore be difficult for Indian vaccine manufacturers to scale-up vaccine production and supply to the levels required by India.

Government of India needs to work out how to overcome this problem. It is recommended that any agreements India signs with COVAX should be within an improved framework and its governance made more multilateral and democratic with a greater role for WHO, and removal of corporate influence. Government should also make public to the Indian people the terms and conditions of agreements with COVAX.

The government should urgently evolve and implement measures for scaling up manufacture of the most appropriate vaccines for our needs, through support to existing manufacturing units in private sector to expand their capacity and by encouraging public sector manufacture in this area irrespective of the vaccine being indigenously developed or licensed from international pharmaceuticals.

5. Strengthen the public health system

Finally it should be emphasized that the vaccination programme will require massive strengthening and mobilization of the public health system in India including for follow-up, monitoring of side-effects and efficacy. The capacity of current cold chain infrastructure is only about 50% of what is required even for the existing package of immunization. The human resources gaps are also huge. Procuring, storing and distributing and administering vaccines to close to 800 million more persons, even if phased is going to require considerable expansion of cold chains equipment, infrastructure, refrigerated transport vehicles, and skilled human resources at the field level.

Therefore any plan for vaccine deployment, must also make a firm and quantified commitment to increased financing of the public health system. In

the absence of such a commitment, the vaccination programme will suffer and other essential health services including child immunization would also be undermined by large scale diversion of existing public health resources.

6. AIPSN Demands

The Government of India needs to urgently undertake the following so as to ensure a safe, effective and free universal vaccination programme against Covid-19:

a) *Scrupulously monitor Phase-3 clinical trials for all indigenously developed vaccines and, after robust and independent scientific assessment of efficacy with peer review of trial results, grant Emergency Use Authorization within a definitive deadline within which such approvals can be applied for;*
b) *Rapidly scale up manufacturing capacity by recruiting and re-tooling both public sector as well as private sector manufacturing units for both internationally and indigenously developed vaccines;*
c) *Ensure transparency of agreements that Indian manufacturers have signed or may sign with COVAX/GAVI and Corporates. These may require further arrangements for systematic transfer of technology from international vaccine developers to Indian manufacturers to enable effective and rapid scaling-up manufacture and deployment in India;*
d) *Make public the basis of approval, including evidence reviewed, provide details of the protocol, process and timelines followed in investigating any reported severe adverse events (SAEs);*
e) *Make public the Government's stand on indemnifying vaccine manufacturers;*
f) *Actively advocate and lobby for declaration of all vaccines developed worldwide as global public goods and, if patents remain an obstacle, take steps to use compulsory licensing if necessary;*
g) *Bring out a white paper on the system and related costs for vaccine procurement and delivery, along with details of the expansion of public health infrastructure and human resources that would go with it;*
h) *Set up a Parliamentary Committee to oversee the implementation of the Covid-19 Vaccination programme in an effective, timely and equitable manner and a broad based Advisory Committee including representation of the scientific community and civil society organizations.*

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