Assessing Measures for India to Tackle Biowarfare Threats

23 April 2019
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This paper can be cited as "Naik, Shambhavi. "Assessing Measures for India to Tackle Biowarfare Threats." Takshashila Discussion Document, April 23, 2019-03."
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Summary</td>
<td>3</td>
</tr>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>The Emerging Biological Weapons Threat</td>
<td>6</td>
</tr>
<tr>
<td>Treaties Preventing the Use of Biological Weapons</td>
<td>12</td>
</tr>
<tr>
<td>India and the Biological Weapons Threat</td>
<td>23</td>
</tr>
<tr>
<td>Policy Recommendations</td>
<td>25</td>
</tr>
<tr>
<td>Conclusion</td>
<td>29</td>
</tr>
<tr>
<td>Appendix I: Articles of the Biological Weapons Convention</td>
<td>30</td>
</tr>
<tr>
<td>References</td>
<td>35</td>
</tr>
</tbody>
</table>
Executive Summary

Gene editing, synthetic biology, and improved delivery systems have reinvigorated the attention to biological weapons. Furthermore, the Biological Weapons Convention has repeatedly failed to agree to a verification mechanism, giving rise to suspicions that state actors may still be experimenting with biological weapons. Further, non-state actors have also dabbled with biological weapons, with isolated reports of incidences in recent decades.

This discussion document assesses three major impacts of new technologies on biological weapons. Firstly, increased access to scientific methods, resources and reduced barriers to scientific expertise has led to the proliferation of bioweapons to non-state actors. Secondly, advanced knowledge of biology and programmable-delivery weapons has converted biological weapons from a weapon of mass destruction to a covert targeted weapon of tactical importance. Finally, in light of these developments, existing preventive measures have become inadequate to curb the threat of biological warfare.

This discussion document recommends:

1. Key measures – such as improved surveillance mechanisms, education and inculcation of industry biosafety standards – need to be adopted to protect Indian citizens, flora and fauna and the economy from potential external and internal attacks.

2. India must stay prepared for a potential biological attack given our geopolitical situation and vulnerability to infectious disease outbreaks. A robust healthcare programme, improved diagnostics and quick responses to outbreaks is required for India to build effective bio-defence capabilities.

3. Collaborations with international partners for sharing resources/expertise to create an effective programme will help India fend off disease outbreaks – both natural or of man-made origin.

4. Finally, India needs to take a lead at the Biological Weapons Convention to ensure stricter action against non-compliant countries and create a mechanism for mandatory reporting of activities related to technology with dual purposes.
Introduction

Over the past century, weapons systems have evolved in concert with humankind's understanding and mastery over the sciences – physics, chemistry and biology. Nuclear weapons, and other advanced weapons and delivery systems have brought far-flung targets closer. While debate of arms and potential disarmament rages on, biowarfare remains the one arena where most countries have signed up to not only disallow use, but even destroy their own arsenal. In a landmark announcement in 1969, the President of the United States, Richard Nixon, addressed the world with his intention to eliminate all existing US stockpiles of biological weapons. Major powers including UK and Russia followed suit under the auspices of the Biological Weapons Convention which came into force in 1975. No intentional use of bioweapons by a state has been known to occur since then.

But does this stand to change with the advent of new gene editing technologies such as CRISPR which can potentially transform bioweapons from a weapon of mass destruction to a targeted killing system?

This discussion document briefly studies the history and development of biological weapons, the impact of recent technological advances on the field, the Biological Weapons Convention and related treaties, and the threat of bioweapons to India and the means of strengthening bio-defence capabilities of India.
Definition

A biological weapon can technically be anything of biological origin that could be used to harm another living thing – may it be an individual, a population of humans, animals or agriculture. The exact definition of biological weapons is open to multifarious interpretations and this discussion document uses the term biological weapons as defined in the Biological Weapons Convention:

“(1) Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.”

Bioweapons can be of different origins – bacteria, virus, fungi, or toxins. Insects can also be used as bioweapons and are covered under the Biological Weapons Convention\(^5\). While weaponisation of lethal organisms such as Anthrax or Ebola is easy to ban, decisions to ban research on relatively harmless organisms that could lead to biowarfare agents are difficult to make. Such research applications are usually considered on a case-by-case basis: for example, the US had put a moratorium on research involving gain-of-function mutations that can make infectious agents more pathogenic\(^6\). Scientists routinely perform gain-of-function research to create highly virulent forms of the pathogens and test vaccines against such agents. The ban ended in December 2017 following multiple pleas from scientists\(^7\). The dual nature of research using biological agents makes it difficult to create a precise definition for the storage and use of biological weapons.
The Emerging Biological Weapons Threat

Bioweapons are not only a threat to human life but also can be used to harm agriculture and animals in a bid to cripple economies or starve human populations. The threat to agriculture is more pronounced because the widespread use of gene editing in creating better plant varieties\(^8\) has created tools and knowledge that make impacting plants easier. In 2018, concerns\(^9\) were raised about the DARPA-sponsored Insect Allies Program\(^10\) - a program meant to respond to natural agricultural requirements by using insect vectors to deliver engineered plant viruses that can deploy gene editing tools to modify the plants. The knowledge to create tools to modify plants to fight drought or pests is still being canvassed; and the use of technology developed through Insect Allies Program is currently very limited and requires fine-tuning. However, the technology can be easily usurped to deliver pathogenic viruses or viruses to adversely affect the plant system. The usurper would only need to change the cargo that the insects will deliver - a pathogenic virus instead of a courier. This abuse of the technology could be harnessed quicker than its peaceful purpose. Yet the discussion of agricultural threat is often neglected and does not receive as much attention as threats to human health.

However, with the availability of multiple options, the target of a bioweapon will depend on the outcome desired by the perpetrator. Bioweapons could be used for the following purposes:

1. For mass killing of human populations
2. For infecting human populations leading to lowered human productivity.
3. For destruction of natural resources - agriculture or drinking water.
4. To cause panic, disrupt peace or divert responders/armed forces
5. To take out targeted individuals in an unsuspecting manner.

Though the use of bioweapons is currently banned, they have been used before and several countries are known to have created bioweapons arsenals particularly in the wake of the World Wars. In the next section we will briefly overview the history of bioweapon use.
Short History of Biological Weapons

The use of bioweapons is not new. Bioweapons have often been used in addition to chemical and traditional weapons in warfare. Early Persians, Greeks, and Romans were known to use infected arrows or contaminate wells.\textsuperscript{11, 12} During the Second World War, Japan used plague-infested fleas in Manchuria, China\textsuperscript{13}. Germany was also rumoured to have weaponised biological agents; but even if they did, they were never used in actual war\textsuperscript{14}. USA, Russia and UK also weaponised biological agents, sometimes experimenting on unsuspecting human populations. In 1966, the US for example, trialled the spread of biological agents by releasing a (then considered) harmless variant in the New York subway\textsuperscript{15}. The US “germ warfare testing” programme lasted for 20 years – from 1949 to 1969 – and involved 239 field tests.\textsuperscript{16} In 1942, UK released anthrax on the Gruinard Island for testing its retaliatory power in case Germans attacked with a bioweapon\textsuperscript{17}. This experiment left the island in a state of quarantine for 48 years during which decontamination processes were conducted. An accident at a factory in Russia released pathogens raising suspicion that although Russia was a signatory to the Biological Weapons Convention, it continued harbouring weaponised biological agents.\textsuperscript{18} In 1995, Iraq admitted to have created bioweapons using anthrax, botulium toxin, and aflatoxin and prepared bioweapons filled Scud-variant missile warheads, aerial bombs and aircraft spy tanks before the Gulf war\textsuperscript{19}.

In the last few decades, there have been a few incidents of non-war related use of biological weapons. Most of these attacks have been carried out by non-state actors. Notably, in 1984, 751 people were intentionally infected\textsuperscript{20} with Salmonella in Oregon, USA by members of Rajneeshpuram, who were devotees of Sri Bhagwan Rajneesh in a bid to manipulate local elections. In 1994, members of the Japanese cult group Aum Shinrikyo attempted to disperse aerosols of anthrax from their headquarter building near Tokyo, but that attempt failed\textsuperscript{21}. In 2001, anthrax was mailed through the postal system to many members of US government leading to five deaths.\textsuperscript{22} In June 2018, German police foiled a possible bioweapons attack using ricin\textsuperscript{23}.

Bioweapons hold much appeal to both state and non-state actors in addition to other weapons. Bioweapons offer two advantages over traditional weapon systems:
1. **They are easy to mass-produce:** Unlike nuclear and chemical weapons, biological weapons do not need to be stored in huge quantities; they can be easily mass-produced at short notice. Thus, storage costs and precautionary measures are minimal for biological weapons.

2. **Stocks can be easily destroyed and restored:** In the event of inspection, a miniscule quantity of the stock bioweapons can be retained and regrown if required, making it easier to escape scrutiny. Thus, bioweapons need not be stockpiled in huge quantities.

Yet, there has been no official state-mediated use of biological weapons in the past 80 years. Potential reasons for state actors refraining from the use biological weapons are:

1. **Biological weapons are difficult to control:** The use of biological weapons can lead to mass casualties on both sides of war. Unlike conventional weapons which can directed against the enemy, biological agents can multiply and not differentiate between friend and foe in a conflict.

2. **Biological weapons are difficult to deliver:** Biological weapons have been easy to make and store – yet their delivery is not easy. The high temperatures of missile explosions will typically kill any biological agent transported with it. This restricts the use of biological weapons depending on human transport and presence behind enemy lines.

3. **The fear of biological weapons utilisation by non-state actors:** Most technologies can be usurped by non-state actors who could use the technology for their own benefit. For instance, while the adoption of nuclear weapons is difficult due to the high cost and scrutiny of raw materials, it is easy for non-state actors to procure raw materials for developing biological weapons. The scooping of this technology also drove the US to announcing the shutting down of its own biological weapons programme.

Biological weapons are slow acting and most would take a few days to take any effect on enemy forces.

They are also unpredictable, i.e. the extent of damage is difficult to anticipate making their use unreliable in any tactical capacity.
Despite the many limitations, as regulation over other weapon systems gets tighter, the experimentation with biological weapons may gain traction. Further, new technologies such as gene editing, artificial intelligence, and robotics can help mitigate some of these restraining factors. The advances in knowledge of human, plant, animal and microbial biology has also revealed vulnerable points that could be easily targeted using biological agents. Moreover, given the persistent threat of bio-weapons, countries have invested in bio-defence capabilities and continue to monitor possible deployment of biological agents.
Known Biological Weapons

The U.S. National Institute of Allergy and Infectious Diseases has compiled a list of emerging threats. This list is primarily comprised of infectious agents that attack humans. Infectious agents can be highly lethal and have been the primary targeted for weaponisation.

There are 3 categories of biological weapons:

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<th>Category</th>
<th>Properties</th>
<th>Diseases</th>
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| A        | can be easily disseminated or transmitted from person to person; result in high mortality rates and have the potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness. | **Anthrax** (*Bacillus anthracis*)  
**Botulism** (*Clostridium botulinum* toxin)  
**Plague** (*Yersinia pestis*)  
**Smallpox** (variola major)  
**Tularemia** (*Francisella tularensis*)  
**Viral hemorrhagic fevers**, including  
**Filoviruses** (*Ebola*, *Marburg*)  
** Arenaviruses** (*Lassa*, *Machupo*) |
| B        | are moderately easy to disseminate; result in moderate morbidity rates and low mortality rates; and require specific enhancements of CDC’s diagnostic capacity and | **Brucellosis** (*Brucella* species)  
Epsilon toxin of *Clostridium perfringens*  
**Food safety threats** (*Salmonella* species, *Escherichia coli* O157:H7, *Shigella*)  
**Glanders** (*Burkholderia mallei*)  
**Melioidosis** (*Burkholderia pseudomallei*) |
enhanced disease surveillance.

<table>
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<tr>
<th>Pathogen</th>
<th>Description</th>
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<tr>
<td>Psittacosis</td>
<td><em>(Chlamydia psittaci)</em></td>
</tr>
<tr>
<td>Q fever</td>
<td><em>(Coxiella burnetii)</em></td>
</tr>
<tr>
<td>Ricin toxin</td>
<td>from <em>(Ricinus communis)</em> (castor beans)</td>
</tr>
<tr>
<td>Staphylococcal enterotoxin B</td>
<td></td>
</tr>
<tr>
<td>Typhus fever</td>
<td><em>(Rickettsia prowazekii)</em></td>
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<tr>
<td>Viral encephalitis</td>
<td>(alphaviruses, such as eastern equine encephalitis, Venezuelan equine encephalitis, and western equine encephalitis)</td>
</tr>
<tr>
<td>Water safety threats</td>
<td><em>(Vibrio cholerae, Cryptosporidium parvum)</em></td>
</tr>
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Many of these agents are emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; and potential for high morbidity and mortality rates and major health impact.

Emerging infectious diseases such as Nipah virus and hantavirus

Many of these agents are naturally occurring and have been known to cause disease outbreaks and/or epidemics. It is often impossible to distinguish a biological weapons attack from a natural disease outbreak, except in cases of diseases such as small pox which are no longer found in nature.

However, given the morbidity of these weapons, the difficulty to exert control and the likelihood that the technology might be used by non-state actors in one’s own
Treaties Preventing the Use of Biological Weapons

The first treaty that banned the use of biological agents was signed in the aftermath of the First World War. The Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or other Gases, and of Bacteriological Methods of Warfare, or the Geneva Protocol prohibited the use of germ-based warfare in international armed conflicts. While this treaty effectively banned the use of bacteriological methods of warfare, it did not take into consideration the production or storage of weaponised biological agents.

In 1972, British representatives put out a draft for a biological weapons convention which would address the development and stockpiling of biological weapons in addition to their use. The Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (or Biological Weapons Convention (BWC)) or Biological and Toxin Weapons Convention, (BTWC) came into force in 1975 with twenty-two signatories, becoming the first multilateral disarmament treaty banning the production of an entire category of weapons.

The US joined the treaty in 1969 with President Nixon ordering the destruction of all US stockpiles of biological weapons. Many political and strategic reasons pushed this step – biological weapons were not as tactically useful as other weapon systems and the US had realised that the acquisition of such weapons by other hostile countries could threaten public safety in the US main land.

Through XV articles, the Convention empowers states to prevent the development of bioweapons on their own territory and increases cooperation between member-states for responding to potential weapons use.
Articles of the BWC

This section provides a brief overview of the Biological Weapons Convention. The detailed text can be found in Appendix I.

The Convention broadly bans the storage of biological agents and toxins unless they have been diverted to peaceful purposes. It prohibits the transfer of any bioweapons technology or resources and empowers state parties to take necessary measures to prevent weapons development in their jurisdiction. The BWC encourages cooperation between its state-parties – to formulate best practices and to assist in case of an epidemic outbreak. There is also a mechanism for countries to lodge complaints against other states on the suspicion of a bioweapons convention violation and stipulates the accused state party has to cooperate with the investigation. Finally, the BWC encourages peaceful use of biological agents and transfer of technology and resources for development of useful applications.

The Convention currently has 182 state-parties and 5 signatories - Egypt, Haiti, Somalia, Syria, and Tanzania. Ten states have neither signed nor ratified the BWC - Chad, Comoros, Djibouti, Eritrea, Kiribati, Micronesia, Namibia, South Sudan, Tuvalu and most notably, Israel. While the Convention could be assessed to have been largely successful given the absence of any major bioweapons use, the Convention itself has come under severe criticism.

Criticism of the Biological Weapons Convention

The main criticism of the Convention is the lack of a verification process that confirms whether or not member states are developing new or have destroyed existing stocks of bioweapons. This lack of verification means that member states have to voluntarily affirm their compliance to the convention and attest to the absence of biological weapons in their territories. The accident in Russia provided evidence that countries, though signatories to the BWC, may still be researching bioweapons. As many as 12 countries including Iraq, Iran, Libya, China, Russia, and North Korea, who are parties to the Convention, are thought to have an ongoing bioweapons programme.

There are two main factors responsible for failure of verification:
Technologies used in biological weapon development are dual use in nature. Technologies used for bioweapons could also be used in biological research and particularly vaccine research and the production process utilises many of the same processes as bioweapons. Thus verification mechanisms would thoroughly examine the intent for facilities and it would be easy for any violator to mask any untoward activity.

Member states have failed to come to a consensus on a verification mechanism. Given the dual nature of the technologies and their use by pharmaceutical companies, there has been resistance from many commercial ventures who don’t want inspectors coming around to investigate their trade secrets or patented products under the guise of checking for potential bioweapons. In 1994, VEREX group formulated a 21-point verification measure, but political negotiations over this mechanism failed in 2001 and has not been revisited.

In the absence of a verification instrument, the biological weapons convention is considered to be toothless and ineffective at curbing the development of bioweapons. Even the voluntary confidence-building measures which require member parties to voluntarily exchange information on vaccine production plants, biodefence programs, and unusual disease outbreaks have seen little active participation. From 1987 to 1995, only 70 of the then 139 member states of the BWC submitted data declarations, and only 11 took part in all rounds of the information exchange.

Another recurring criticism is that the language of the Convention, particularly the definition is ambiguous and open to various interpretations. For example, the definition bans the use of agents or toxins in quantities that have no justification for prophylactic, protective, or other peaceful purposes. However, there is no clarity on what quantities are justified or what accounts for peaceful purposes. Many biological agents are held for purposes of bio-defence – to create vaccines or diagnostic kits for detection. The WHO still continues to keep reserves of smallpox virus in laboratories in Russia and US for global security reasons. This makes distinguishing between the peaceful and harmful uses of biological agents or toxins more difficult. This is further complicated because unlike nuclear and chemical weapons, biological weapons can be easily multiplied to a desired amount from a small starting stock. They need not be necessarily stocked at quantities required for offensive purposes, making the true intent behind possessing even minute amounts questionable.
Finally, the Convention does not have enough infrastructure to perform its duties. For example, the Secretariat of the International Atomic Energy Agency consists of a team of “over 2,500 professional and support staff” and the Organisation for the Prohibition of Chemical Weapons\textsuperscript{29} staff number around 500, while the Biological Weapon Convention’s Implementation Support Unit (ISU) consists of three people (with some additional support through the European Union)\textsuperscript{30}.

The biological weapons convention’s eighth expert’s meeting was held in November 2018 to address concerns over the increased use of genetic editing and its potential exploitation in creating dangerous biological weapons. The next section surmises the impacts of genetic editing on the various articles of the biological weapons convention.

**Biological Weapons Convention Under a CRISPR Lens**

CRISPR is the latest technology that has made gene editing cheaper and more precise. Further, the expertise required for carrying out gene editing via CRISPR is easy to obtain. Already DIY kits for CRISPR at home have been advertised in the market. Further, our knowledge of genetics – microorganisms, human, animal and plant – has increased manifold in the previous decades. Extensive research on gene editing -delivery systems to deliver gene therapies in humans to genetically editing plants through air sprays of virus -has led to efficient tools that can quickly cause gene modifications (albeit not always correctly) across a range of species. In the hands of scientists – in state or non-state capacities – CRISPR is a remarkable tool that can be experimented with to create a superior weapon or to create a tailored weapon that can pick out specific gene sequences to lethally target someone.\textsuperscript{31} In this broad context, CRISPR has few immediate ramifications to consider\textsuperscript{32}:

1. Bioweapons of the future may be created so that they do not impact the host country’s own forces – so far the biggest deterrent to biological warfare has been the fear of repercussion on the attacking forces. The unreliability and unpredictability associated with the release of a biological agent has been an unsurmountable confounder that has so far prevented effective use. However, now with an advanced and readily available technology coupled with increased understanding of disease pathologies, it may be possible to create weapons and antidotes for specific applications. Thus, a bioweapon attack may be possible while keeping the attacker’s own
forces immune to the attack. Even stopping the released agent from further mutating may become possible, thus precluding the risk that the agent may transform naturally.

2. Bioweapons may be tailored to impact specific varieties of crops or animals that provide sustenance to enemy forces - With increased understanding of how plant, animal and micro-organism genomes work and interact, it may now be possible to manipulate weapons that could target certain plant or animal species, crippling the country’s economy or depriving the population of food. The ecosystem devastation that such a move would cause is obviously dread-worthy.

3. Bioweapons may be tailored transforming them from a weapon of mass destruction to a tool for sabotage – As more humans get genetically tested for presence of mutations, we are also determining which mutations may be present in specific groups of people. The DNA of a person could also reveal a lot of information about that person, including potential susceptibility to diseases or unique sequences that could be targeted to gene editing without affecting other people. Agents developed with such purposes could be used on specific ethnic populations or even on individual targets, perhaps averting a large-scale traditional war. Even if designer bioweapons seem distant, viruses could be engineered to deliver gene editing tools that could permanently turn on or off some genes. Such a tool could also have disastrous consequences for the victim and may remain undetectable to an undiscerning medical establishment. While such technologies may be still a few years away, defence options would be certainly limited and greater regulation is needed to ensure such weaponised bio-agents are not created.

CRISPR will also bring to front the following implementation challenges for the biological weapons convention:

1. **Identification of bioweapons use**: Many microbial agents are found in naturally occurring reservoirs and are in a constant flux of changing their genetic code. Thus, a minor acquisition of a code that could turn a relatively mild agent into an aggressive one could happen accidentally in nature and cannot be easily designated as an intended malicious change. Similarly, consider something like the hepatitis infection – a taxing infection, but one that does not spread easily from person-to-person. Now consider that the
hepatitis virus were to gain the capability to transmit in an airborne manner like the common cold, and these changes could occur either naturally or intentionally be introduced via human efforts. With the genetic manipulation tools that were available so far, any intentional changes could have been easily identifiable through genetic studies. However, with CRISPR, it would be difficult to detect artificially-induced changes rendering it impossible (if done cleverly) from evolving natural outbreaks. Further, exploiting advances in synthetic biology, highly pathogenic agents could be engineered indigenously with the requirement of minimum biological raw materials. This would make follow up action and determination of a perpetrator difficult precluding the convention from effectively curbing the use of bioweapons.

2. **Need for lesser quantities and delivery modes**: In Article I, the convention states that biological agents in “quantities that have no justification for peaceful purposes” should not be stockpiled. However, with genetic manipulation, biological agents can be made more virulent and pathogenic – thus decreasing the amount of the agent required to create a similar impact. The convention needs to clarify the quantities clause to remove ambiguity in its meaning. Further, viral vectors are being developed for administering gene therapies, but these can also be re-purposed for delivering bio-weapons targeting humans and agriculture. Through genetic screening, it may now become possible to identify individuals such as Typhoid Mary who are themselves immune to a certain disease and convert them into carriers, capable of spreading a disease in a target population without it affecting the host. Improved diagnostics and quick healthcare responses are required to prevent the rapid onset of disease and for identifying its source. Further, states also hold limited quantities of infectious agents for bio-defence research. It is unclear whether or not these quantities and the associated research would fall under the purview of the convention. Additionally, CRISPR is being pursued to engineer changes in species which can inherit and quickly spread the modified gene in a population. Originally aimed for reducing the population of malaria-transmitting mosquitoes, the technology can be easily adapted to other species, making the demise of the entire species relatively simple. However, such systems are slow and still unpredictable. The Insect Allies Program is much more adept at targeting a large population of crop systems and incites further investigation as a bioweapons threat.
3. **Technology transfer**: CRISPR has already been widely used in various model systems (humans, animals, plants, micro-organisms) and the expertise required to perform CRISPR can be obtained without extensive experience. The ease of use has raised concerns that non-state actors may also try to usurp the technology for creating their own biological weapons. On the other hand, there is a need for the technology to be made accessible given its vast therapeutic and agricultural potential. Thwarting the technology is not a viable option and unlike nuclear weapons, there are no critical gene editing components which can be controlled via their supply chain. Thus the transfer of technology for peaceful purposes remains a priority and in the absence of stringent monitoring the same technology could be re-purposed for creation of bioweapons.

**Gene Editing Changes the Process of Biological Weapons Development**

Gene editing changes not only the severity of biological weapons, but also the process for biological weapons development. (adapted from 34)

How recent technology advancements are altering the process for bioweapon development:

**Step 1: Access to pathogens:**
Typically, in most biological weapons development, the intended perpetrators have accessed biological agents through scientists or technicians working in life science laboratories who may possess such agents for research purposes. However, as gene editing becomes cheaper, it may be easy to manipulate relatively harmless microorganisms that can be easily obtained from local natural sources. This would reduce dependency of attackers on obtaining biological agents from other certified spaces. With synthetic biology advances, it may be possible to create biological agents from basic raw material (DNA, etc.) further reducing the requirement for a harmful biological agent\textsuperscript{35}.

**Step 2 Technical information:**

As mentioned before, CRISPR itself is a fairly simple process. Further, much of the technical knowledge used to be earlier published in pay-walled and closed journals; however, in the recent decades, open access policies and pre-print archives have put much knowledge in the open space. This is of course much needed; the availability of knowledge is the bedrock on which further innovation can be based. However, the same knowledge can also be misused to create hazardous biological agents. This is particularly true when whole genomes are published in an open domain for anyone to use.

**Step 3 Resources:**

Previously the development of bioweapons was contingent on the presence of specialised equipment that were costly and difficult to procure. Further, there was a need to protect oneself while handling hazardous agents in large quantities. With increased pathogenicity and virulence, biological agents can now be handled in smaller quantities. Further, advances in biomedical technology has significantly improved equipment and techniques that can be used to achieve similar outcomes. Equipment like thermal analysers can be easily bought locally and most do not require any specific license that can monitor users. Many of the equipment are multi-purpose making it impossible to track their usage.

**Step 4: Create and grow Biological weapon**

Innovative ways of creating biological weapons have been opened by the advent of gene editing technologies and their delivery methods. A viral vector could easily be re-purposed to deliver targeted gene editing tools that could edit the genome of a specific individual. The biochemical expertise that was earlier required to
handle and manipulate biological agents is quickly being replaced by easy-to-obtain knowledge and off-the-shelf tools, making biological weapons one of the cheapest and dirtiest of weapon systems of all.

**Step 5: Weaponise**

One of the major issues with bioweapons delivery was the creation of airborne transmissible biological agents.

However, controlling many of these factors is now possible with advances in gene editing and other related technologies. Weaponising biological agents or creating newer delivery systems is simpler, particularly because of the massive research being undertaken to help improve delivery of gene therapies.

**Step 6: Disperse:**

All the changes to step 1 to 5 result in an agent that can made in small quantities, in a local lab without much expertise thus decreasing the costs for dispersal.

Overall, recent technological changes have made biological weapons an attractive weapons system that could be utilised by either state or non-state actors.

**Biological weapons prospective uses by state or non-state actors**

So far, biological weapons have only been considered the prerogative of state actors who have the wherewithal of deploying biological agents as a weapon of mass destruction. However, with the democratisation and popularisation of science and the significant cost reduction of technologies has made biological weapons as a viable option for non-state actors as well. Below, we consider the incentives and possible motives for state and non-state actors to engage in biological warfare.

As has been noted throughout this document, biological weapons have clear advantages over nuclear or other traditional weapons. As opposed to chemical weapons, only a tiny amount of biological agent could replicate to have devastating effects. Significant amounts of chemical weapons on the other hand would be needed to create the same impact.
Understanding motivations for biological weapons use

State and Biological Weapons

Most countries are participants in the biological weapons convention, yet in the absence of a robust inspection and verification process, it is difficult to confirm that these countries do not possess any bioweapons. The state governments do have a considerable reputation costs to bear and further economically sanctioned by other countries if caught perpetrating a biological weapons attack. As a weapon of mass destruction or in traditional armed conflict, conventional weapons are likely more useful for a state’s activities.

However, the possibility of using gene edited bioweapons as a targeted weapon against key individuals or groups of people may appeal to the state. This is particularly applicable since it would be impossible to track the culprit if an appropriate pathogen is used. Further, while a state has to invest copious funds on maintaining a nuclear arsenal, a bioweapons facility would be minimalist in nature. Stocks could be easily destroyed and replenished when required.

The use of biological weapons in taking out key individuals may avert or delay full-fledged armed conflicts and be in the nation’s interest. This is a key facet of the biological weapon’s convention which allows member-countries to leave if they deem using biological weapon is in their national interests. While framed as a measure against the use of biological weapon as a weapon of mass destruction, the convention now needs to take cognisance of the fact that perhaps a specified, limited, and defined use of biological agents may be in a government’s self-interest.
Non-state actors and biological weapons

Many non-state actors have been known to dabble with biological weapons yet the expertise needed so far to create any consequential weapons has eluded them. However, in the current scenario, bioweapons may be an attractive avenue for non-state actors. They are cheap to make, relatively easy to procure and in many religious contexts, have been justified by the occurrence of disease as a destroyer of the sinned in various texts. Finally, disease is an excellent way to strike fear and panic in a population; which is usually the goal of non-state threats.

Since these actors have no reputational worries and are not even party to the biological weapons convention, the likelihood of these people carrying out a mass attack is higher. The panic that sets in with an infectious disease is likely the outcome non-state actors would aim for.

Thus while both state and non-state actors might find biological weapons appealing, they are likely to use them for different purposes. A review needs to be made to discuss if non-state actors should be legislated under the convention or if targeted use of bioweapons should be included in the convention's remit.
India and the Biological Weapons Threat

India has so far not had any major bioweapons attack on its territory. However, the consequences to India if a threat emerges are higher because not only is Indian weather suitable for multiple organisms to grow, the paucity of good primary healthcare leaves populations at a high risk of epidemics. India is a large land mass, making effective implementation of anti-disease treatments cumbersome and difficult. Further India remains accessible through multiple fronts with air, sea, and land connectivity making it easy to transport biological agents. The instability of political connections in the neighbouring region and ongoing conflicts raise the threat of a potential bioweapons attack from across India’s borders. A comprehensive threat awareness of the various state and non-state actors in conflict with India and their bioweapons status needs to be done to ensure India is prepared for a potential attack. A preliminary analysis of threats against India was conducted based on the following factors:

1. **Geographical location**: The closer the perpetrator state is to India, the easier they will find to disperse a biological agent in Indian territory, land or water. While geographical location was originally a deterrent for engaging in biowarfare, the capability of creating targeted weapons or a combination of weapon and antidote may lower the barriers for considering the development of biological weapons. A possible exception to this is agricultural attacks: lands in vicinity may be producing similar food crops and the possibility of a blow back may be higher in this sector.

2. **Connectivity with India (through air, water, or land)**: Increased access to India would increase the chances of delivering a biological weapon through these ports of entry. Further, the more access points, the less likely would it be to detect the entry and dissemination of a biological agent.

3. **Possession of weapons of mass destruction/prior history of armed conflict lead to the following observations**: Prior history of use of weapons or ongoing conflicts with India would increase the likelihood of these countries attempting to engage in biological warfare against India.

4. **Signatory status** to the Biological Weapons Convention or reports of alleged bioweapon possession.
Two countries stand out on the bioweapons monitor radar – Pakistan and China. Particularly the presence of non-state actors in Pakistan and ongoing conflicts with the state demand increased preparedness for a biological attack. Non-state actors affiliated to other territories including Al Qaeda and Daesh have pursued training for biowarfare and there is no major hurdle that could stop such training to spread to non-state actors in geographies closer to or in India.

China, on the other front, has been widely believed to have an advanced biowarfare programme. Recently, China has also focussed on developing expertise in gene editing technologies. Taken together, China represents a major threat for the creation of targeted bioweapons against India.

While this assessment is likely relevant when considering biological weapons as a weapon of mass destruction, the use of biowarfare as a tool of sabotage is free of any concerns of a blow back or substantial delivery systems. Any state or non-state actor with a preliminary scientific infrastructure may be able to orchestrate such an attack. In this case, the security of targeted individuals may be paramount and an attack through biological weapons should be considered when detailing out a security regime.

In either context, India needs to focus on its immediate neighbours and monitor for intent of bioweapons use. One possible way is to monitor publications coming
out of these regions and look for scientists who may have been previously publishing on gene editing or biological agents use, but have not published recently.\textsuperscript{40}

**Vulnerability to a Biological Attack**

In any event, India needs to be prepared for the eventuality of biological warfare. In the recent Nipah outbreak in Kerala, a strong healthcare response saw the containment of the disease with few casualties. Unlike developed countries, India reels from a weak and underserved primary healthcare system.\textsuperscript{41} Therefore, if a similar outbreak had happened elsewhere or the patients had gone to a private hospital, the casualty list may have been significantly higher.\textsuperscript{42} Further, though efforts are being made to improve mechanisms, real-time surveillance for disease outbreaks remains poor.\textsuperscript{43} Diagnosis of febrile cases, for example is much lower in India as compared with the global rate.\textsuperscript{44}

Two additional factors make India vulnerable to infectious outbreaks: one, India inherently suffers from seasonal infectious diseases and second, there is widespread migration of people across the country, thereby making control of outbreaks difficult. Finally, lack of hygiene and areas of high population density also contribute to faster spread of diseases. These factors, which can aggravate natural outbreaks can also make masking a bioweapons attack easier.

Further India has a strong dependency on agriculture to sustain its population and any interference with agriculture would strongly affect farmers and the economy. In this context, the threat to Indian agriculture may be higher and more impactful than an attack targeting human diseases.

**Policy Recommendations**

India is vulnerable to a biological weapons attack and needs to develop strong surveillance and bio-defence programmes to tackle a possible attack.

**Surveillance Mechanisms**

The process for detection of an agricultural bio-attack is difficult to assess, but surveillance is primary for reporting cases of insect attack or mass crop failure for no apparent reason.
In either case, real-time surveillance and data analysis remain central to detection and swift response to an attack. While check-points at ports of entry or even internal inspections at suspected bio-weapons development sites could be carried out, their effectiveness at identifying biological agents may not be adequate. Further, the development of quick responses to disease outbreaks will aid India against natural outbreaks as well. In this context, an upgrade of select laboratories to biosafety level (BSL) 3 or ideally 4, where infectious diseases can be tested would reduce the time to detection. Currently only National Virology Institute in Pune has a BSL-4 laboratory, but as was seen in the Nipah outbreak case, precious time was saved because the closer Manipal Centre for Virus Research had the necessary facilities to detect the virus.

The National Disaster Management Authority has issued advisories on managing biological disasters and capacity building is key in their guidance. Emphasis is placed on collection of specimen and its safe delivery to the laboratory. Training for these activities to early responders and at-risk civilians would aid in a rapid response. India has also developed Muntra, an unmanned tank with capabilities of detecting bio-threats. However, the usefulness of such a tank in areas of high population density or locations with road connectivity is poor or lanes are too short is questionable.

Instead, the presence of a networked primary healthcare system in all parts of the country is required. A staggered chain of protocols, including quarantine, personal protection equipment for healthcare workers, sample collection and delivery, etc. should occur in response to an infectious outbreak – particularly for those cases where a disease cannot be easily identified.

Along with handling and delivery of samples, a strong focus needs to be made on improving diagnostic capabilities – kits or tests which are used for detection of diseases. The development of point-of-care diagnosis kits would be ideal in quick response to outbreaks. The introduction of new technologies – such as Nanopore sequencing – for diagnosing unidentified or new infections may aid in prescribing relevant medication. In the diagnosis of unusual infections, an effort needs to be made to sequence the entire DNA of the infectious agents. In many cases, an antibody or specific DNA based tests are used for diagnosis. However, the sequencing of the entire DNA would help identify if the agent has been tampered with using artificial agents. Though this is not always reliable, treating unusual cases as a likely bioweapons attack and documenting genome sequences of the
biological agent would provide a repository that could lend useful information for future use.

Biosafety Standards, Ethics, and Penalties

A responsive healthcare system would help contain the effects of a biological weapons attack but not the proliferation of biological agents itself. While verification remains a political non-starter at the biological weapons convention, national mechanisms to increase biosafety levels at institutions would reduce the chances of accidental leakage of biological agents. Further sensitising scientists and students to the possibility of misuse of science and ethical practices in research is paramount. Scientists could also be the best resource to use in detecting potential malpractices or anomalous disease behaviour and should be tapped for such requirements.

The first step to prevent misuse of biological agents is to educate students and researchers in biosafety procedures and ethical use of biological materials. Indian academic and private institutions need to adopt safety standards – Good Lab Practices, National Accreditation Board for Testing and Calibration Laboratories or others – to ensure safe use and disposal of biological agents. The guidelines on biosafety of recombinant DNA research and biocontainment were released in 2017, but do not include penalties for guideline violation. A stricter approach to ensure laboratories do not accidentally leak biological materials to non-state actors is needed.

Identifying the correct set of standards requires discussion with multiple stakeholders. While the idea of standards makes sense, there is a cost attached to adhering to them and a very high cost could affect the budding biotechnology start-up industry in India. Balancing the threat of bioweapon proliferation with the need to encourage biotechnology-based start-ups is extremely important as India looks to exploit these dual-use technologies for its benefits.

Further, education of scientists and students to understand the implications of their research being misused is necessary. Ethical training of all personnel working in a laboratory environment should be mandatory.

Leader at the Biological Weapons Convention
As India remains particularly vulnerable to biological threats and has a history of hostile political conflicts, India needs to take a lead in ensuring the Biological Weapons Convention is effective in its aim at curbing use of biological agents or toxins.

The primary focus of India at the BWC should be to instil and participate in a scientific advisory board on the same lines as the one attached to the Chemicals Weapons Convention. The board should have scientists representing various participating countries, industry, societies, and academies. The responsibility of the board would be to monitor new technologies for the feasibility of weaponisation and suggest mechanisms to prevent proliferation of such technologies.

While instilling a verification mechanism is not considered as a feasible option at the convention, inculcating a cooperative atmosphere for sharing vaccine and diagnostic technologies across the state parties would definitely be in India's interest.

India could also push for transforming the voluntary system for reporting on national activities to a mandatory reporting. Further penalties can be put in for parties who are not compliant with the confidence building measures dictated by the BWC. Doing so will help India with gaining access to technologies that could improve India's primary health care response.

**Treaties with Other Nations**

Within and outside the BWC, India needs to forge strategic partnerships with countries who can share their expertise on biosecurity.

The US-India Strategic Dialogue on biosecurity started in 2016, but a broader conversation with other countries who remain similarly threatened by biological attacks would help create a community that shares best practices and means/resources to curb the problem of biological warfare.

In 2018, India joined the Australia Group, an informal arrangement between interested parties to work together to effectively curb chemical and biological weapon proliferation through export controls. But a more intense internal discussion and identification of biological threats to India is required to make most use of such informal meetings.
Public Engagement

Most people are aware of various weapon systems and there is a certain degree of awareness of how to react in case of say lone wolf attacks. However, the spread of an infectious disease can quickly cause panic and fear. Societal education on how to behave in response to a potentially lethal infectious outbreak has to be instilled. This is particularly important while discharging sensitive procedures including patient visitations, handling of personal items and funerals.

A public engagement initiative that can educate the citizens on maintenance of personal hygiene, possibility of infectious outbreak and protocols in response to an outbreak is definitely required. Bangladesh has published an in-depth guideline for response to a Nipah outbreak – escalating from a suspicious incident to a confirmed case, detailing the roles for local government authorities and civilians.50

Conclusion

Bioweapons have once again come into the limelight and India needs to be prepared for defending against biological warfare. The mere fact that biowarfare has caught the eye of agencies in US and Europe has generated interest around the world. And this attention will propel biowarfare onto the radar of non-state actors as well. Even if attacks aimed at India do not use advanced technologies, the poor primary healthcare system51 makes India vulnerable to even a simple biological agent which would have not made significant damage in more developed economies.

The biological weapons convention, despite its good intention, is a toothless treaty that is incapable of curbing the spread of bioweapons. Stronger regulation and global co-operation can be the only means to fighting this threat. India is particularly vulnerable to biological warfare and needs to focus on improving diagnostics, grassroot reach, data analytics and healthcare response to contain the spread of disease. Education and biosafety standards need to be adopted to prevent proliferation of biological agents. Public engagement and discussion is necessary to make the society aware of the threat of disease and ensure preparedness in case of an attack.
Appendix I: Articles of the Biological Weapons Convention

Article I

Each State Party to this Convention undertakes never in any circumstances to develop, produce, stockpile, or otherwise acquire or retain:

(1) Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.

Article II – Destruction of existing stockpiles

Each State Party to this Convention undertakes to destroy, or to divert to peaceful purposes, as soon as possible but not later than nine months after the entry into force of the Convention, all agents, toxins, weapons, equipment and means of delivery specified in Article I of the Convention, which are in its possession or under its jurisdiction or control. In implementing the provisions of this Article all necessary safety precautions shall be observed to protect populations and the environment.

Article III – Prohibition of technology transfer

Each State Party to this Convention undertakes not to transfer to any recipient whatsoever, directly or indirectly, and not in any way to assist, encourage, or induce any State, group of States or international organisations to manufacture or otherwise acquire any of the agents, toxins, weapons, equipment or means of delivery specified in Article I of the Convention.

Article IV – Prevention of bioweapons development

Each State Party to this Convention shall, in accordance with its constitutional processes, take any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition or retention of the agents, toxins, weapons, equipment and means of delivery specified in Article I of the Convention, within the territory of such State, under its jurisdiction or under its control anywhere.
Article V – Co-operation for problem solving

The States Parties to this Convention undertake to consult one another and to co-operate in solving any problems which may arise in relation to the objective of, or in the application of the provisions of, the Convention. Consultation and cooperation pursuant to this Article may also be undertaken through appropriate international procedures within the framework of the United Nations and in accordance with its Charter.

Article VI – Co-operation in investigations

(1) Any State Party to this Convention which finds that any other State Party is acting in breach of obligations deriving from the provisions of the Convention may lodge a complaint with the Security Council of the United Nations. Such a complaint should include all possible evidence confirming its validity, as well as a request for its consideration by the Security Council.

(2) Each State Party to this Convention undertakes to co-operate in carrying out any investigation which the Security Council may initiate, in accordance with the provisions of the Charter of the United Nations, on the basis of the complaint received by the Council. The Security Council shall inform the States Parties to the Convention of the results of the investigation.

Article VII – Provide assistance

Each State Party to this Convention undertakes to provide or support assistance, in accordance with the United Nations Charter, to any Party to the Convention which so requests, if the Security Council decides that such Party has been exposed to danger as a result of violation of the Convention.

Article VIII

Nothing in this Convention shall be interpreted as in any way limiting or detracting from the obligations assumed by any State under the Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare, signed at Geneva on 17 June 1925.

Article IX – Prohibition of chemical weapons
Each State Party to this Convention affirms the recognised objective of effective prohibition of chemical weapons and, to this end, undertakes to continue negotiations in good faith with a view to reaching early agreement on effective measures for the prohibition of their development, production and stockpiling and for their destruction, and on appropriate measures concerning equipment and means of delivery specifically designed for the production or use of chemical agents for weapons purposes.

Article X – Peaceful use of technologies

(1) The States Parties to this Convention undertake to facilitate, and have the right to participate in, the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes. Parties to the Convention in a position to do so shall also cooperate in contributing individually or together with other States or international organisations to the further development and application of scientific discoveries in the field of bacteriology (biology) for the prevention of disease, or for other peaceful purposes.

(2) This Convention shall be implemented in a manner designed to avoid hampering the economic or technological development of States Parties to the Convention or international co-operation in the field of peaceful bacteriological (biological) activities, including the international exchange of bacteriological (biological) agents and toxins and equipment for the processing, use or production of bacteriological (biological) agents and toxins for peaceful purposes in accordance with the provisions of the Convention.

Article XI – Amendments to the Convention

Any State Party may propose amendments to this Convention. Amendments shall enter into force for each State Party accepting the amendments upon their acceptance by a majority of the States Parties to the Convention and thereafter for each remaining State Party on the date of acceptance by it.

Article XII – Review the Convention
Five years after the entry into force of this Convention, or earlier if it is requested by a majority of Parties to the Convention by submitting a proposal to this effect to the Depositary Governments, a conference of States Parties to the Convention shall be held at Geneva, Switzerland, to review the operation of the Convention, with a view to assuring that the purposes of the preamble and the provisions of the Convention, including the provisions concerning negotiations on chemical weapons, are being realised. Such review shall take into account any new scientific and technological developments relevant to the Convention.

**Article XIII – Duration of Convention**

(1) This Convention shall be of unlimited duration.

(2) Each State Party to this Convention shall in exercising its national sovereignty have the right to withdraw from the Convention if it decides that extraordinary events, related to the subject matter of the Convention, have jeopardised the supreme interests of its country. It shall give notice of such withdrawal to all other States Parties to the Convention and to the United Nations Security Council three months in advance. Such notice shall include a statement of the extraordinary events it regards as having jeopardised its supreme interests.

**Article XIV – Signature and Ratification Process**

(1) This Convention shall be open to all States for signature. Any State which does not sign the Convention before its entry into force in accordance with paragraph 3 of this Article may accede to it at any time.

(2) This Convention shall be subject to ratification by signatory States. Instruments of ratification and instruments of accession shall be deposited with the Governments of the United Kingdom of Great Britain and Northern Ireland, the Union of Soviet Socialist Republics and the United States of America, which are hereby designated the Depositary Governments.

(3) This Convention shall enter into force after the deposit of instruments of ratification by twenty-two Governments, including the Governments designated as Depositaries of the Convention.
(4) For States whose instruments of ratification or accession are deposited subsequent to the entry into force of this Convention, it shall enter into force on the date of the deposit of their instruments of ratification or accession.

(5) The Depositary Governments shall promptly inform all signatory and acceding States of the date of each signature, the date of deposit of each instrument of ratification or of accession and the date of the entry into force of this Convention, and of the receipt of other notices.

(6) This Convention shall be registered by the Depositary Governments pursuant to Article 102 of the Charter of the United Nations.

Article XV – Languages for Convention

This Convention, the English, Russian, French, Spanish and Chinese texts of which are equally authentic, shall be deposited in the archives of the Depositary Governments. Duly certified copies of the Convention shall be transmitted by the Depositary Governments to the Governments of the signatory and acceding States.
References

1 https://www.armscontrol.org/factsheets/bwcsig
3 The Biological Weapons Act 1974, UK
6 https://www.nature.com/news/us-suspends-risky-disease-research-1.16192
7 https://www.emedicinehealth.com/biological_warfare/article_em.htm#what_is_the_history_of_biological_warfare
9 Reeves RG, Voeneky S, Caetano-Anollés D, Beck F and Boëte, C. Agricultural research or a new bioweapon system? 2018 Science 362;6410:35-37.
12 https://emergency.cdc.gov/agent/agentlist-category.asp
26 https://issues.org/tucker/
27 ibid
29 https://www.opcw.org/
30 https://www.brookings.edu/blog/order-from-chaos/2017/09/06/the-biological-weapons-convention-at-a-crossroad/
38 https://etc.usma.edu/the-islamic-state-and-wmd-assessing-the-future-threat/
39 https://www.globalsecurity.org/wmd/world/china/cbw.htm
41 https://idronline.org/primary-healthcare-rural-areas/
43 Bagcchi, S. Dengue surveillance poor in India. 2015 The Lancet 386:1228. doi: https://doi.org/10.1016/S0140-6736(15)00315-3
44 https://www.indiaspend.com/nipah-contained-but-more-than-80-cases-from-similar-brain-fevers-are-undiagnosed-4958/
45 https://www.theweek.in/health/cover/2019/03/08/The-virus-busters.html
47 http://www.dbtindia.nic.in/regulations-and-guidelines-on-biosafety/
49 https://australiagroup.net/en/participants.html
50 National Guideline for Management, Prevention and Control of Nipah Virus Infection including Encephalitis Directorate General of Health Services Ministry of Health & Family Welfare Government of the People’s Republic of Bangladesh