

South Asia Biosafety Program

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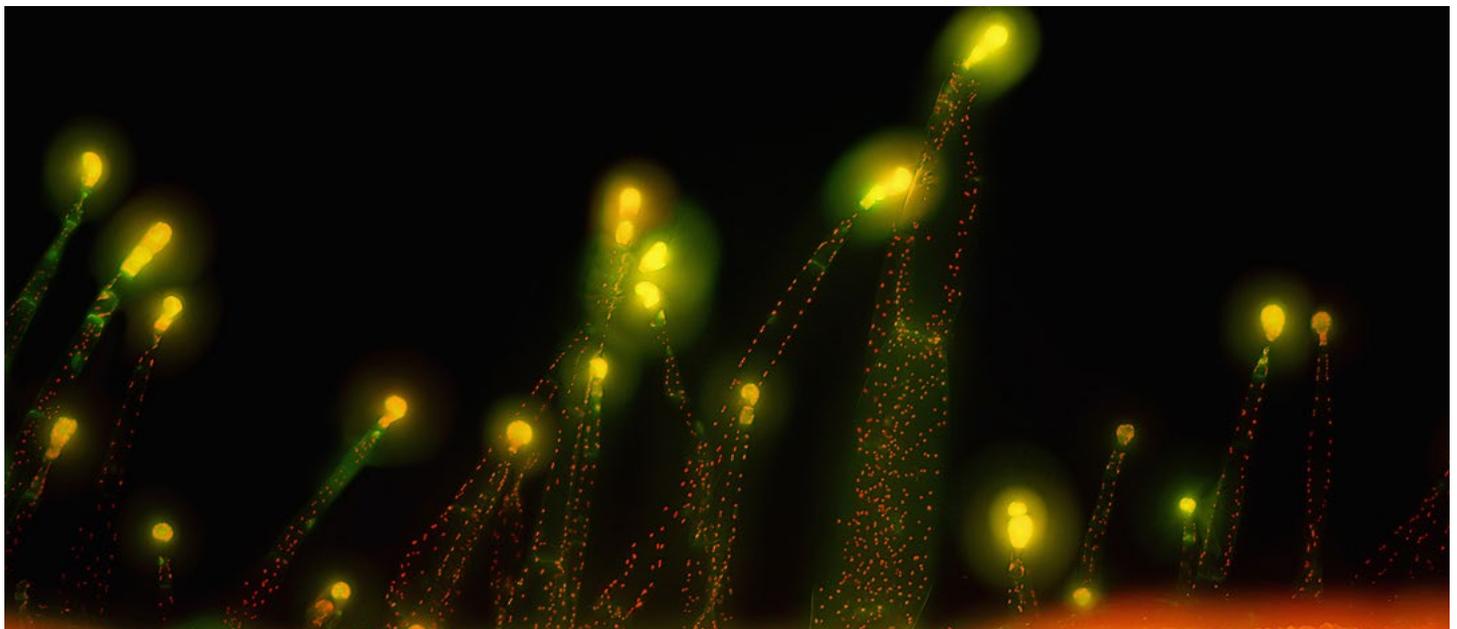
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BANGLADESH

Plant-Based Techniques to Fight Against COVID-19

Mr. Sium Ahmed, Biosafety Support Office



Nicotiana benthamiana leaf hairs captured via fluorescence microscopy with 20x objective lens © Heiti Paves | Dreamstime.com

The world is suffering from the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the cause of coronavirus disease 2019 (COVID-19). As of June 30, 2020, the virus has emerged in 213 countries and territories, with 10,450,207 cases and 509,142 deaths¹. Amid the current situation, the World Health Organization (WHO) declared a pandemic and an international public health emergency. As the situation is getting worse and there is no effective drug or vaccine available yet, the whole world is scrambling to solve the puzzle. Researchers are now trying to find an effective cure, and hundreds of different drugs and vaccines are in the developmental stage.

Vaccines are biological preparations that improve immunity by stimulating antibody production in humans and animals. Vaccination is the most efficient health intervention to fight against viral diseases. However, high cost or lack of availability often drives attention towards more efficient, fast, and cost-effective alternatives. Traditional vaccines are generally developed by incorporating inactivated or attenuated pathogens. But, they have some technical limitations, which often challenge or slow large scale production and distribution—including the need to ensure inactivation of live or attenuated pathogens, potential

for failure of quality control, specialized storage and transport needs, etc. Moreover, complex production systems, significant costs associated with fermentation and purification, and additional expenses associated with adjuvants make them expensive and inaccessible in developing countries².

Plant-made vaccines and therapeutics are protein products with clinical or veterinary implications that are produced in recombinant plant systems. The idea of plant-made vaccines was introduced three decades ago by Andrew Hiatt and colleagues from the Research Institute of Scripps Clinic, USA and further developed by Charles J. Arntzen and his colleagues, who developed the concept of utilizing transgenic plants to produce and deliver subunit vaccines.

For SARS-CoV-2, the straightforward approach for developing a vaccine candidate is the technology of inactivated vaccines by chemical or physical treatments while another possible approach is a vaccine based on live-attenuated virus. More advanced is the development of subunit vaccines using the coronavirus spike glycoproteins, as they are considered the primary target for neutralizing antibodies. Virus-like particles (VLPs), Cytotoxic T-lymphocyte (CTL) responses, generation

In the run to find the cure for COVID-19, in line with other scientists, plant biotechnologists are also working hard to develop a viable vaccine candidate using plant-based technology.

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of artificial antigen presenting cells through transduction as a way to express viral antigens and immune modulatory genes to ultimately activate T cells are also considered as promising strategies. These strategies have the potential to be successfully integrated into plant systems to produce possible vaccine candidates³.

Plant-made vaccines are heat stable, free from pathogen contamination, and can be engineered to contain multiple antigens. Plants are amenable to large-scale economic production, product safety, and ease of storage and distribution, while reducing costs by bypassing fermentation, purification, cold storage, and transportation². Moreover, plant-based edible vaccines offer a better choice, predominantly in developing countries, because they are cost-effective, needleless, convenient, safe, easily administrable, and bio-friendly. However, there are still several limitations remaining, such as the selection of antigen and plant expression host, consistency of dosage, and manufacturing of vaccines according to Good Manufacturing Practice (GMP) procedures^{4,5}.

According to the WHO, the regulatory evaluation of plant-based vaccines should follow the existing guidelines for development, evaluation, and use of vaccines made by conventional methods, while they are also clinically tested under US investigational new drug applications and also must follow all the regulatory and GMP requirements⁵.

In the run to find the cure for COVID-19, in line with other scientists, plant biotechnologists are also working hard to develop a viable vaccine candidate using plant-based technology. Researchers from the Spanish Research Council (CSIC) at the Centre for Research in Agricultural Genomics (CRAG) are trying to produce SARS-CoV-2 antigens in different plant expression systems. A team from the Queensland University of Technology are using an ancient Australian plant (*Nicotiana benthamiana*) to make larger quantities of high-quality vaccine and antibodies. Canadian biopharmaceutical company Medicago has made

significant progress toward producing an experimental plant-based vaccine by using a virus-like particle (VLP). Kentucky BioProcessing (KBP), is developing a potential vaccine for COVID-19 using fast-growing tobacco plants. Researchers from the Institute of Biotechnology of the Autonomous University of Nuevo León (UANL) in Mexico are trying to develop a tomato with SARS-CoV-2 antigens, which can be consumed as edible vaccines. ZYUS Life Sciences Inc. is collaborating with the Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac) at the University of Saskatchewan to produce SARS-CoV-2 antigens in plant expression systems⁶⁻¹¹.

The global emergence of COVID-19 demands the development of new biologics, especially vaccines, to counteract against this threat. In this scenario, plant-based approaches may represent a viable strategy to rapidly respond to this need.

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- ⁸ <https://www.pmi.com/media-center/news/medicago-develops-a-plant-based-vaccine-for-coronavirus>⁹ https://www.bat.com/group/sites/UK_9D9KCY.nsf/vwPagesWebLive/DOBN8QNL
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BIOSAFETY DISCOURSES

Sium Ahmed
Biosafety Support Officer
Biosafety Support Office, Dhaka, Bangladesh
Email: biosafetyofficedhaka@gmail.com

BANGLADESH

Biosafety Research in Bangladesh Grants Program 2019: Progress Review Meeting

Dr. Aparna Islam, South Asia Biosafety Program

SABP launched the Biosafety Research in Bangladesh Grants Program (BRBGP) in 2019, supported by the USAID Mission in Dhaka. This grant program has multiple objectives. It focuses on engaging researchers to build awareness and understanding around the science and practice of biosafety, and it aims to expand the locally produced knowledge and technical resources to support risk assessment for agricultural biotechnologists in Bangladesh.

The first call for proposals was issued in January 2019. After several tiers of assessment, three projects were selected for the year 2019. The awardees are Dr. Abdun Noor Muhammad Iftakhar Alam, National Institute of Biotechnology, Savar; Prof. Dr. Md. Shahidul Haque, Bangladesh Agricultural University, Mymensingh; and Prof. Dr. Mohammad Zabed Hossain, University of Dhaka, Dhaka. All three projects were survey-based and collected baseline data on agricultural practices. The projects commenced in November 2019 and reached the mid-year completion mark in May 2020.

On June 15, 2020, a virtual meeting was held to review the progress of these projects. All the principal investigators presented their

project updates and shared their future plans. Dr. Joe Smith, President, International Society for Biosafety Research and Dr. Joerg Romeis, Head of the Biosafety Research Group, Agroscope, Zurich, Switzerland were present at the meeting to review the progress of the projects.

All the projects have progressed considerably since their inception. Training of project personnel and questionnaire development have been achieved in all three projects. However, the projects were not able

to make progress as planned due to the imposed lockdown at the end of March 2020. At the meeting, the scientists discussed the challenges that they are facing due to the pandemic. The challenges

range from not being able to collect seasonal data, to not being able to go forward with chemical analysis of the collected samples and delay in data analysis, etc. But, both experts observed that the projects had progressed well and expressed interest in seeing the final results of the projects. To take the projects further, both experts suggested some ideas for assessment parameters and analysis to reach the final result. The meeting was also attended by Dr. Andrew F. Roberts, Dr. Aparna Islam, and Mr. Sium Ahmed.

Training of project personnel and questionnaire development have been achieved in all three projects.

South Asia Biosafety Program Organizes Webinars on Biosafety for Bangladeshi Universities

Mr. Sium Ahmed and Dr. Aparna Islam, South Asia Biosafety Program

Over the past three decades, significant progress has been made in Bangladesh's biosafety regime and in the field of biotechnology research. Courses on biosafety are integrated within the biotechnology curriculum offered at universities to make students aware of the existing regulations. Understanding the biosafety processes at various stages of research and development is an absolute necessity for proper implementation. To improve perception towards biosafety and further enhance the knowledge of future researchers, a series of webinars are being organized by the South Asia Biosafety Program (SABP) for tertiary students, in collaboration with different universities of Bangladesh, starting with two public universities in June 2020.

The first lecture in the *SABP Webinar Series* was held on June 1, 2020. "Biosafety in Agricultural Biotechnology: In the Eyes of Future Researchers" was organized in collaboration with the Department of Biotechnology of Sher-e-Bangla Agricultural University in Dhaka. It was attended by ten master's degree students and five faculty members. Prof. Dr. Md. Ekramul Hoque, Chairman of the Department of Biotechnology, presided over the online event. In his welcome remarks, Prof. Hoque introduced the academic and research activities of the department, with an emphasis on crop biotechnology and biosafety. He was followed by Dr. Aparna Islam of SABP, who delivered the keynote lecture. Dr. Islam's presentation covered biosafety interventions at various stages of biotechnology research for the production of genetically engineered crops. Later, she introduced the Bangladesh Biosafety Portal and open-access eLearning courses offered by the Agriculture & Food Systems Institute (AFSI) to the audience. In his concluding remarks, Prof. Hoque thanked Dr. Islam for an informative and easily understandable lecture: "the teachers and students will be benefitted from the knowledge acquired through the lecture and discussions." He also expressed interest in having similar programs with SABP in the near future.

The second lecture in the *SABP Webinar Series*, "Biosafety in Crop Biotechnology Research," was held on June 18, 2020 with the Department of Biotechnology and Genetic Engineering of Jahangirnagar University, Dhaka. This online event was attended by 17 students and five faculty members. Prof. Dr. Abdul Jabber Howlader,

Dean, Faculty of Biological Sciences, was the Chief Guest of the event, while Dr. Md. Sharif Hossain, Chairman of the Department of Biotechnology and Genetic Engineering was the Special Guest.

In his welcome address, Prof. Dr. Abdullah Mohammad Shohaheel of the Department of Biotechnology and Genetic Engineering introduced departmental initiatives on biotechnology and biosafety. Dr. Hossain welcomed the capacity building initiative taken by SABP to enable students to enhance their knowledge, which will help in the effective implementation of biosafety during their research. Prof. Howlader mentioned the benefits of modern biotechnology in various sectors and the importance of biosafety for the protection of biological diversity. In her talk, Dr. Aparna Islam of SABP discussed the structure and composition of the biosafety committees in Bangladesh and the documents shaping the national biosafety regime. She also explained the regulatory approval system at various stages of crop biotechnology research and development. Later, Dr. Islam encouraged students to visit the Bangladesh Biosafety Portal and eLearning courses offered by AFSI for further enhancement of their understanding.

In both events, the keynote presentation was followed by lively discussions among the participants. The questions on development of plant-based vaccines against the novel coronavirus reflected concerns of the students over the current pandemic situation. Questions on biosafety requirements for transformation experiments, vector importation, time required in processing of different applications, and stewardship of the decision showed the intense interest of students to understand Bangladesh's biosafety system. Due to the pandemic, since mid-March, all universities have been closed in Bangladesh. But, the enthusiasm among the attendees showed their eagerness to learn and prepare themselves for the future.

Dr. Aparna Islam of SABP discussed the structure and composition of the biosafety committees in Bangladesh and the documents shaping the national biosafety regime. She also explained the regulatory approval system at various stages of crop biotechnology research and development.

RESOURCE SPOTLIGHT

Access the Bangladesh Biosafety Portal:

<https://bangladeshbiosafety.org>

Access AFSI eLearning Courses on Biosafety and Biotechnology:

<https://foodsystems.org/elearning>

Algae: A New Source of Antivirals

Ms. Shradha Nirwan, Biotech Consortium India Limited



Marine (red) algae © Somprasong Wittayanuakorn | Dreamstime.com

Algae have been recognized as promising organisms for production of different metabolites, primarily due to their high growth rates compared with those of other photosynthetic organisms. Scalable and

contained growth, rapid transformation, easily obtained stable cell lines, and consistent transgene expression levels are important characteristics, making algae an attractive host for therapeutic production.

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Reliance Industries Research and Development Centre (based in Mumbai, India) is exploring the creation of a safe and sustainable source of bio-chemicals and antivirals from marine algae sources. The Reliance Biology R&D Team has been continuously running a 20-acre open pond algae facility for the last few years and has a diverse germplasm repository of algal strains.

Novel initiatives include:

1. A heteropolymer *Porphyridium*, carrageenan-like sulfated polysaccharides from red algae, are being investigated as selective inhibitors of several enveloped and non-enveloped viruses, which act predominantly by inhibiting the binding or internalization of virus into the host cells¹. The cells pre-treated with carrageenan are well protected against the infection due to coronaviruses. These algae can be used as a coating material on sanitary items and for the production of antiviral drugs.
2. Algal oil and their components like linoleic acid, oleic acid, palmitic acid, and stearic acid are being studied for their preventive role in virus infection². These oils act by inhibiting the binding virus into the host cells or suppressing virulence activity by destabilization of the bilayer of viral envelopes. The purified oil from algal sources could be considered as a potential preventive measure for spread of virus from person to person to fight disease like COVID-19 in the form of oil-based nasal sprays and other formulations.
3. Several cyclic or linear peptides and depsipeptides isolated from cyanobacteria act as protease inhibitors, which are being studied for their antiviral properties. Seven extracts derived from microalgae and cyanobacteria have been shown to inhibit

There has been some debate as to whether or not genetically modified (GM) algae fall under GM Microorganisms (GMMs) or GM Plants, or even both categories, and questions as to how this might impact any risk assessments that would need to be performed.

seasonal influenza A and B replication in host cells to the extent of 80% and could be important for bioprospecting in antiviral research³.

There are reports of scientific groups from Italy and Israel working to develop algae-based edible vaccines for coronavirus⁴. The DNA sequence from a portion of the SARS-COV2 spike protein has been used as a transgene to insert into *Chlamydomonas reinhardtii*. It is proposed that modified algae would be lyophilized to generate an oral capsule. The scientists are working in parallel with gene editing, a tool that would allow them to introduce additional modifications to the algae nuclear genome, which could improve the productivity of its biomass.

There has been some debate as to whether or not genetically modified (GM) algae fall under GM Microorganisms (GMMs) or GM Plants, or even both categories, and questions as to how this might impact any risk assessments that would need to be performed. Regulatory and biosafety

obstacles rather than technical and experimental constraints are critical in the approval process of algal-based biologicals.

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INDIA

Identification of Rice Genomic Region: A Step Towards Improved Productivity

Dr. Jyoti Batra, Biotech Consortium India Limited

Rice is one of the main staple foods across the world, as it has high carbohydrate content, provides instant energy, and accounts for more than 75 percent of the calorie intake. Traits like the number of grains per plant and weight of the grain mainly determine the yield in rice. Thus, one of the main aims of researchers and breeders has been to develop superior rice varieties with heavier grains, which can give higher yield and better nutrition. However, the genetic basis for contrasting grain size/weight trait among Indian germplasms and their association with domestication-driven evolution is not well understood.

In a new study, researchers from the Department of Biotechnology's National Institute of Plant Genome Research (DBT-NIPGR), ICAR-Indian Agricultural Research Institute (ICAR-IARI), ICAR-National Rice Research Institute (ICAR-NRRI), Cuttack, and the University of Delhi South Campus (UDSC) have identified a region in the genome of rice, which appears to have the potential for improving productivity. A long (~6 Mb) genomic region termed 'low diversity region' (LDR) was identified by studying 3000 rice accessions from across the world along with the four Indian genotype (LGR, PB 1121, Sonasal, and Bindli) sequences that show contrasting phenotypes in seed size/weight. LDR has an unusually suppressed nucleotide diversity region across the centromere of rice chromosome and has been identified as an evolutionary important site with significant positive selection and multiple selection sweeps, showing association

In a new study, researchers [...] have identified a region in the genome of rice, which appears to have the potential for improving productivity.

with many domestication-related traits, including grain size/weight. All the data and analyses can be accessed from the RiceSzWtBase database.

Higher presence of the LDR region in most of the cultivated rice genotypes belonging to *japonica* and *indica* varieties than the wilder *aus* group varieties further advocate its potential towards improving rice yield. Thus, the LDR region could be utilized for enhancing rice production by targeting various traits, including the seed size Quantitative Trait Loci identified by genomic studies. This new study highlights an important and long domestication-related genomic region, which was found to be evolutionarily crafted to carry multiple agronomic traits associations.

Further Readings

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NBA-UNDP Webinar Series on 'Biodiversity and Biological Diversity Act 2002'

Dr. Sanchita Choudhary, Biotech Consortium India Limited

The Government of India enacted the Biological Diversity (BD) Act in 2002, notified the Biodiversity Rules in 2004, and formulated the guidelines for Access and Benefit Sharing (ABS) of biological resources in 2014. This legal framework has served the goals of conservation of biodiversity, sustainable utilization of biodiversity, and fair and equitable sharing. Nevertheless, the understanding of this legal framework and issues related to its implementation have not been completely understood by a large number of stakeholders.

In order to effectively address these issues, a webinar series is being organized by the National Biodiversity Authority (NBA) in partnership with United Nations Development Programme (UNDP) to bring in leading experts and practitioners to share their professional expertise

and respond to various Q&A. Based on the experience, the webinar series will be expanded in both content and coverage.

The webinar series was launched on the International Day for Biological Diversity (May 22, 2020) by Sh. Prakash Javadekar, Honorable Minister for Environment, Forest and Climate Change, Government of India. This webinar series will run from May 2020-Feb 2021, and the format of the webinar series will be expanded in content and coverage depending upon the experience generated from engagement of various stakeholders.

For more information, please email secretary@nba.nic.in or mohini.thakur@undp.org. Topics, speakers, and dates for the webinars are as follows (all webinars will be held from 11:00-11:30AM IST):

No.	Title	Speakers	Date
1	<i>COVID-19 and One Health Initiative*</i>	<i>Representatives: MoEF&CC; MoFAH&D; NCBS; DBT; ICMR; NCDC; WHO; UNEP; UNDP Moderator: Dr. V.B. Mathur</i>	<i>May 22, 2020</i>
2	<i>Introduction to Biological Diversity Act: Historical Perspectives*</i>	<i>Dr. P.L. Gautam Former Chairperson, National Biodiversity Authority</i>	<i>June 24, 2020</i>
3	Biological Diversity Act 2002: Part I	Sh. Rabi Kumar Former Secretary, National Biodiversity Authority	July 22, 2020
4	Biological Diversity Act 2002: Part II (The Biological Diversity Rules, 2004)	Shri A.K. Goyal Former Special Secretary, Government of India	August 19, 2020
5	National Biodiversity Authority	Sh. Justin Mohan Secretary, National Biodiversity Authority	September 23, 2020
6	State Biodiversity Boards	Sh. R.S. Murthy Member Secretary, M.P. State Biodiversity Board	October 21, 2020
7	Biodiversity Management Committees	Dr. Pradip Sarmokadam Member Secretary, Goa State Biodiversity Board	November 25, 2020
8	People's Biodiversity Registers	Prof. Anil Gupta Indian Institute of Management, Ahmedabad	December 23, 2020
9	The Nagoya Protocol	Dr. Sarat Babu Gidda Senior Programme Management Officer, Convention on Biological Diversity	January 27, 2021
10	Access & Benefit Sharing: Process & Outcomes	Dr. Shivendu Shrivastava Former PCCF, Government of Madhya Pradesh	February 24, 2021

* Already completed

CALENDAR OF EVENTS

EVENT	ORGANIZED BY	DATE	WEBSITE
INDIA			
India Bio @ Bengaluru Tech Summit	Department of Information Technology Biotechnology and Science and Technology, Government of Karnataka	September 21-23, 2020 Bengaluru, Karnataka	http://www.indiablo.in/
4 th International Conference on NANOFORAGRI 2020 - Application of Nanotechnology for Sustainable, Productive and Safer Agriculture and Food System	The Energy and Resources Institute	November 5-6, 2020 Gurugram, Haryana	https://www.teriin.org/event/4th-international-conference-nanoforagri-2020-application-nanotechnology-sustainable
Indian Seed Congress 2021	National Seed Association of India	February 24-26, 2021 Bengaluru	https://isc2021.nsai.co.in/
INTERNATIONAL			
5 th International Conference on Genome Editing and Gene Therapy	Meetings International	August 19-20, 2020 Osaka, Japan	https://www.meetingsint.com/conferences/genomeediting
7 th Plant Genomics and Gene Editing Congress: Asia	Global Engage Ltd.	September 14-15, 2020 Bangkok, Thailand	http://www.global-engage.com/event/plant-genomics-asia/
24 th Meeting of the Subsidiary Body on Scientific, Technical, and Technological Advice	Secretariat of the Convention on Biological Diversity	November 2-7, 2020 Montreal, Canada	https://www.cbd.int/meetings/?thm=CPB
3 rd Meeting of the Subsidiary Body on Implementation	Secretariat of the Convention on Biological Diversity	November 9-14, 2020 Montreal, Canada	https://www.cbd.int/meetings/?thm=CPB
The 3 rd Asian Horticultural Congress 2020 (AHC 2020)	Horticultural Science Society of Thailand, International Society for Horticultural Science, Department of Agriculture, Department of Agricultural Extension, Ministry of Agriculture, Kasetsart University, and VNU Exhibitions Asia Pacific	December 15-17, 2020 Bangkok, Thailand	http://ahc2020.org/
10 th Meeting of the Conference of the Parties Serving as the Meeting of the Parties to the Cartagena Protocol on Biosafety	Secretariat of the Convention on Biological Diversity	Second Quarter of 2021, Kunming, China	https://www.cbd.int/meetings/?thm=CPB



SOUTH ASIA
BIOSAFETY PROGRAM

The South Asia Biosafety Program (SABP) is an international developmental program implemented in India and Bangladesh with support from the United States Agency for International Development. SABP aims to work with national governmental agencies and other public sector partners to facilitate the implementation of transparent, efficient, and responsive regulatory frameworks for products of modern biotechnology that meet national goals as regards the safety of novel foods and feeds, and environmental protection.



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CONTACT SABP
BANGLADESH

Dr. Aparna Islam
Country Manager
South Asia Biosafety Program
c/o CIMMYT
House-10/B, Road-53, Gulshan-2
Dhaka-1212, Bangladesh
Email: aparnaislam@southasiabiosafety.org

UNITED STATES

Ms. Layla Tarar
Communications Manager
Agriculture & Food Systems Institute
740 Fifteenth Street NW, Suite 600
Washington, DC 20005, USA
Email: ltarar@foodsystems.org
Twitter: @AgFoodSystems

INDIA

Dr. Vibha Ahuja
Chief General Manager
Biotech Consortium India Limited
Anuvrat Bhawan, 5th Floor
210, Deendayal Upadhyaya Marg
New Delhi 110 002, India
Email: vibhaahuja@biotech.co.in

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