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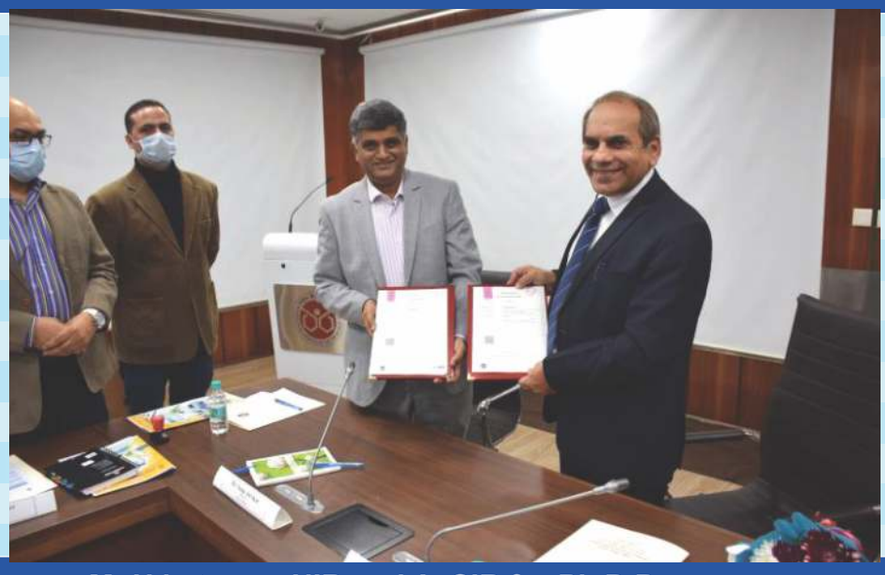
Azadi Ka Amrit Mahotsav

NATIONAL INSTITUTE OF BIOLOGICALS
NEWSLETTER

Visit of Honourable Union Minister- Health & Family Welfare



MoU between NIB and AcSIR for Ph.D Programme

Issue 1, January - March, 2022

Director's Desk

NIB is committed to nurturing future scientists who will empower the organization in the area of Biotechnology and Biologicals. At the same time, the Institute remains deeply rooted in its mandate. An underlying priority is to instill in our staff a sense of commitment to have a socially responsible impact; and to expand their knowledge and their intellectual horizons so they emerge transformed and prepared to have an impact on the world of science and society at large. We have consciously created a culture that values collegiality and accessibility, with open doors at all levels.

With a great delight and to initiate new horizons in the field of Research and Development, NIB, Noida signed an MoU with Academy of Scientific & Innovative Research, Ghaziabad (AcSIR) on 28th February, 2022 for conducting Ph.D. programs in Biotechnology with a special emphasis on Quality of Biologicals at NIB, Noida. Where, AcSIR will collaborate and recognize NIB as its Associate Academic Center.

It is a great moment of honor and pleasure that Hon'ble Health Minister Dr. Mansukh Mandaviya along with Hon'ble Minister of State, Health & Family Welfare Dr. Bharati Pravin Pawar visited National Institute of Biologicals (NIB), Noida during Chintan Shivir - Heal in India event organized by NHA to discuss medical value travel to India held on 4 - 5th, March 2022.

NIB hosted the Laboratory visit to B. Pharm students along with Faculty members from the College of Pharmaceutical Sciences, Govt. Medical College Calicut, Kerala on 17th March 2022. The students were given a basic overview of NIB and visited various Laboratories, and interacted with Scientists.

I wish Good Luck to All !!

Anup Anvikar
Director

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Ms. Y. Madhu Editor	**Mr. Jaipal Meena** Associate Editor	**Dr. Manjula Kiran** Associate Editor	**Ms. Apoorva Anand** Associate Editor

In-vivo Quality Control Testing of Biologicals and Implementation of 3Rs

Dr. Shikha Yadav, Scientist Grade II (Vet)

Biologicals are products that have been derived from natural sources like humans, animals, or microorganisms and include a wide range of medicinal products such as blood and blood components, recombinant therapeutic proteins, vaccines, enzymes, hormones, monoclonal antibodies, allergenics, somatic cells, tissues and gene therapy. It is believed that in some time, biologicals may offer the most effective means to treat a variety of medical illnesses and conditions for which presently no other treatments are available.

As manufacturing of biologicals involves complex processes and use of living cells, they are also vulnerable to microbial contamination by bacteria, viruses and fungi. Further, as biologicals are relatively large complex molecules, with an inherently heterogeneous structure, they are often extremely sensitive to physical conditions like temperature and enzymatic action. Therefore, compared to the chemical drugs, it is difficult to scale up their production from small quantities used for early analysis and preclinical testing to larger-scale batches, maintaining the product's purity and batch-to-batch equivalence. Due to this complexity, regulators require quality control (QC) testing to be performed on each batch of some biologicals by the manufacturers as well as on regular basis by regulatory bodies before it can be placed on the market.

The production and particularly the quality control of biologicals are closely intertwined with laboratory animal use as these products usually require complex *in vivo* bioassays for batch release in order to assure the safety, purity, identity and potency of these products. There has always been extensive use of laboratory animals in the development, production as well as quality evaluation of biologicals as use of animals can provide important information on pharmacokinetics and pharmacodynamics, insights into their mechanism of action, physiologic distribution, potency and potential toxicity. It is estimated that globally more than 10 million animals are used annually in development of biologicals and that 80% of these animals are used for routine quality control and batch release tests of licensed products.

The regulatory requirements for the QC safety and potency batch release testing of biologicals and vaccines are typically incorporated in pharmacopoeia monographs and guidelines. The Animal Facility of National Institute of Biologicals (NIB) functions as a central support laboratory for performing *in-vivo* quality control tests as per Indian or other Pharmacopoeias for quality control evaluation of the batches of various biologicals received in the institute.

The potential safety concerns for a biological product or vaccine include those due to inherent toxicities of the product, toxicities of impurities and contaminants, toxicities that result from interactions between the components present in the biological or vaccine formulation or due to the immune response induced by them. Regulations also make it mandatory to ensure that each batch of biologicals that are intended for parenteral administration is free from pyrogens as they can initiate fever and a multitude of other biological reactions like chills, body aches, rise in blood pressure and possibly a state of shock and death. Therefore, in-vivo quality control tests like abnormal toxicity test and pyrogen test are performed to ensure that the finished batches of various biologicals are safe for use in humans.

Potency of biologicals is also a Critical Quality Attribute (CQA) and is examined by regulators for their characterization. Identity and potency of several biologicals like hormones i.e. Human Chorionic Gonadotropin, Urofollitropin, Menotropin, Follicle Stimulating Hormone, Erythropoietin etc and several vaccines are established using bioassays in animal models. Potency assays measure the clinical response anticipated from a dose of biologicals and ensures that the manufacturing process is reliable to produce a consistent dose based on particular attribute of the product that is linked to the relevant biological property.

However biologicals and conventionally produced vaccines in particular are the subjects of great animal welfare concern because of the large number of animals being used and also the pain and distress caused to them. Therefore manufacturers, regulatory authorities as well as the society as a whole have the moral obligation to support the development and implementation of 3Rs alternatives i.e. use methods which result in the replacement of animals or reduction in the numbers used in that procedure or a refinement of techniques that may minimize pain and suffering in the animals.

Various international and European regulatory bodies such as European Medicines Agency (EMA), Food and Drug Administration (FDA), World Health Organization (WHO) have compelled the development of alternative methods as well as their implementation by various National Control Laboratories (NCL) for quality control of biological products. The European Centre for the Validation of Alternative Methods (ECVAM) has also validated a number of alternative methods and implementing the Three Rs in the production and quality control of biologicals has been one of its main priority areas.

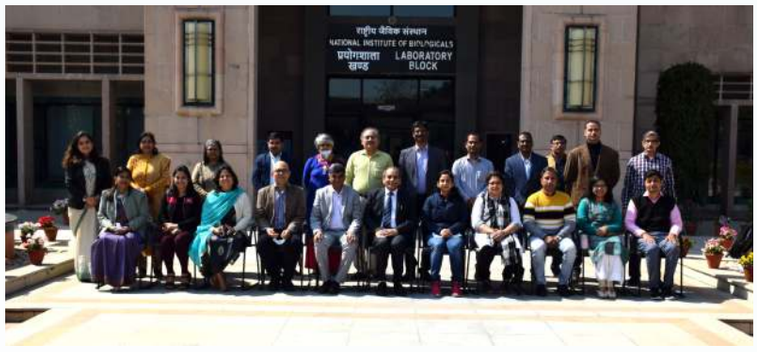
Several alternatives have been developed and validated in the last two decades for assessing the quality of sera, immunoglobulins, vaccines and other biologicals. With the advancement in technologies, the animal-based pyrogen test has gradually been replaced by alternative tests like Bacterial Endotoxin Test (BET) and Monocyte Activation Test (MAT) in several products, although suitability of these alternatives has to be demonstrated in a product-specific validation to ensure quality control of parenteral drugs. The benchmark success has started with replacement of the animals-based potency assays with in-vitro antigen quantification and in-vitro assay models for routine batch release of biological products. Further, some potency assays have been refined by establishment of humane endpoints in the lethal challenge test of human & veterinary vaccines like Rabies vaccines. The number of animals being used have also been reduced by replacing the multiple-dilutions with single-dilution mouse immunogenicity assay.

The Scientists at NIB are also highly committed towards the implementation of the 3R's in specific quality control and batch release testing and make efforts to adopt the validated alternative methods as and when they are accepted by the regulatory bodies and published in the Pharmacopeia.

The WHO guidelines and recommendations on biologicals are considered by most regulatory authorities and manufacturers. Therefore, recently in 2019, National Centre for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs), UK and the World Health Organization (WHO) have collaborated on a project to conduct a systematic review of the WHO written standards for the animal based testing requirements and procedures recommended for use in the post-licensure quality control and batch release of biologicals and also to determine to identify where updates can lead to a more harmonized adoption of 3Rs principles (i.e. Replacement, Reduction, and Refinement of animal tests) in batch release testing by national regulatory authorities (NRAs), NCLs and manufacturers and also to evaluate barriers to the adoption of 3Rs principles.

With new, stricter regulations and scientifically validated alternatives being developed by scientists, we can certainly be hopeful that the number of animals used in regulatory testing will continue to decline in the future.

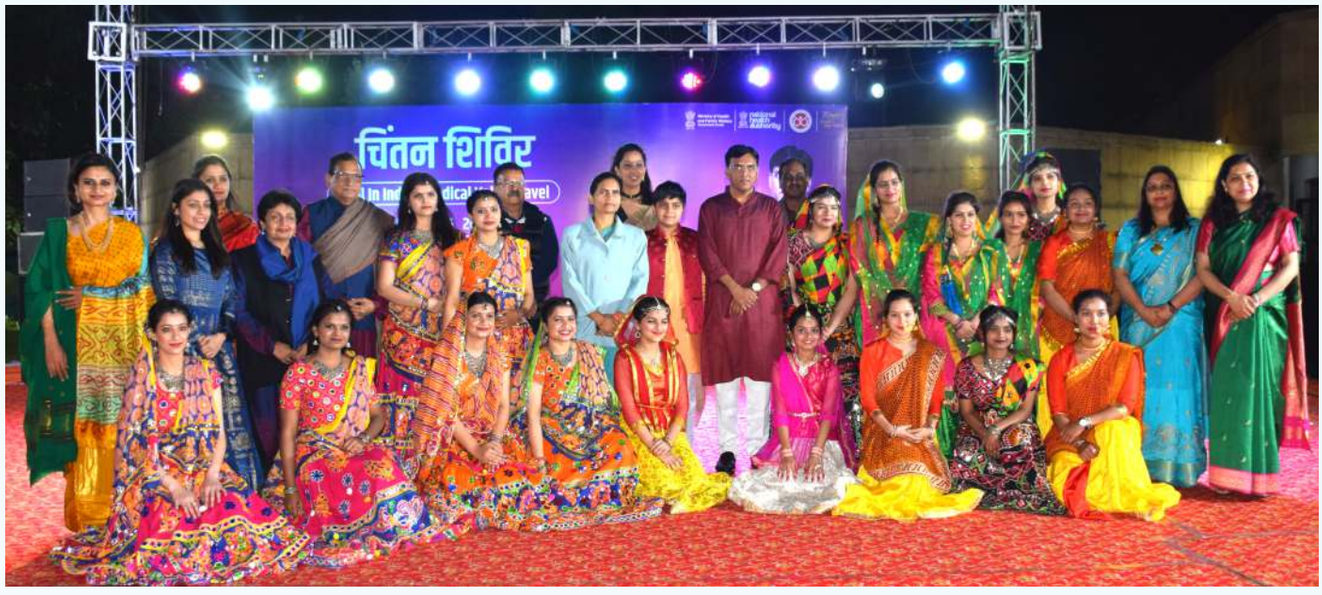
MoU BETWEEN NIB AND AcSIR FOR Ph.D PROGRAMME

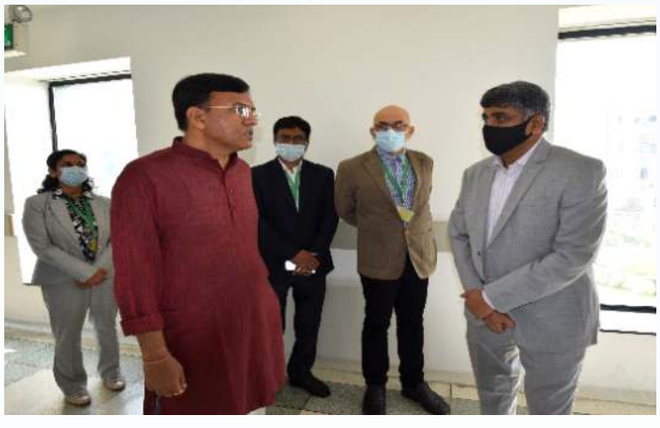


National Institute of Biologicals (NIB), Noida signed an MoU with Academy of Scientific & Innovative Research, Ghaziabad (AcSIR) on 28th February, 2022 for conducting Ph.D. programme in Biotechnology with special emphasis on Quality of Biologicals at NIB, Noida. Where, AcSIR will collaborate and recognize NIB as its Associate Academic centre.

CHINTAN SHIVIR – Heal in India

National Health Authority (Ministry of Health and Family Welfare) and the National Institute of Biologicals, organized a two-day "Chintan Shivir – Heal in India" at the National Institute of Biologicals, NOIDA on 4 & 5th March 2022 in order to have a discussion on bringing policy promoting medical tourism to promote India as a destination for wellness travel, Indian traditional medicine and wellness systems, the potential of health insurance, and digital health. Further discussions over strengthening medical infrastructure and improving primary and tertiary healthcare were also held in the workshop. Hon'ble Union Health Minister Dr. Mansukh Mandaviya, Minister of State for Health Dr. Bharati Pravin Pawar, senior officials from the Centre and States, and industry experts, participated in the 'Chintan Shivir.' Hon'ble Union Health Minister Dr. Mansukh Mandaviya visited various laboratories of the Institute and interacted with the scientists.





COVID-19 SAMPLE TESTING:

- NIB continued testing of COVID-19 suspected patient samples receiving from various hospitals, and quarantine centres of Uttar Pradesh (Baghpat, Gautambudh Nagar, Ghaziabad). During January to March 2022, NIB tested 8,966 samples reporting 4.45% positive.

PROFICIENCY TESTING (PT)/ EXTERNAL QUALITY ASSURANCE SCHEME (EQAS)

- Biochemical Kit Laboratory continued its enrolment into the Association of Clinical Biochemists of India/ Christian Medical College (ACBI/CMC) External Quality Assessment Scheme (EQAS) - 2022 for Chemistry II (Glucose, Cholesterol & Triglycerides), conducted by the Department of Clinical Biochemistry, Christian Medical College, Vellore.

TECHNICAL EXPERT COMMITTEE MEETINGS:

- Dr. Akanksha Bisht, Scientist Grade –II & Head, HvPI & Secretary of International Haemovigilance Network (IHN) attended the GAPP (facilitatinG the Authorisation of Preparation Process for blood, tissues and cells), final Dissemination Conference online with the host location Thessaloniki, Greece on 20th - 21st January 2022.

- Second meeting of advisory committee was held on 8th February 2022 for setting up of BSL-3 facility at NIB, Noida.

- Dr Gauri Misra, Scientist Grade-II & Head, SRRDU attended the First hub experts meeting (External Expert) to discuss the queries of the innovators organised by BIRAC through virtual mode on 4th March 2022.

- Scientists of Vaccine and Antisera Laboratory attended the 10th Meeting of Expert Working Group– Vaccine & Immuno-sera for Human Use through video conferencing on 14th March 2022 organized by Indian Pharmacopeia Commission (IPC), Ghaziabad.

- Dr. Harish Chander, Scientist Grade-I & In-charge DD(QC) Chaired a Session in DST-SERB Sponsored "Post Covid-19 Pandemic Era: Prospective Shift towards Clinical and Translational Research" at Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab on 17th March 2022.

- Institutional Biosafety Committee (IBSC) along with DBT Nominee organized its first meeting on 22nd March 2022, to discuss the IBSC Guidelines applicable for NIB, action plan for the next year 2022-23 and to review IBSC applications for R&D projects.

- Dr. Akanksha Bisht, Scientist Grade –II & Head, HvPI and Secretary of IHN board attended the "2022 virtual mini-seminar of the International Hemovigilance Network on plasma vigilance" organized by IHN on 29th March 2022.

INVITED TALK/ LECTURES

- Dr. Harish Chander, Scientist Grade-I & In-charge DD(QC), delivered a talk on: "Global Scenario of IVD Medical Device Regulation" in BIS Webinar "In-Vitro Diagnostic Medical Devices: Standardization and Regulation" held on 9th Feb, 2022.

- Dr Shikha Yadav, Scientist Grade-II & Head Animal Facility delivered a talk on in the Regional Workshop on "Role of Laboratory Animals in Bio-medical Research" organized by North Eastern Indira Gandhi

Regional Institute of Health & Medical Sciences (NEIGRIHMS), Ministry of Health & Family Welfare, Shillong in Hybrid Mode on "Occupational Hazard for Laboratory Animal Workers" on 22nd March 2022.

TRAININGS & WORKSHOPS

- Under the ongoing National AIDS Control Programme (NACP)-IV of National AIDS Control Organization (NACO), the National Reference Laboratory (NRL) of National Institute of Biologicals has organized one day virtual EQAS Workshop for distribution of HIV Proficiency test penal (Round 1I, 2021-22) to SRLs of Utter Pradesh & Uttaranchal on 8th February, 2022.

- Ms. Shalini Tewari Scientist Grade-III & Head QMU and Ms. Rashmi Srivastav Scientist Grade-III & Member QMU participated in Pharma Investigation & CAPA: Quality Management System for continual improvement; Online Workshop held on 24th -25th February 2022 organised by BlueTech Media.

- Vaccine & Antisera laboratory imparted training to the scientists of the National Institute of Animal Biotechnology (NIAB), Hyderabad from 14th -17th March 2022 on quality control testing of Covid vaccines (Covishield and Covaxin).

- Blood Reagent Laboratory imparted training to an official from Indian Red Cross Society (IRCS), New Delhi on Cryopreservation and thawing of Red blood cells from 14th - 16th March 2022.

- 23 Scientists of NIB attended a 4 day online Training Program on Laboratory Quality Management System & Internal Audit as per ISO 17025:2017, organised by National Institute of Training for Standardization, NOIDA from 10th to 13th January 2022.

- NIB facilitated a technical Laboratory tour to B. Pharm students from the College of Pharmaceutical Sciences, Govt. Medical College, Calicut, Kerala on 17th March 2022. The students were given a basic overview of NIB and visited various Laboratories, and interacted with Scientists.

PUBLICATIONS

- Kumar S, Perumal, N, Raj VS. Evaluation of Gut Microbial Changes in Human and Murine Models in Response to Antibiotics. Indian J Pharm Sci 2021;83(6):1308-13141 https://doi.org/10.36468/pharmaceutical-sciences.887

- Kumar Suresh, Bharti VK, Yadav Shikha, "Quality evaluation of vaccines, immunoglobulins and other biologicals", QUEST Magazine (July-Dec. 2021). Directorate of Quality, Reliability & Safety (DQR&S), DRDO Head Quarters, New Delhi.

- Rashmi Shrivastava1, Shalini Tewari2*, Charu Mehra Kamal3, Niharika Trivedi, Manisha Varshney, Aakanksha Yadav, Anupkumar R Anvikar. National Control Laboratories in Quality healthcare- a roadblock for substandard biopharmaceuticals. https://doi.org/10.1016/j.biologicals.2022.02.002.

- Birendra Kumar, Charu Mehra Kamal, Gurminder Bindra et al. Evaluation of Potency of Erythropoietin Injection Available in Indian Market to Assess its Quality. Inventi Rapid: Biosimilars & Biopharmaceuticals, 2022(1):1-5, 2022.

- Rajawat J, Misra G, Anvikar AK, Era B. Therapeutic targeted approaches for Covid-19 treatment. Curr Pharm Biotechnol. 2022 Mar 4. doi: 10.2174/1389201023666220304163903. PMID: 35249480 [Epub ahead of print].

- Polisety A., Misra G., Rajawat J., Katiyar A., Singh H., Bhatt A.N. Therapeutic natural compounds Enzastaurin and Palbociclib inhibits MASTL kinase activity preventing breast cancer cell proliferation. Medical Oncology in Press.

- Prabhat Suman, Vikrant Mehta, Andrew W B Craig, Harish Chander, Wild-type p53 suppresses formin-binding protein-17 (FBP17) to reduce invasion, Carcinogenesis, 2022;, bgac015, https://doi.org/10.1093/carcin/bgac015.

WOMENS' DAY CELEBRATION ON 08.03.2022

With great zeal and enthusiasm, NIB celebrated International Women's day 2022 with the theme "Gender equality today for a sustainable tomorrow". Dr. (Mrs.) Shashi Khare, former Deputy Director (Quality Control) – NIB was the Chief Guest for this year's International Women's day celebration. She emphasised that the purpose of the day is not only to honour a woman's accomplishments but also to raise awareness about bias. She shared her experiences of her scientific journey during her interaction with the women staff and motivated them to continue to contribute to the nation's growth.

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For any other Information/ Suggestions/ Queries related to Newsletter kindly contact: Dr. Manjula Kiran, Associate Editor, Email: mkiran@nib.gov.in. Please feel free to share your valuable thoughts & feedback for the betterment of the edition. We look forward to hear from you!!!