PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Balram Bhargava, MBBS, MD, DM
Director General
Indian Council of Medical Research

06 August 2020

Via e-mail: balrambhargava@yahoo.com

Subject: For Dr Balram Bhargava, from PETA India: Request to cancel permission for the capture of wild monkeys for use in research by NIV

Dear Dr Bhargava,

I am writing on behalf of People for the Ethical Treatment of Animals (PETA) India and our more than 2 million members and supporters to draw your attention to the Maharashtra government's recent decision to grant permission for the capture of rhesus monkeys for use by the National Institute of Virology (NIV) in the testing of a vaccine for the novel coronavirus (SARS-CoV-2).

This letter is co-signed by my colleague Dr Lisa Jones-Engel, a recognised authority on the role that free-ranging Asian primates play in the maintenance and transmission of infectious agents as well as their suitability as biomedical models of infectious diseases. Her decades of research and expertise have informed our response to NIV's misguided decision to capture wild rhesus macaques for use in SARS-CoV-2 studies.

Based on the scientific information presented below, we respectfully ask that you instruct NIV to halt this research and that you help the institute adopt superior, human-relevant, animal-free research methods instead.

Scientific Challenges and Zoonotic Risks

The recent decision by the Maharashtra government to grant permission for the capture of wild rhesus monkeys for use in SARS-CoV-2 vaccine testing by NIV is at odds with basic scientific principles. For decades, the international biomedical research community has acknowledged that rigorous scientific investigation requires a thorough understanding of any potentially confounding factors that may obscure scientists' knowledge of the immune function of their research subject.[1,2,3] When the decision is made to use an animal model, the scientific community has consistently used well-characterised, specific-pathogen-free (SPF) animals capable of exhibiting a normal immune response to viral infection or vaccination.[4] The use of SPF animals is also critical in protecting the health of laboratory workers and scientists who are exposed to them.

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Wild-caught rhesus macaques will not be well characterised and will most certainly not be SPF. More than 80% of rhesus macaques in India are in close proximity to human settlements.[5] Infectious agents move with ease between human and non-human primate populations. It should be expected – and has been repeatedly shown – that pathogens such as *Mycobacterium tuberculosis* complex, picornaviruses, paramyxoviruses, influenza viruses, astroviruses, a broad range of enteric pathogens, and enzootic viruses are present in free-ranging rhesus macaque populations in Asia, and these pathogens can be shared among humans and monkeys.[6,7,8,9,10,11,12] There is also a risk that zoonotic pathogens such as Kysanur forest disease virus would be spread to those who trap and handle free-ranging monkeys in Maharashtra.[13]

The presence of these and other infectious agents in recently captured macaques, as well as the act of trapping and transporting them, will compromise their immune function and distort the interpretation of the results of the vaccine studies at NIV. Finally, serologic tests for SARS-CoV-2 have been shown to perform poorly even in well-characterised SPF macaques.[14]

Animal models have consistently failed to replicate the pathology of disease observed in humans infected with severe acute respiratory syndrome coronavirus (SARS-CoV) or Middle East respiratory syndrome coronavirus (MERS-CoV). Please see the review by Gretebeck and Subbarao for a detailed discussion of the limitations[15] of all animal models, and also see an editorial by

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Leist and colleagues discussing novel animal-free test methods for the development of COVID-19 drugs and vaccines.[16]

Coronavirologist Professor Dave Matthews and colleagues recently published[17] a study demonstrating that SARS-CoV-2 can mutate when undergoing replication in cell culture and/or during vaccine challenge studies in animals, including non-human primates. The authors state, "**This has clear implications for the use of Vero cells to propagate and grow large batches of the virus for research and especially virus batches grown for use in vaccine challenge studies. Moreover, it also raises the possibility that even virus stocks which have been carefully assayed for homogeneity could still spontaneously generate this deletion during animal challenge studies – particularly in non-human primates.**"[18]

This study and others demonstrate that it is reasonable to expect that some of the SARS-CoV-2 virus used to inoculate monkeys will mutate in order to more efficiently adapt to or infect this novel host. This, in turn, means scientists will have difficulty distinguishing the effects of the treatments or vaccines they're testing from the effect of the virus mutation.

NIV's critical research to develop treatments and/or vaccines to protect humans from COVID-19 can and should be conducted using cutting-edge research methods and tools. The use of wild, non-SPF monkeys will only delay and possibly derail these efforts.

Regulatory Agency Preference

The report of the first global regulatory workshop on COVID-19 vaccine development of the International Coalition of Medicines Regulatory Authorities advises researchers developing vaccines to draw on their experience of vaccine platforms and suggests that toxicology data and clinical data from other vaccines from the same platform can be used to support first-in-human (FIH) clinical trials. It also states that developers do not need to demonstrate vaccine efficacy in "animal challenge models" before proceeding to FIH clinical trials.[19] The Central Drugs Standard Control Organisation has also reduced unnecessary requirements for animal toxicity tests in the development of therapies for COVID-19.[20]

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Experimenting on animals is not only unethical but also unjustifiable from a scientific perspective, since it repeatedly fails to produce results that address pressing human health issues.[21]

Regulations Require the Use of Available Non-Animal Methods
Section 17(2)(d) of The Prevention of Cruelty to Animals (PCA) Act, 1960, states that "experiments on animals [must be] avoided wherever it is possible to do so".[22]

We humbly request that, in consideration of the fundamental scientific concerns surrounding the use of wild-caught, non-SPF monkeys, you instruct NIV to halt this research immediately. Additionally, we urge you to help NIV invest in and make the transition to non-animal research techniques in order to accelerate the development of vaccines and treatments for COVID-19.

We would be happy to arrange a teleconference to discuss this important issue. Dr Jones-Engel can be contacted via Skype at jones-engel or at LisaJE@peta.org, and I can be contacted on +91 8800897382 or at DiptiK@petaindia.org. We look forward to hearing from you.

Kind regards,

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Science Policy Adviser
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Lisa Jones-Engel, PhD
Primatologist
Senior Science Adviser, Primate Experimentation
PETA US

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Harsh Vardhan, MBBS, MS(ENT)
Union Minister of Health and Family Welfare

06 August 2020

Via e-mail: drhrshvardhan@gmail.com; dr.harshvardhan@sansad.nic.in; hfm@gov.in

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Kind regards,

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Priya Abraham, MD, PhD
Director
National Institute of Virology

06 August 2020

Via e-mail: priya.abraham@icmr.gov.in; director.niv@icmr.gov.in

Subject: For Professor Abraham, from PETA India: Dangers of using wild Indian rhesus monkeys in SARS-CoV-2 research

Dear Professor Abraham,

Further to our letter sent via e-mail on 14 July 2020 (copy attached), I am writing on behalf of PETA India and our more than 2 million members and supporters to share additional scientific concerns regarding the use of captured wild monkeys in biomedical research.

This letter is co-signed by my colleague Dr Lisa Jones-Engel, a recognised authority on the role that free-ranging Asian primates play in the maintenance and transmission of infectious agents as well as their suitability as biomedical models of infectious diseases. Her decades of research and expertise have informed our response to the National Institute of Virology's (NIV) misguided decision to capture wild rhesus macaques for use in SARS-CoV-2 studies.

In consideration of the information presented below regarding international standards and the lack of scientific value of research performed on animals who are not specific-pathogen-free (SPF), we respectfully request that NIV not proceed with its proposed use of wild monkeys in experiments for SARS-CoV-2. Additionally, we urge you to adopt and invest in non-animal techniques to accelerate the development of vaccines and treatments for COVID-19.

The recent decision by the Maharashtra government to grant permission for the capture of wild rhesus monkeys for use in SARS-CoV-2 vaccine testing by NIV is at odds with basic scientific principles. For decades, the international biomedical research community has acknowledged that rigorous scientific investigation requires a thorough understanding of any potentially confounding factors that may obscure scientists' knowledge of the immune function of their research subject.[1,2,3] When the decision is made to use an animal model, the scientific community has consistently used well-characterised, SPF animals capable of exhibiting a normal immune response to viral infection or

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[13]Sayyed N. Maharashtra takes measures against spread of Kyasanur forest disease. *Hindustan Times*, 23 January 2019. https://www.hindustantimes.com/pune-news/maharashtra-takes-measures-against-spread-of-kyasanur-forest-disease/story-niFej2v3yFqR7K1ShIIrEL.html
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discussion of the limitations[15] of all animal models, and also see an editorial by Leist and colleagues discussing novel animal-free test methods for the development of COVID-19 drugs and vaccines.[16]

Coronavirologist Professor Dave Matthews and colleagues recently published[17] a study demonstrating that SARS-CoV-2 can mutate when undergoing replication in cell culture and/or during vaccine challenge studies in animals, including non-human primates. The authors state, "**This has clear implications for the use of Vero cells to propagate and grow large batches of the virus for research and especially virus batches grown for use in vaccine challenge studies. Moreover, it also raises the possibility that even virus stocks which have been carefully assayed for homogeneity could still spontaneously generate this deletion during animal challenge studies – particularly in non-human primates.**"[18]

This study and others demonstrate that it is reasonable to expect that some of the SARS-CoV-2 virus used to inoculate monkeys will mutate in order to more efficiently adapt to or infect this novel host. This, in turn, means scientists will have difficulty distinguishing the effects of the treatments or vaccines they're testing from the effect of the virus mutation.

NIV's critical research to develop treatments and/or vaccines to protect humans from COVID-19 can and should be conducted using cutting-edge research methods and tools. The use of wild, non-SPF monkeys will only delay and possibly derail these efforts.

We'd be happy to arrange a teleconference to discuss this important issue. Dr Jones-Engel can be contacted via Skype at jones-engel or at LisaJE@peta.org, and I can be contacted on +91 8800897382 or at DiptiK@petaindia.org. We look forward to hearing from you.

Kind regards,

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