**IN THE HON'BLE NATIONAL GREEN TRIBUNAL, SOUTHERN ZONE BENCH, CHENNAI**

**APPEAL NO. 65 of 2024**

**IN THE MATTER OF: -**

**Inventprise**

**…. Applicant**

**Versus**

**The Union of India & Anr.** **…. Respondents**

**REPLY AFFIDAVIT FILED ON BEHALF OF RESPONDENT NO. 1 & 2**

Filed by:
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**BEFORE THE HON'BLE NATIONAL GREEN TRIBUNAL (SZ)**
**AT CHENNAI**
**APPEAL No. 65 of 2024**

***IN THE MATTER OF***:

Inventprise, INC **... Appellant**

***Versus***

1. Union of India through Secretary,

Ministry of Environment, Forest and Climate Change,
New Delhi – 110 003.

2. National Biodiversity Authority

Represented by the Secretary, National Biodiversity Authority,
Chennai – 600 113. **... Respondents**

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**DATE:** .01.2025

**PLACE:** CHENNAI

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**BEFORE THE HON'BLE NATIONAL GREEN TRIBUNAL (SZ)**

**AT CHENNAI**

**APPEAL No. 65 of 2024**

***IN THE MATTER OF:***

Inventprise, INC
18133 NE 68th Street, d150,
Redmond, Washington – 98052, USA **... Appellant**

**Versus**

1. Union of India through Secretary,
   Ministry of Environment, Forest and Climate Change,
   Indira Paryavaran Bhawan,
   Jorbagh Road, New Delhi – 110003.

2. National Biodiversity Authority
   Represented by the Secretary, National Biodiversity Authority,
   5th Floor, TICEL Bio Park, CSIR Road, Taramani,
   Chennai – 600 113 **... Respondents**

**REPLY AFFIDAVIT ON BEHALF OF RESPONDENT NO. 1 & 2**

**MOST RESPECTFULLY SHOWETH:**

I, Dr. B. Balaji, son of G. Badrinarayanan, aged 51 years, Occupation: Government service residing at Chennai, do hereby solemnly affirm and sincerely state as follows:

I. I am serving as the Member Secretary of the National Biodiversity Authority (NBA), the 2nd Respondent herein, having Office at 5th Floor, TICEL Bio Park, CSIR Road, Taramani, Chennai – 600 113, Tamil Nadu and as such, well acquainted with the facts of the case, borne out of records. I am duly authorized to sign, verify and file this Counter Affidavit and, as such, competent to defend this case on behalf of the 1st (MoEF&CC) and 2nd Respondents (NBA).

II. That the answering Respondent had perused the instant Appeal filed by the Appellant against the 1st Respondent to frame rules for a single window clearance for patent application against the order dated 09.03.2024 issued by the 2nd Respondent and the annexures thereto. At the outset, the Respondents deny each and every averment and/or submission made in the Appeal, which is contrary to and inconsistent with the averments made and facts stated in the present reply. The Appeal is liable to be dismissed *in limine* as not maintainable as it seeks relief which is not maintainable in law. It is submitted that nothing stated in the Appeal may be deemed to have been admitted by the Respondents unless the same is expressly admitted in the present reply.

III. It is respectfully submitted that the subject matter of this Memorandum of Appeal filed under Section 52A of the Biological Diversity Act, 2002 hereinafter referred to as the (BD Act) read with clause (j) of Section 16 of the National Green Tribunal Act, 2010 and clause (l) of Rule 8 of the National Green Tribunal (Practices and Procedure) Rules, 2011 pertains to matter against the alleged order of the Respondent No. 2 dated 09.03.2024.

IV. It is submitted that the Appellant does not have any *locus standi* in this Appeal to challenge the orders/notices issued by the 2nd Respondent to the Appellant calling upon the Appellants to sign the access and benefit sharing agreement for commercial utilization of biological resources. The Appellant is filing the instant appeal after 3 years since the approval and clearance of the application granted on 23.03.2021 by Respondent

No. 2. The instant appeal is liable to be dismissed based on the above-mentioned preliminary objections.

Without prejudice to the foregoing preliminary objections as to the very maintainability of the appeal, this Respondent wishes to place the correct facts relating to the issue, subject matter of the Appeal as follows:

1. It is respectfully submitted that the Appellant had placed all his submissions wholly on one aspect of the issue, *i.e.,* the 'Rotavirus strain 116E' used by the Appellant in his invention is not a biological resource. That the said virus is a non-living substance, processed off-the shelf product and has to be extracted from the host by human intervention, and thus, by virtue of this process, it becomes a value-added product, which is exempted under the provisions of the BD Act, 2002.

2. It is submitted that the Biological Diversity Act, 2002 and the subsequent Biological Diversity (Amendment) Act, 2023 which was passed by the Parliament of India to meet the obligations under the Convention on Biological Diversity, 1992 ("CBD") signed in Rio de Janeiro. The Act provides for the conservation of biological diversity, sustainable use of its components and fair and equitable sharing of the benefits arising out of the use of biological resources and knowledge associated thereto. It is further submitted that the 2nd Respondent is the Authority established under Section 8 of the Biological Diversity Act, 2002, and it functions as enumerated under Section 18 of the Act.

3. The NBA is a statutory body, and it performs facilitative, regulatory and advisory functions for the Government of India under the Ministry of Environment, Forest and Climate Change (MoEF&CC) on the issues relating to the conservation of biodiversity, sustainable use of its components and fair and equitable sharing of benefits arising out of the use of biological resources.

राष्ट्रीय जैव विविधता प्राधिकरण National Biodiversity Authority Chennai - 600 113 चेन्नई - 600 113

4. It is submitted that under Section 6 of the BD Act, without obtaining prior approval of the National Biodiversity Authority, no person shall apply for any intellectual property rights in or outside India for any invention based on any research or information on any biological resource obtained from India. The Appellant had filed an application on 11.09.2020 in Form – III No. INBA3202002159 (4228) **(Annexure – R1)** before the National Biodiversity Authority for obtaining approval as per the provisions of the BD Act for obtaining a patent on the invention titled "Heat stable liquid rotavirus vaccine". The invention is directed to an oral vaccine composed of a micronized freeze-dried rotavirus particle emulsion with buffering excipients in a non-aqueous liquid. The Appellant had procured the biological resources from M/s Bharat Biotech International Ltd. Hyderabad, India which was used in the patent invention.

5. This case of unwarranted access came to the notice of Respondent No. 2 in the usual monitoring of published patents conducted by Respondent No. 2 to identify such non-compliance cases in and outside India. Based on these results, Respondent No.2 sent an official communication to the Indian patent notifying them of the non-compliance and requesting them to direct the applicant to obtain the required statutory approvals. Subsequently, the applicant filed the said Form-III application. It is submitted that while the application filed in Form – III with NBA for the invention titled "Heat stable Liquid Rotavirus vaccine" ( Patent Application No. 201917035818 ) was under process, it was found during the internal patent search by NBA that the patent was already granted to the Appellant by the US Patent Office on 17.09.2019 (US Patent Number 10,413,604) and patent applications were pending in US, China, Indonesia, Korea, Malaysia, and Philippines **(Annexure – R2)** without prior approval of the NBA. While processing the application on merits, the Appellant reiterated that he was already exempted from the BD Act and the application was filed as a formality

to get a 'No Objection Certificate' (NOC) from NBA to be submitted before the Indian Patent Office. It is submitted that the Appellant is an entity (non-Indian) categorised under Section 3(2) of the BD Act, and having violated the provisions of the BD Act, the Appellant does not have the right to claim a no objection certificate and subsequently withdraw his application filed under Form - III.

6. The Appellant, *vide* their communication dated 26.04.2021 **(Annexure – R3)**, stated that they had procured the particular rotavirus strain for research and development. The biological resource is a processed off-the-shelf product and not a naturally occurring material *per se*. However, it is respectfully submitted that irrespective of the source from where the biological resources were collected, either wild or culture collections or traders or vendors, prior approval of NBA is required for access to biological resources occurring in or obtained from India for commercial utilization, or IPR or research done by entities categorized under Section 3 (2) of the BD Act. Furthermore, as per the definition under Section 2 (c) of the BD Act, only the access to human genetic material is exempted, not the microorganisms such as (Rotavirus) in the present case.
7. The Appellant had obtained US patent rights using the biological resources obtained from India without the prior approval of the NBA, thereby violating Sections 3 and 6 of the BD Act. Respondent No. 2 examined the communication sent by the Appellant, and a clarification dated 29.04.2021 was also sent, rejecting the claims of the Appellant and stating that the invention requires prior approval of Respondent No. 2.
8. It is submitted that as per Rule 18 (1) of the Biological Diversity Rules, 2004, any person desirous of applying for a patent or any other intellectual property based on research on any biological resources and or associated knowledge obtained from India shall apply in Form – III. The Authority, after due appraisal of the application on merits, may

grant approval for applying for a patent or any other IPR subject to terms and conditions. The approvals are granted in the form of a written agreement. The Authority may also reject the application if it considers that the request for approval cannot be acceded to after recording the reasons and also an opportunity for a hearing duly given before any order of rejection is passed.

9. It is submitted that Section 6 of the BD Act mandates that no person shall apply for any intellectual property right, by whatever name called, in or outside India for any invention based on any research or information on any biological resources occurring in or obtained from India without prior approval of the National Biodiversity Authority before making such application. After obtaining patents in the USA without approval from the NBA, the Appellant applied for a patent in India.

10. It is submitted that the Appellant in the Application in Form – III stated that the biological resource, *i.e.*, rotavirus, used in the said invention was obtained from India. The Appellant mentioned in the application that he had sourced the biological resource from Bharat Biotech International Ltd., Hyderabad. On the scrutiny of the application by the NBA, it was found that the Appellant, being a Section 3(2) entity, did not get the prior approval of the NBA for obtaining the biological resources from India for research as well. The Appellant had applied for a patent in the USA and other countries by utilizing the Indian biological resources for their research without obtaining prior approval from the NBA, thereby violating Sections 3 and 6 of the BD Act.

11. The Respondent No. 2, based on the information received during the usual monitoring of published patents, had sent an objection communication dated 18.02.2020 **(Annexure – R4)** to the Patent Office to direct the Appellant to seek approval from Respondent No.2 before obtaining a patent as stipulated under Section 6 of the Biological Diversity Act, 2002.

It is further submitted that though the Appellant had submitted the application in Form – III on 11.09.2020 to the NBA seeking prior approval, the Appellant had already obtained the Patent Rights on the invention (*using the biological resources taken from India)* in the USA without the prior approval of the Respondent No.2 in 2019.

The patent application filed in India (Patent Application No. 201917035818) was granted by the Indian Patent Office on 29th December 2023 without considering the necessary NBA approvals for accessing biological resources. The patent grant constitutes a violation of the order/direction given by the Honourable High Court of Delhi on 20.12.2023.

12. It is submitted that the Appellant has declared in Form – I submitted to the Indian Patent Office affirming that no Indian biological resources are used in the invention claiming patent. However, the complete specification of the invention submitted by the applicant to the patent office acknowledges that the virus was procured from India, which was also mentioned in the Form – III application. The Office Circular dated 23.05.2017 **(Annexure – R5)** issued by the Controller General of the Patent Office to claim exemption under Value Added Products (VAP). However, this is an internal circular of the Patent Office, hence, not binding to the Respondent No. 2. It is submitted that as per Section 6 of the Act, products that fulfil the criteria given in Section 2 (p) are alone considered as value-added products and exempted from the Act. The instant case does not qualify the conditions in Section 2 (p) of the Act, but it squarely falls under the definition of biological resources, as rotavirus is a microorganism. However, access to biological resources to prepare VAP is not an exempted activity under the Act and requires prior approval of the NBA. Hence, the contention of the Applicant cannot be accepted.

As this was a clear violation of the BD Act's provisions, after due consideration, the NBA observed that the necessary approvals

could not be given for the 'past access' of biological resources. Accordingly, the application was placed before the 60th Expert Committee Meeting on Access and Benefit Sharing (EC on ABS) constituted under Section 13 of the BD Act held on 03rd November 2020 **(Annexure – R6).** The Expert Committee comprises a body of scientific and legal experts in the respective fields from the recognized government research organisations and departments to examine the applications filed in the NBA for approvals under the BD Act.

13. It is submitted that the Expert Committee (EC), after examination of the application and the documents filed by the appellant, observed that the applicant, being a Section 3 (2) entity, had accessed the biological resources from Bharat Biotech Pvt. Ltd. without prior approval of NBA as required under Section 3 of the BD Act. It was also observed that the applicant had obtained Patent in USA without prior approval of NBA as required under Section 6 of the Act. Hence, the applicant had contravened Sections 3 and 6 of the BD Act. The Expert Committee noted the Appellant's contraventions and decided to determine the highest benefit-sharing component in such cases. Accordingly, the Appellant was duly informed by the Respondent No. 2 about the Expert Committee (EC) recommendations *vide* the official communication dated 28.01.2021 and also to apply in Form – I for regularizing biological resources already accessed to conduct research for developing the said invention **(Annexure – R7)**.

14. It is submitted that as the Appellant was not complying, reminder letters dated 12.10.2022 and 17.10.2022 **(Annexure – R8)** sent through post and email to execute the agreement as a part of the approval required in Form III. However, the Appellant replied *via* their email dated 05.11.2022 (**Annexure – R9)** that they were not interested in proceeding further and would like to abandon the Form III application. In response to the reply sent by the Appellant, Respondent No. 2 on 09.11.2022 **(Annexure – R10)** had communicated to the Appellant that

the application could not be closed as the Appellant had already obtained a patent in the US and filed patent applications in India and other foreign countries without the statutory prior approvals from the Respondent No.2.

15. On 17.11.2022, **(Annexure – R11)** the Appellant through their counsels had sought time to reply as the Appellants are based in foreign jurisdiction, further requesting Respondent No. 2 not to pass any adverse order without giving opportunity of hearing. It is respectfully submitted that Respondent No.2 did not initiate any legal action or criminal proceedings against the Appellant. Hence, there is no need to grant a hearing opportunity. Respondent No.2 had given sufficient time to execute the agreement and directed the Appellant to comply with the laws. However, the Appellant did not send the signed agreement nor communicate it to Respondent No.2 even after three months of seeking time to reply. Hence, Respondent No.2 had to send another reminder dated 22.02.2023 **(Annexure – R12)** to the Appellant to execute the agreement and comply with the provisions of the BD Act.

16. On 25.02.2023 **(Annexure – R13)**, the counsel for the Appellant via email stated that they had sought time (for three months) to get instructions from their client only, i.e. the Appellant, and not to execute the agreement. The counsel reiterated that the Appellant does not fall under the purview of the BD Act and requested to issue a 'No Objection Certificate' and grant a hearing before the order is passed. Further, the counsel informed Respondent No. 2 that the subject matter proceedings are pending with the National Green Tribunal, Chennai. As the matter is *sub-judice*, any action taken by the Respondent No. 2 in the subject matter shall be unilateral and not binding on the Appellant. It is submitted that while extending time on one pretext or the other to execute the agreement, the Appellant later informs Respondent No. 2 that the matter is now '*sub-judice*' before the Green Tribunal.

17. The Appellant had neither sent any legal notice to Respondent No. 2 nor served the notice ordered by the National Green Tribunal. On the one hand, the Appellant says the matter is *sub-judice* and, on the contrary, seeks an opportunity for a hearing before passing an order. It is respectfully submitted that Respondent No. 2, a statutory and autonomous body under the BD Act, does not pass any orders or grant the opportunity of hearing if the matter is *sub-judice*.

18. It is submitted that in response to the Appellant's communication that the matter is *sub-judice*, Respondent No. 2 had sent a communication dated 02.03.2023 **(Annexure – R14)** to the Appellant to provide the details of the case pending before the National Green Tribunal, Chennai. On 21.03.2023, the Counsel for the Appellant stated that the matter filed with the NGT is under objection/defects, and once the objection/defects have been addressed, the details of the case filed will be provided to Respondent No. 2 **(Annexure – R15)**.

19. It is submitted that the Appellant has misled the National Biodiversity Authority (Respondent No. 2) by stating the matter is *sub-judice* when the case is not even numbered or admitted by the Registry, NGT. It is respectfully submitted that the Appellant had abused the process of law and misled the statutory authorities. The Appellant informed Respondent No. 2 that the matter is *sub-judice* and the defect in the case will be corrected, and the case details will be provided in due course. However, without providing the details of the case filed before the NGT, Chennai, the Appellant had filed a writ petition in WP. No. 26 of 2023 before the Hon'ble High Court of Delhi against the Controller of Patents and the 2nd Respondent the instant Appeal seeking grant of patent, issuance of NOC and quashing the communication requiring execution of benefit sharing agreements.

20. The Hon'ble High Court, *vide* its order dated 20.12.2023, directed the 2nd Respondent to give a personal hearing to the Appellant before

the Expert Committee of the NBA and to decide whether the biological resource falls within the purview of the BD Act. The order stipulated that the decision was to be taken within three months. In compliance with the orders/directions passed by the Hon'ble High Court, the 2nd Respondent constituted an Expert Committee (comprising of Scientists, a virologist from ICMR (NIV) and a representative of the Indian Patent Office) on 17.01.2024 to examine the application filed by the Appellant and also provided an opportunity for a hearing. The NBA constituted an Expert Committee of 26 members and 2 special invitees as subject experts, Dr. Mallika Lavania representing National Institute of Virology, NIV (ICMR) Pune and Dr. Bhanumathi, Deputy Controller of Patents Designs, Chennai representing, Controller of Patents Designs and Trademark (CGPDTM). Accordingly, the Patent Attorney of the Appellant, Dr. Sudipta Banerjee, attended the hearing in person and submitted the contentions.

The Expert Committee deliberated in detail on the following contentions/ issues raised by the Petitioner/applicant:

- Whether Virus is considered a microorganism as per the available scientific literature?
- Can the rotavirus accessed by the Petitioner/applicant be considered as human genetic material?
- Whether 'Rota virus strain 116E' accessed be considered a value-added product (VAP) as claimed by the Petitioner/applicant?

The following are the critical points of the observations made by the EC Members on the above issues:

i. That the virus strain Rotavirus 116E fits into the definition of "biological resource", and the details submitted by the Petitioner/applicant's statement that the rotavirus strain is an isolated strain clearly suggests that the resource under question

is living and has genetic material in it and its components can be isolated.

ii. The Appellant can only multiply the virus in the lab because the strain contains genetic material.

iii. The experts clarified that a virus contains its own genetic material, which can be either DNA or RNA. This genetic material carries the instructions necessary for the virus to replicate and produce new viral particles. This genetic material carries the genetic instructions necessary for the virus to replicate and produce new viral particles within host cells. The virus uses the host cell machinery to replicate its own genetic material. Studies prove that the rotavirus infects both humans and animals. The said virus strain could not be considered human genetic material as it replicates its own genetic material, thereby producing new viral particles using the human or animal body only as a host.

iv. The EC clarified that all major rotavirus vaccines are usually developed using strains of the viruses, and this particular invention follows the same mechanism (as per the complete specification of the patent application submitted by the Petitioner/applicant). The virus itself or its components serve as an essential biological resource for the production of vaccines to prevent rotavirus infection.

v. Petitioner/applicant accessed a rotavirus strain in its recognizable and separable form, which does not qualify as a value-added product under Section 2(p) of the Biological Diversity Act of 2002.

vi. That even part thereof is considered a biological resource as per the definition of Section 2(c) and is in "separable and recognizable form". The EC was of the opinion that even the final vaccine produced by the Petitioner/applicant does not qualify as a value added product under Sec 2(p) of the Biological Diversity Act, 2002.

vii. The EC also observed that the Indian Patent Office granted a patent to the Appellant on 29.12.2023 without waiting for the approval of the 2nd Respondent **(Annexure R16).**

21. The 2nd Respondent, based on the recommendations of the Expert Committee, passed an order on 09.03.2024 directing the Appellant to execute the agreement and file Form – I for the already accessed biological resources.

22. However, aggrieved by the order passed by the 2nd Respondent, the Appellant filed an appeal in WP No. 65 of 2024 before the Hon'ble High Court of Delhi. During the initial hearings, the counsel for the 2nd Respondent raised preliminary objections on the maintainability of the writ petition as the appellant has to file an appeal before the Hon'ble National Green Tribunal against any orders passed by the National Biodiversity Authority. In view of the same, the counsel for the Appellant withdrew the writ petition with liberty to avail appellate remedy (NGT). Hence, the petition was dismissed by the Hon'ble High Court as withdrawn.

**Applicable International treaties and conventions:**

23. It is submitted that the objective of the Convention on Biological Diversity (CBD), 1992 is stated in Article 1:

> *"The objectives of this Convention, to be pursued in accordance with its relevant provisions, are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies, and by appropriate funding."*

The Precautionary Principle was explicitly framed in 1992 via the Rio Declaration by representatives of 178 nations as:

*"Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." [Rio Declaration on Environment and Development, Principle 15, U.N. Doc. A/CONF. 151/26 (Aug. 12, 1992)].*

It is submitted that the precautionary principle under International environmental law is enshrined in the Preamble of the CBD which states that:

*"Where there is a threat of significant reduction or loss of biological diversity, lack of full scientific certainty should not be used as a reason for postponing measures to avoid or minimize such a threat."*

The Precautionary Principle is of particular relevance and importance in the context of conservation and sustainable use of biodiversity and living natural resources. Application of the Precautionary Principle helps sustain the biodiversity assets and ecosystem services that underpin all societies and economies and can thereby contribute to the eradication of poverty; maintenance of a natural and social environment supportive of human dignity, bodily health, and spiritual well-being; and the rights of indigenous peoples to their spirituality, knowledge, lands, resources and livelihoods.

24. Under Article 3 of the CBD, the sovereign has national rights over biological resources. This principle enables developing countries to get better benefits from their biological resources and traditional knowledge pertaining to them. Under Article 8(j), CBD requires each state party to respect, preserve and maintain knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity. These two are the most important articles in the CBD, concerning biodiversity. CBD commits member countries to conserve and develop biological resources for sustainability. Sustainable

use of biological resources means finding new drugs, crops and industrial products while conserving the resources for future generations.

25. Access and benefit-sharing (ABS) refers to the way in which genetic resources may be accessed, and how the benefits that result from their use are shared between the people or countries using the resources (users) and the people or countries that provide them (providers). It is submitted that India is *a signatory to the Convention on Biological Diversity* (CBD) in 1994 *and the Nagoya Protocol* of the CBD in 2014, *which are concerned with the trade in biological resources and the use of traditional knowledge.* This international agreement deals explicitly with ensuring Access and Benefit Sharing (ABS). The benefits obtained from using genetic resources are shared in a "fair and equitable way" with indigenous and local communities that possess the traditional knowledge regarding its use.

26. It is submitted that the CBD is a multilateral international treaty that provides national governments with sovereign rights over genetic resources and associated traditional knowledge. The CBD aims to ensure that countries receive a fair share of the benefits from their biological resources and traditional knowledge in return for conserving and allowing access to these resources.

**The following are excluded under the Biological Diversity Act from seeking approval:**

1. Normally traded commodities (provided the material is used only as a commodity).

2. Uses by cultivators and breeders, e.g. farmers, livestock keepers and beekeepers and traditional healers, e.g. vaids and hakims.

3. Collaborative research between Indian and foreign institutions that conform to the notified guidelines by the Ministry of Environment and Forest, Government of India has its approval.

K.C

राष्ट्रीय जैव विविधता प्राधिकरण National Biodiversity Authority Chennai - 600 113 चेन्नई - 600 113

4. Human Genetic material and Value Added Products.

5. Application for protection under the Protection of Plant Varieties and Farmers Rights Act, 2001.

27. India's legislation to ratify the Nagoya Protocol came in the form of the ABS Guidelines notified by the NBA in 2014. These guidelines regulate various aspects of benefit sharing. The Appellant has to provide ABS in return for the commercial use of a genetic resource to reach the local communities who are directly involved in the conservation of traditional knowledge.

28. India became one of the pioneering countries to enact a special law, the Biological Diversity Act, 2002, to implement the CBD within its borders and protect valuable biological resources. The National Biodiversity Authority (NBA) at the helm "performs facilitative, regulatory and advisory functions" to conserve genetic resources and ensure fair benefit sharing.

29. The provisions of the BD Act ensure that the protection of the sovereign rights of our country over these biological resources are protected and conserved for future uses. If the access is not regulated or restricted it will lead to exploitation or further extinction of the valuable resources. Also, this Act seeks to prevent bio-piracy of India's biological resources. Hence, the BD Act does not stand as an impediment to economic activity or human consumption; it only regulates the usage of biological resources and protects traditional knowledge.

To safeguard our precious biological resources, the Biological Diversity Act, 2002 has provided for stringent penalties for violations under Sections 3, 4 & 6 of the Act, which include imprisonment of up to 5 years and a fine that may extend up to Rs. 10 lakhs or proportionate to the damage caused by the offender if it is an entity under Section 3 (2) of the BD Act. In the present case, the Appellant is a Section 3 (2) entity and is liable to be prosecuted under Section 55 of the Act.

However, the Biological Diversity (Amendment) Act, 2023 substituted imprisonment with an increment in penalty amount for violation of provisions of the Act. The penalty imposed for contravention of the provisions of Sections 3, 4, 6 and 7 has been revised with the lower limit of penalty being one lakh rupees, which may reach a maximum of fifty lakh rupees. However, where the damage caused exceeds the amount of penalty, the penalty shall be commensurate with the damage caused.

If the failure or contravention continues, an additional penalty may be imposed, which shall not exceed one crore rupees. The amendment omits the imprisonment and appoints an adjudication officer under Section 55(A) to hold an enquiry or impose penalties under the Act. Any person aggrieved by the order made by the Adjudication Officer may appeal to the National Green Tribunal established under Section 3 of the National Green Tribunal Act, 2010.

30. **Regulatory framework for obtaining IPR:** At the national level, the BD Act was enacted, which mandates prior approval of the National Biodiversity Authority is necessary before applying for any kind of intellectual property rights (IPRs) based on any research or information on a biological resource obtained from India. The Act primarily addresses access to genetic resources and associated knowledge by foreign individuals, institutions or companies to ensure equitable sharing of benefits arising out of the use of these resources and knowledge to the country and the people.

**Earlier litigation initiated by the Appellant on the same subject matter:**

31. The patent attorney of the appellant, vide their email dated 25.02.2023, informs the 2nd Respondent that the subject-matter proceedings are pending with NGT, Chennai, but fails to give the case details.

32. The Appellant had filed a Writ Petition No. 26 of 2023 before the Hon'ble High Court of Delhi against the Controller of Patents and the 2nd Respondent

seeking grant of patent, NOC and quashing of communication requiring execution of benefit sharing agreements. The Hon'ble High Court, vide its order dated 20.12.2023, directed the 2nd Respondent to give a personal hearing to the Appellant before the Expert Committee of the NBA and decided whether the biological resource comes within the purview of the BD Act. The decision to be taken within three months.

33. The Appellant filed a Writ Petition in WP No. 23 of 2024 before the Hon'ble High Court against the Ministry of Environment, Forest and Climate Change and the 2nd Respondent seeking a direction to create a single window clearance for patent applications and quash the impugned order dated 09.03.2024 passed by the 2nd Respondent. However, the Counsel for the Petitioner withdrew the petition with liberty to avail of alternate remedy. Hence, the petition was dismissed as withdrawn.

34. It is submitted that the Appellant has violated Sections 3 and 6 of the BD Act. Moreover, there are two different approvals required under the BD Act for access of biological resources and prior approval for intellectual property laws, hence the applicant has to take approvals from the National Biodiversity Authority. Further, if any invention involves utilization of biological resources or knowledge taken from India, the applicant has to take prior approval from NBA. Hence, a single window system for obtaining patent and approvals from NBA is not feasible under the two different Acts and Rules. The Appellant is not entitled to seek the reliefs prayed in the Special Appeal and is liable to be dismissed. The Respondents reserve their right to raise any additional pleas or reply statement, if necessary, with the leave of the Honorable Court at the time of the hearing.

Without prejudice to the above contentions, this Respondent now set forth the para-wise remarks to the Appeal.

**Paras 1 to 33** - The contents are denied as false and misleading and the Appellant is put to strict proof of the same. Respondent No.2 denies the

averments and the grounds from A to X as the same are baseless without any merits and not tenable.

In the light of the above, it is most respectfully prayed that this Hon'ble Tribunal may kindly be pleased to dismiss the present Appeal with exemplary costs, direct the Appellants to pay the necessary ABS as levied by the NBA and comply with the provisions of the Act and pass any other directions as this Hon'ble Tribunal may deem fit and proper in the case.

डॉ. ब. बालाजी, भा.व.से. / Dr. B. Balaji, IFS
सचिव / Secretary
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
भारत सरकार / Govt. of India
5वां तल, टायसल बायोपार्क / 5th Floor, TICEL Biopark
सी एस आई आर रोड / CSIR Road
तरमणि, चेन्नई / Taramani, Chennai-600113

**DEPONENT**

23/1/25

**VERIFICATION**

Verified that the statements made above Paras 1 to 34 are true to my knowledge and belief. No part of it is false and nothing material has been concealed therefrom.

Verified at Chennai on the ___ day of January, 2025.

डॉ. ब. बालाजी, भा.व.से. / Dr. B. Balaji, IFS
सचिव / Secretary
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
भारत सरकार / Govt. of India
5वां तल, टायसल बायोपार्क / 5th Floor, TICEL Biopark
सी एस आई आर रोड / CSIR Road
तरमणि, चेन्नई / Taramani, Chennai-600113

**DEPONENT**

23/1/25

**Respondent No. 2**

राष्ट्रीय जैव विविधता प्राधिकरण National Biodiversity Authority Chennai - 600 113 चेन्नई - 600 113

**Through:**

**(COUNSEL)**

**Place: Chennai**
**Dated: .01.2025**

Attested by
K. C

के. सिद्धरसु / K. Chitrarasu
सलाहकार (विधि) / Advisor(Law)
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
भारत सरकार / Govt. of India
5वां तल, टायसल बायोपार्क / 5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तरमणि, चेन्नई / Taramani, Chennai-600113.

A228 13/L 3

# FORM-III

(See Rule 18 of Biological Diversity Rules, 2004)

Application form for applying for Intellectual Property Right.

Submitted on:2020-09-11 **Application No:** INBA3202002159

| | | | |
|---|---|---|---|
| **Type of the Applicant** | | : | **Entity** |
| **1** | **Full particulars of the applicant** | | |
| | **(A) Applicant 1** | | |
| | **(i) (a) Name of the Entity** | : | INVENTPRISE, LLC |
| | **(b) Type of Entity** | : | Company/Industry |
| | **(c) Status** | : | Not incorporated or registered in India |
| | **(ii) Permanent address** | : | 18133 NE 68th St d150, Redmond, Washington 226<br>**Zip /Pincode-** 98052<br>**Mobile-** +1-9811402998<br>**Phone-** +1-9811402998<br>**Email-** info@inventprise.com<br>**Website-** www.inventprise.com |
| | **(iii) Profile of the organization** | | |
| | **(a) Nature of Business** | : | Others-Research and Development and Manufacturers |
| | **(b) Attach a copy of document of incorporation or registration duly attested by the competent authority** | : | Registration Document |
| | **(iv) Details of authorized representative of Entity** | | |
| | **(i) Name** | : | Mr Praneet Singh Davar |
| | **(ii) Designation** | : | Patent Attorney |
| | **(iii) Mobile Number & Email Id** | : | **Mobile-** +1-9811402998<br>**Email-** psdavar@psdavar.com |
| | Attachments | : | Passport Copy, Id Number: **Z3540631**<br>Authorization Letter, Authorization Number: **N/A** |

org.nba.application.AgentProfile : 45259

| | | | |
|---|---|---|---|
| **(v)** | Address of the contact person / agent in India, if any | : | Yes |
| | Full particulars of Contact person | : | **(a) Profile-** Attorney<br>**(b) Name-** MR PRANEET DAVAR<br>**(c) Address-** N-220 N-BLOCK GREATER KAILASH-1<br>**State / UT-** Delhi<br>**City-** NEW DELHI<br>**Zip / Pincode-** 110048<br>**Mobile-** +91-9811402998<br>**Email-** psdavar@psdavar.com |
| | Attachments | : | **(a) Authorization Letter**<br>**(b) Passport** |

| | | | |
|---|---|---|---|
| **(2)** | **Details of invention on which IPR is sought** | | |
| | **(a)** Title of the invention | : | HEAT STABLE LIQUID ROTAVIRUS VACCINE |

| | | |
|---|---|---|
| (b) | Abstract of the invention | : The invention is directed to an oral vaccine composed of a micronized freeze-dried rotavirus particle emulsion with buffering excipients in a non-aqueous liquid. This IVT-06 formulation has imparted heat stability by protecting the virus at temperatures of 30 degree Celsius and 40 degree celsius for at least twelve months. Extrapolations from the 12-month stability data indicate shelf life of more than two years at 30 degree Celsius, and six months at 50 degree Celsius. In addition, for ease of administration, the formulated dose has a volume of 0.5 mL. |
| (c) | Details of territories / patent offices where the applicant intends to apply for the present invention | : Korea, Republic of, United States, Malaysia, Philippines, Indonesia, China. |
| (d) | Whether IP application filed for the present invention | : Yes |

| S.no | Country/Territory name | Patent Application No. | Date | Status | Patent no. & date if granted | Specify reason |
|---|---|---|---|---|---|---|
| 1 | India | 201917035818 | 05/09/2019 | Others-Application Published | | N/A |

**(3) Details of biological resources and/ or associated knowledge used in the invention**

(I) Identification (scientific name) of biological resources and its traditional use

| Sl.No | Accessed | Common name | Scientific name | Nature of biological resources | Part of biological resources |
|---|---|---|---|---|---|
| 1 | Biological Resources | Virus | Rotavirus | Micro-organism | Others- Naturally attenuated Rotavirus |

**(4) Geographical location of proposed collection**

| Sl.No | Name of biological resource | Source of access | Village / Panchayat | Town / Taluk | District | State | Name | Contact Details |
|---|---|---|---|---|---|---|---|---|
| 1 | Rotavirus | Market | N/A | N/A | N/A | N/A | Bharat Biotech International, Ltd. | Genome Valley, Shameerpet, Hyderabad-500078, TS, India |

| | | |
|---|---|---|
| (a) | **Whether any biological resources and/ or traditional knowledge used in the invention was obtained outside India** | : Yes |
| (b) | **Scientific name(s) and common name(s) of biological resource(s) and / or details of traditional knowledge used** | : Rotavirus strain 116E |
| (c) | **Whether approval of the country (ies), obtained for accessing the biological resources and / or associated traditional knowledge for the said invention.** | : No |
| (d) | **If no, specify the reasons thereon** | : The Applicant was still in the process of collecting the required information for obtaining permission from NBA at the time of filing of the said Patent Application |

u/c

| | | |
|---|---|---|
| (5) | **Details of any traditional knowledge used in the invention and any identified individual / community holding the traditional knowledge:** | |
| | Is applicable? | : No |
| (6) | **Details of institution where Research and Development activities carried out** | |
| | | : Inventprise LLC, 18133 NE 68th Str., d150 Redmond, Washington 98052, United States of America |
| (7) | **Details of economic, biotechnological, scientific or any other benefits that are intended, or may accrue to the applicant due to commercialization of the invention** | |
| | | : The present invention is directed to manufacture of bulk vaccine and overcomes the problems and disadvantages associated with current strategies and designs and provides new vaccines. |

**Declaration:**

| | |
|---|---|
| (a) | Declaration without digital signature |
| | I / We further declare that information provided in the application form is true and correct and I / we shall be responsible for any incorrect / wrong information. |

**Payment Details:**

| | | | |
|---|---|---|---|
| (a) | Transaction Id | : | QBPJPB6BWC8J |
| (b) | Payment Reference Number | : | DUD5017583 |
| (c) | Payment Amount | : | Rs. 500/- |
| (d) | Payment Receipt | : | |

# INDIA NON JUDICIAL

## Government of National Capital Territory of Delhi

## e-Stamp

सत्यमेव जयते

| | | |
|---|---|---|
| Certificate No. | : | IN-DL67129242977938R |
| Certificate Issued Date | : | 11-Oct-2019 11:38 AM |
| Account Reference | : | IMPACC (IV)/ dl717803/ DELHI/ DL-DLH |
| Unique Doc. Reference | : | SUBIN-DLDL71780342782878568387R |
| Purchased by | : | P S DAVAR AND COMPANY |
| Description of Document | : | Article Others |
| Property Description | : | Not Applicable |
| Consideration Price (Rs.) | : | 0 (Zero) |
| First Party | : | P S DAVAR AND COMPANY |
| Second Party | : | Not Applicable |
| Stamp Duty Paid By | : | P S DAVAR AND COMPANY |
| Stamp Duty Amount(Rs.) | : | 100 (One Hundred only) |

----------Please write or type below this line----------

**POWER OF ATTORNEY**

**IN THE MATTER OF**: Indian National Phase Patent Application No. **201917035818 dated 05.09.2019** based on International Application No. **PCT/US2018/018226 dated 14.02.2018** claiming priority from American Patent Application No. **62/458,904 dated 14.02.2017**, titled **"HEAT STABLE LIQUID ROTAVIRUS VACCINE"** in the name of **INVENTPRISE, LLC.**

Statutory Alert:
1. The authenticity of this Stamp Certificate should be verified at "www.shcilestamp.com". Any discrepancy in the details on this Certificate and as available on the website renders it invalid.
2. The onus of checking the legitimacy is on the users of the certificate.
3. In case of any discrepancy please inform the Competent Authority.

**FORM-26**
**THE PATENTS ACT, 1970**
**(39 OF 1970)**
**FORM OF AUTHORISATION OF A PATENT AGENT/OR ANY PERSON IN A MATTER OR PROCEEDING UNDER THE ACT,**
**(See Section 127 & 132 rule 121)**

We, **INVENTPRISE, LLC**, an American Company, of 18133 NE 68th Street, d150 Redmond, Washington 98052, USA, hereby authorise Praneet Singh Davar, C.M. Gaind, Tarannum Khan, V.K. Bali, Dr. Rekha Chaturvedi, S. Moktan, of P.S. Davar & Co., having their offices at N-220, Greater Kailash-1, New Delhi 110048, INDIA, all of Indian nationality to act on my / our behalf in connection with securing a Letters Patent for our invention titled, **"HEAT STABLE LIQUID ROTAVIRUS VACCINE"**, based on International Application No. **PCT/US2018/018226** dated **14.02.2018** claiming priority from American Patent Application No. **62/458,904** dated **14.02.2017**, including substituting and/or authorising any other person/s on their behalf and request that all notices, requisitions and communications relating thereto may be sent to such a person at the above address unless otherwise specified.

I/We hereby revoke all previous authorisation, if any made, in respect of the same matter or proceeding.

I/We hereby assent to the action already taken by the said person in the above matter.

Dated this 22nd day of October, 2019

** Signature (Full name): **Subhash V. Kapre**
Designation: **President**

To be signed**
By the person making this authorisation
Name of the natural**person who has signed along with designation and official seal, if any

**To**
**The Controller of Patents**
**The Patent Office**

# INDIA NON JUDICIAL

## Government of National Capital Territory of Delhi

### e-Stamp

सत्यमेव जयते

| | | |
|---|---|---|
| Certificate No. | : | IN-DL67129242977938R |
| Certificate Issued Date | : | 11-Oct-2019 11:38 AM |
| Account Reference | : | IMPACC (IV)/ dl717803/ DELHI/ DL-DLH |
| Unique Doc. Reference | : | SUBIN-DLDL71780342782878568387R |
| Purchased by | : | P S DAVAR AND COMPANY |
| Description of Document | : | Article Others |
| Property Description | : | Not Applicable |
| Consideration Price (Rs.) | : | 0 (Zero) |
| First Party | : | P S DAVAR AND COMPANY |
| Second Party | : | Not Applicable |
| Stamp Duty Paid By | : | P S DAVAR AND COMPANY |
| Stamp Duty Amount(Rs.) | : | 100 (One Hundred only) |

.....Please write or type below this line.....

**POWER OF ATTORNEY**

**IN THE MATTER OF**: Indian National Phase Patent Application No. **201917035818 dated 05.09.2019** based on International Application No. **PCT/US2018/018226 dated 14.02.2018** claiming priority from American Patent Application No. **62/458,904 dated 14.02.2017**, titled **"HEAT STABLE LIQUID ROTAVIRUS VACCINE"** in the name of **INVENTPRISE, LLC.**

Statutory Alert:
1. The authenticity of this Stamp Certificate should be verified at "www.shcilestamp.com". Any discrepancy in the details on this Certificate and as available on the website renders it invalid.
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3. In case of any discrepancy please inform the Competent Authority.

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**THE PATENTS ACT, 1970**
**(39 OF 1970)**
**FORM OF AUTHORISATION OF A PATENT AGENT/OR ANY PERSON IN A MATTER OR PROCEEDING UNDER THE ACT,**
**(See Section 127 & 132 rule 121)**

We, **INVENTPRISE, LLC**, an American Company, of 18133 NE 68th Street, d150 Redmond, Washington 98052, USA, hereby authorise Praneet Singh Davar, C.M. Gaind, Tarannum Khan, V.K. Bali, Dr. Rekha Chaturvedi, S. Moktan, of P.S. Davar & Co., having their offices at N-220, Greater Kailash-1, New Delhi 110048, INDIA, all of Indian nationality to act on my / our behalf in connection with securing a Letters Patent for our invention titled, **"HEAT STABLE LIQUID ROTAVIRUS VACCINE"**, based on International Application No. **PCT/US2018/018226** dated **14.02.2018** claiming priority from American Patent Application No. **62/458,904** dated **14.02.2017**, including substituting and/or authorising any other person/s on their behalf and request that all notices, requisitions and communications relating thereto may be sent to such a person at the above address unless otherwise specified.

I/We hereby revoke all previous authorisation, if any made, in respect of the same matter or proceeding.

I/We hereby assent to the action already taken by the said person in the above matter.

Dated this 22nd day of October, 2019

** _____

Signature (Full name): **Subhash V. Kapre**

To be signed**

Designation: **President**

By the person making this authorisation

Name of the natural**person who has signed along with designation and official seal, if any

**To**
**The Controller of Patents**
**The Patent Office**

6/c

UNITED STATES OF AMERICA

# The State of Washington

## Secretary of State

**I, KIM WYMAN**, Secretary of State of the State of Washington and custodian of its seal, hereby issue this

### CERTIFICATE OF EXISTENCE

**OF**

**INVENTPRISE LLC**

**I CERTIFY** that the records on file in this office show that the above named entity was formed under the laws of the State of Washington and that its public organic record was filed in Washington and became effective on 03/30/2012.

**I FURTHER CERTIFY** that the entity's duration is Perpetual, and that as of the date of this certificate, the records of the Secretary of State do not reflect that this entity has been dissolved.

**I FURTHER CERTIFY** that all fees, interest, and penalties owed and collected through the Secretary of State have been paid.

**I FURTHER CERTIFY** that the most recent annual report has been delivered to the Secretary of State for filing and that proceedings for administrative dissolution are not pending.

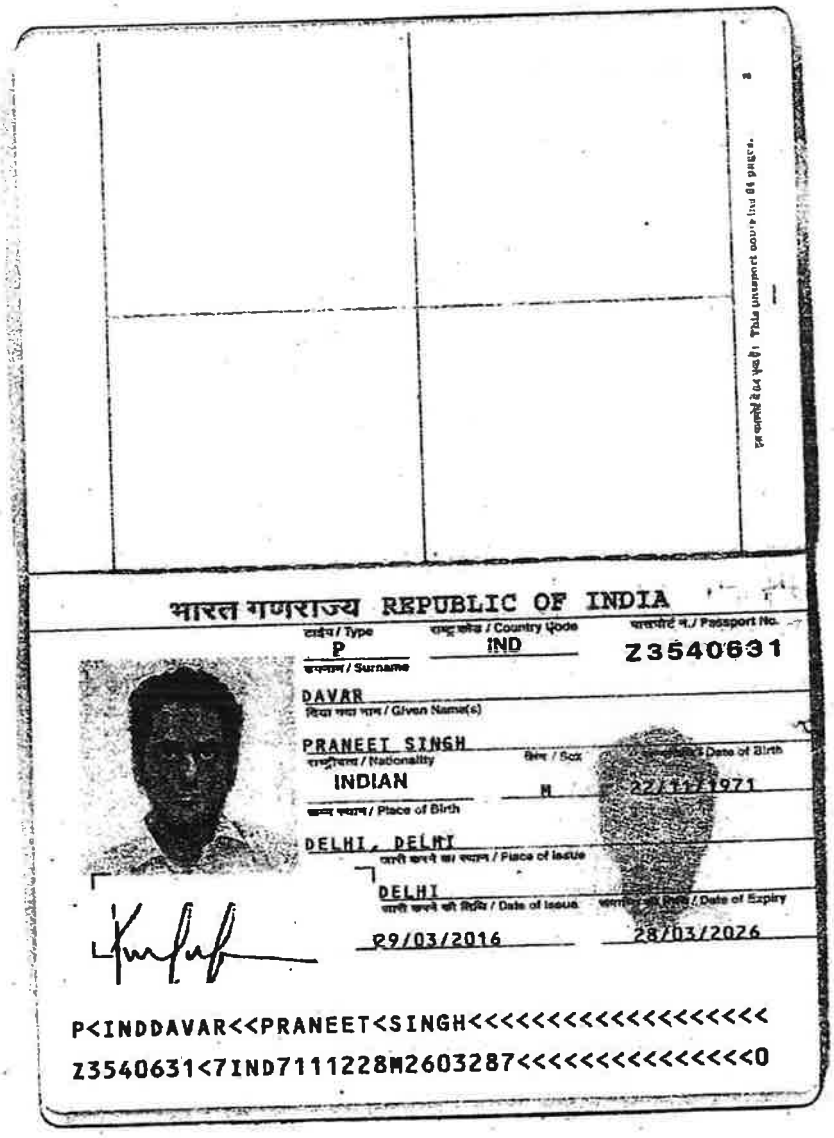
Issued Date: 09/08/2020
UBI Number: 603 194 814

Given under my hand and the Seal of the State of Washington at Olympia, the State Capital

Kim Wyman

Kim Wyman, Secretary of State

Date Issued: 09/08/2020

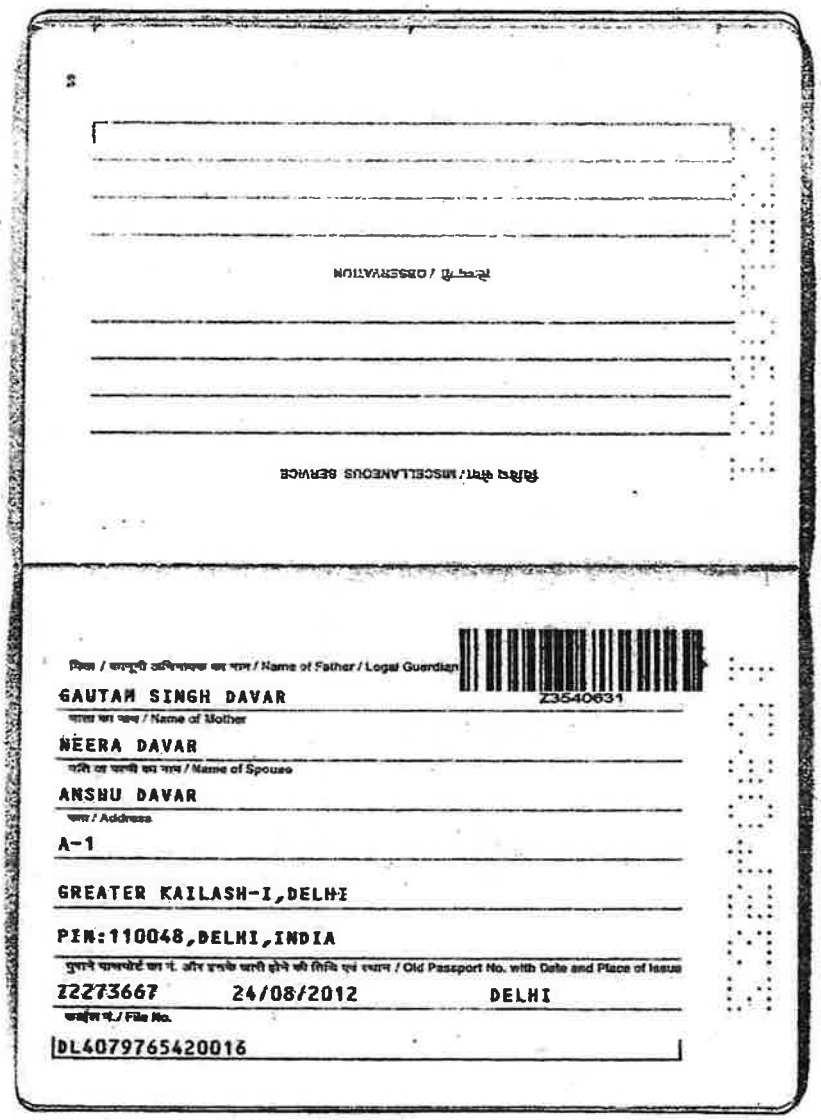


भारत गणराज्य REPUBLIC OF INDIA

प्रकार / Type: P
राष्ट्र कोड / Country Code: IND
पासपोर्ट नं./ Passport No.: Z3540631

उपनाम / Surname: DAVAR
दिया गया नाम / Given Name(s): PRANEET SINGH
राष्ट्रीयता / Nationality: INDIAN
लिंग / Sex: M
जन्म तिथि / Date of Birth: 22/11/1971
जन्म स्थान / Place of Birth: DELHI, DELHI
जारी करने का स्थान / Place of Issue: DELHI
जारी करने की तिथि / Date of Issue: 29/03/2016
समाप्ति तिथि / Date of Expiry: 28/03/2026

P<INDDAVAR<<PRANEET<SINGH<<<<<<<<<<<<<<<<<<<<
Z3540631<7IND7111228M2603287<<<<<<<<<<<<<<<0



पिता / कानूनी अभिभावक का नाम / Name of Father / Legal Guardian

GAUTAM SINGH DAVAR

Z3540631

माता का नाम / Name of Mother

NEERA DAVAR

पति या पत्नी का नाम / Name of Spouse

ANSHU DAVAR

पता / Address

A-1

GREATER KAILASH-I,DELHI

PIN:110048,DELHI,INDIA

पुराने पासपोर्ट का नं. और इसके जारी होने की तिथि एवं स्थान / Old Passport No. with Date and Place of Issue

Z2273667 24/08/2012 DELHI

फाईल नं./ File No.

DL4079765420016

# INDIA NON JUDICIAL

## Government of National Capital Territory of Delhi

### e-Stamp

सत्यमेव जयते

| | | |
|---|---|---|
| Certificate No. | : | IN-DL78634763187927S |
| Certificate Issued Date | : | 11-Sep-2020 11:24 AM |
| Account Reference | : | IMPACC (IV)/ dl717803/ DELHI/ DL-DLH |
| Unique Doc. Reference | : | SUBIN-DLDL71780364572606713005S |
| Purchased by | : | P S DAVAR AND COMPANY |
| Description of Document | : | Article Others |
| Property Description | : | Not Applicable |
| Consideration Price (Rs.) | : | 0 (Zero) |
| First Party | : | P S DAVAR AND COMPANY |
| Second Party | : | Not Applicable |
| Stamp Duty Paid By | : | P S DAVAR AND COMPANY |
| Stamp Duty Amount(Rs.) | : | 100 (One Hundred only) |

.....Please write or type below this line.....

### AUTHORIZATION OF REPRESENTATIVE

**IN THE MATTER OF**: Obtaining permission from the National Biodiversity Authority in relation to Indian Patent Appl. No. 201917035818 dated 05.09.2019.

## AUTHORISATION LETTER FOR AGENT/REPRESENTATIVE

We, **INVENTPRISE LLC** of **18133 NE 68th St., d150 Redmond, Washington-98052, United States of America** hereby authorize P. S. Davar, A. Davar, C. M. Gaind, B.S. Davar, Anushka Singh, Smita Bhatia, S Moktan, T. Khan, and all representatives of P.S.Davar & Co., as our agent/representative to submit an application in Form III of the Biological Diversity Rules, 2004, to the National Biodiversity Authority, India (hereinafter, referred to as the NBA) for the purpose of obtaining the prior approval as required under the Biological Diversity Act, 2002 for an IPR of accessed biological resources.

We hereby authorize and declare that all actions committed by the agent / representative with regard to the above purpose and all communications by the agent/representative with the NBA in this regard shall bind us entirely.

**Authorised Signatory, INVENTPRISE LLC**
Name & Designation: **Subhash V. Kapre, Ph.D.**
Date: **08 September 2020**
Place: **Redmond, WA USA**

**P. S. Davar**
Of P.S. DAVAR & CO.
Date:
Place:

1/2

SBI

NATIONAL BIODIVERSITY AUTHORITY
TICEL BIO PARK,5th FLOOR, , CSIR ROAD TARAMANI , CHENNAI-600113
Date: 11-Sep-2020

## e-Receipt for State Bank Collect Payment

| | |
|---|---|
| SBCollect Reference Number | DUD5017583 |
| Category | FORM-III PAYMENT OFFLINE APPLICATION SUBMISSION |
| Applicant Name (Individual/Firm/Institution) | Inventprise LLC |
| Address 1 | 18133 NE 68th Street |
| Address 2 | d 150 Redmond Washington 98052 |
| Country | United States of America |
| Contact Number | 9811402998 |
| E Mail ID | psdavar@psdavar.com |
| Application Fees (In INR) | 500 |
| Transaction charge | 0.00 |
| Total Amount (In Figures) | 500.00 |
| Total Amount (In Words) | Rupees Five Hundred Only |
| Remarks | Fee submission for Form III (Application form for applying for Intellectual Property Right). |
| Notification 1 | Please input all details correctly and confirm before proceeding for payment. Avoid using special characters. |
| Notification 2 | Save copy of the online payment receipt for future reference and submit the same along with the application. For queries, contact e-mail id: accounts@nbaindia.in |

27/c

4

FORM-3

THE PATENTS ACT, 1970
(39 of 1970)
&
The Patents Rules, 2003
STATEMENT AND UNDERTAKING UNDER SECTION 8
[See section 8, rule 12]

We, INVENTPRISE, LLC, an American Company, of 18133 NE 68th St., d150 Redmond, Washington 98052, USA, hereby declare:

(i) that we who have made this application No. 201917035818 dated 05 September 2019 have made for the same/substantially same invention, application (s) for patent in the other countries, the particulars of which are given below:

APPLICATION NUMBER 201917035818 DATED 05 September 2019

| Name of the country | Date of Application | Application No. | Status of the Application | Publication No. | Date of Publication | Patent No. | Date of grant |
|---|---|---|---|---|---|---|---|
| United States of America | 14 Feb. 2017 | 62/458,904 | Expired | N/A | | | |
| PCT | 14 Feb. 2018 | PCT/US2018/18226 | PUBLISHED | WO/2018/152237 | 23 Aug. 2018 | NA | NA |
| United States of America | 14 Feb. 2018 | 15/896,939 | GRANTED | 20180228889 | 16 Aug. 2018 | 10,413,604 | 17 Sept. 2019 |
| United States of America | 16 Sept. 2019 | 16/751,702 | PENDING | Not yet published | | | |
| China | 14 Oct. 2019 | Not yet assigned | PENDING | Not yet published | | | |
| Indonesia | 11 Sept. 2019 | PID 201907114 | PENDING | Not yet published | | | |
| Korea | 05 Sept. 2019 | 10-2019-7026145 | PENDING | 10-2019-0111117 | 01 Oct. 2019 | | |
| Malaysia | 07 Aug. 2019 | PI 2019004553 | PENDING | Not yet published | | | |
| Philippines | 09 Aug. 2019 | 1-2019-501865 | PENDING | Not yet published | | | |
| | | | | | | | |

ii) that the rights in the application(s) has/have been assigned to NIL.

iii) that we undertake that up to the date of grant of the patent by the Controller, we would keep him informed in writing the details regarding corresponding applications for patents filed outside India within six months from the date of filing of such application.

Dated this 29th day of October 2019

| IP Office | Application | Applicant | Title | Application Date | Priority Number | Publication Number | Publication Date |
|---|---|---|---|---|---|---|---|
| S | 16571702 | 1)INVENTPRISE LLC | Heat Stable Vaccines | 09/16/2019 | US 16571702<br>US 15896939<br>US 62458904 | US 20200009242 A1 | 01/09/2020 |
| S | 15896939 | 1)INVENTPRISE LLC | Heat Stable Liquid Rotavirus Vaccine | 02/14/2018 | US 15896939<br>US 62458904 | US 20180228889 A1<br>US 10413604 B2 | 08/16/2018<br>09/17/2019 |
| R | 20197026145 | 1)INVENTPRISE LLC | | 02/14/2018 | US 62458904<br>US PCT/US18/18226 | KR 20190111117 A | 10/01/2019 |
| N | 201880024968 | 1)INVENTPRISE LLC | HEAT STABLE LIQUID ROTAVIRUS VACCINE | 02/14/2018 | US 62458904<br>US PCT/US18/18226 | CN 110730671 A | 01/24/2020 |
| S | PCT/US18/18226 | 1)INVENTPRISE LLC | HEAT STABLE LIQUID ROTAVIRUS VACCINE | 02/14/2018 | US 62458904 | WO 2018152237 A1 | 08/23/2018 |

(5) 106LC

NBA

Satheesh K <satheesh@nbaindia.org>

# Fwd: Execution of agreement for obtaining IPR underSection 6 of the Biological Diversity Act, 2002 – Reg

**P. Jaishankar** <techasstz@nba.nic.in> Mon, Apr 26, 2021 at 9:33 AM
To: Satheesh Desk <absdesk4@nbaindia.org>
Cc: iprsection <iprsection@nbaindia.org>

FNA pls URGENT

---

**From:** "sudipta banerjee" <sudipta.banerjee@psdavar.com>
**To:** absdesk2@nbaindia.in
**Cc:** "P. Jaishankar" <techasstz@nba.nic.in>, psdavar@psdavar.co
**Sent:** Friday, April 23, 2021 1:53:19 PM
**Subject:** FW: Execution of agreement for obtaining IPR underSection 6 of the Biological Diversity Act, 2002 – Reg

Dear Sir,

This has reference to the trail mail. We may here advise that the strain of the instant Patent application number is 201917035818 is not used as such but rather the same is further processed to produce the Vaccine of the present invention. In this connection, our detailed submissions are enclosed for your kind consideration. Further, based on the submissions we request you to issue a "No objection certificate" and waive the objection.

Yours sincerely,

Dr. Sudipta Banerjee

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Our detailed submissions pertaining to your objection in respect of Patent Application Number 201917035818 is as follows:

Without prejudice, the Applicant submits that they have procured the particular strain of rotavirus from Bharat Biotech International Ltd., Genome Valley, Shameerpet, Hyderabad – 500078, TS India for carrying out research and development. They further submit that the particular strain of rotavirus procured from the said commercial vendor is a processed off-the-shelf product and not a naturally occurring material per se. They have procured the particular strain of rotavirus as over the counter product when offered for sale by the said vendor. The particular strain of rotavirus has been exported to many countries for a number of years and is commonly available material. Further, the strain is also not used as such, it is processed to produce the vaccine of the present invention.

Particular strain of rotavirus was originally isolated in 1985 from asymptomatic new-borns in hospital new natal units in India. The strain is now considered to be the "model" for rotavirus vaccine development and basic research (virology.2010Sep15,405(i):201-213).

Since, the particular strain of rotavirus is not a naturally occurring product per se, the particular strain of rotavirus should not come under the purview of 'biological resource' as per the definition under Section 2(c) of the Biological Diversity Act, 2002.

Further, they are of the opinion that the said particular strain of rotavirus is a value-added product as per Section 2(p) of the Biological Diversity Act, 2002. Because, the particular strain of rotavirus is very old and is available worldwide.

As per Section 2(p) of the Biological Diversity Act, 2002 'value added products means products which may contain portions or extracts of plants and animals in unrecognizable and physically inseparable form'. Moreover, the said particular strain of rotavirus is being processed prior to using it in making the vaccine. Thus, the original strain is not used directly rather it is a value-added form which is used in the present invention. Thus, the rotavirus vaccine formulation comprises a lyophilized rotavirus strain with excipients expected to grant viral titer thermo-stability at 30°C for at least 2 years and 50°C for 3 months. The solid lyophilized material is milled to a uniform particle size mixed with a solid buffer and finally suspended and homogenized in medium-chain triglyceride oil to create the final formulation.

In this connection, please refer to Biological diversity act 2002 definition of Biological resources is as follows:

(http://nbaindia.org/content/565/56/1/explanatorynote.html).

Definition of Biological Resources: Plants, animals, micro-organisms, their parts, genetic material and by-products, having actual or potential use or value.

- Value added products based on biological resources are excluded.
- Human genetic material is excluded.

According to Biological diversity act 2002 value added product implies products containing portions/extracts of plants and animals in unrecognizable and physically inseparable form

(http://nbaindia.org/content/19/16/1/faq.html).

It may be noted that the biological materials **used in the present invention** are procured from commercial vendors. **This is a reassortant strain containing a single bovine**

**gene segment (VP4) in a human background and has been successfully used.** This clearly proves that the particular strain of rotavirus should not come under the purview of biological resource as it a value-added product according to Biological diversity act 2002 and Value-added products based on biological resources are excluded.

Further, we would like to draw the attention of the Ld. Controller to the Preamble of the Biological Diversity Act, which reads as:

> *An Act to provide for conservation of biological diversity, sustainable use of its components and fair and equitable sharing of the benefits arising out of the use of biological resources, knowledge and for matters connected therewith or incidental thereto.*
>
> *AND WHEREAS the said Convention* ***has the main objective of conservation of biological diversity, sustainable use of its components and fair and equitable sharing of the benefits arising out of utilisation of genetic resources;***
>
> *AND WHEREAS it is considered necessary to provide for conservation, sustainable utilisation and equitable sharing of the benefits arising out of utilisation of genetic resources and also to give effect to the said convention.*

The Preamble of The Convention on Biological Diversity, reads as:

> The Contracting Parties,
>
> *Conscious of the intrinsic value of biological diversity and of the ecological genetic, social, economic, scientific, educational, cultural, recreational and aesthetic values of biological diversity and its components,*

*Conscious also of the importance of biological diversity for evolution and for evolution and for maintaining life sustaining systems of the biosphere...*

Further, The Convention on Biological Diversity through its Article 1 reads as:

*The objective of this Convention, to be pursued in accordance with its relevant provision, are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies and by appropriate funding.*

Congruently, the Article 2 of The Convention on Biological Diversity further states that:

*'Genetic material' means any material of plant, animal, microbial or other origin containing functional units of heredity.*

According to Section 2(b) of the Biological Diversity Act, the term 'Biological Diversity' means *'the variability among living organisms from all sources and the ecological complexes of which they are part and includes diversity within species or between species and of eco-system'.*

There it is understandable that term 'biological Diversity' should be applicable only over 'living organisms' of an ecosystem and not on non-living substance/processed off-the-shelf products.

Further, with reference to an **"Office Circular" No.: CG/ Office Circular (P)/ 2017/ 451, dated May 23, 2017**, this instant application may clearly fall under "Value Added Products", which has been excluded from the definition of "Biological Resources" under section 2(c) of the Biodiversity (BD) Act saying, *""**Biological resources**" means plants, animals and micro-organisms or parts thereof, their genetic material and by-products **(excluding value added products)** with actual or potential use or value, but does not include human genetic material*". Section 2(p) of the said Act defines ""***Value Added Product***" *means products which may contain portions or extracts of plants and animals in unrecognizable and physically inseparable form.*" **In the present invention the strain is used to develop a vaccine useful for mankind.**

**As the present invention underlying this instant application merely becomes *"a process of preparation"* of a *"value added product"*, which may be kept outside of the purview of the National Biodiversity Authority, and the patent may be granted with waiving the NBA requirement, subjected to the learned judgment of Hon'ble Controller of Patents.**

In view of the above reasons either individually or in combination, the Applicant submits that they should NOT be under the purview of the Biological Diversity Act, 2002 for procuring the particular strain of rotavirus from commercial vendors. Thus, we request you to issue a "No objection certificate" in respect of the instant application and waive the objection of NBA.

Yours sincerely,

Dr.Sudipta Banerjee

Of P.S.DAVAR AND COMPANY

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# Complete Genome Sequence Analysis of Candidate Human Rotavirus Vaccine Strains RV3 and 116E

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## Abstract

Rotaviruses (RVs) cause severe gastroenteritis in infants and young children; yet, several strains have been isolated from newborns showing no signs of clinical illness. Two of these neonatal strains, RV3 (G3P[6]) and 116E (G9P[11]), are currently being developed as live-attenuated vaccines. In this study, we sequenced the eleven-segmented double-stranded RNA genomes of cell culture-adapted RV3 and 116E and compared their genes and protein products to those of other RVs. Using amino acid alignments and structural predictions, we identified residues of RV3 or 116E that may contribute to attenuation or influence vaccine efficacy. We also discovered residues of the VP4 attachment protein that correlate with the capacity of some P[6] strains, including RV3, to infect newborns versus older infants. The results of this study enhance our understanding of the molecular determinants of RV3 and 116E attenuation and are expected to aid in the ongoing development of these vaccine candidates.

**Keywords:** rotavirus, neonatal, vaccine, attenuated, genome, RV3, 116E

## Introduction

Group A rotaviruses (RVs) are important pathogens that cause acute, dehydrating gastroenteritis in infants and young children. The burden of disease is severe, particularly in developing countries where RV infections lead to more than 500,000 deaths annually (Parashar et al., 2006). RVs are non-enveloped, triple-layered icosahedral particles that enclose an eleven-segmented, double-stranded (ds) RNA genome (Pesavento et al., 2006). Together, the genome codes for six structural proteins (VP1-VP4, VP6, and VP7) and five or six non-structural proteins (NSP1-NSP5, and sometimes NSP6) (Estes and Kapikian, 2007). Individual RV strains have traditionally been classified into serotypes based on the antibody responses generated against the outermost structural proteins VP7 (G-serotypes) and VP4 (P-serotypes) (Estes and Kapikian, 2007). Due to the ease of sequencing, RVs are now classified into G/P-genotypes based on the relatedness of the genes encoding VP7 and VP4 (Estes and Kapikian, 2007; Matthijnssens et al., 2008a). Molecular sequencing of RVs has also led to the development of a

classification system for the internal genes (i.e., dsRNA segments encoding proteins other than VP7 and VP4). In this system, each internal gene is assigned a particular genotype based on established nucleotide identity cut-off percentages (Matthijnssens et al., 2008a; Matthijnssens et al., 2008b). Now, the acronym Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx is used to classify the VP7-VP4-VP6-VP1-VP2-VP3-NSP1-NSP2-NSP3-NSP4-NSP5/6-encoding segments. The majority of human RVs sequenced to date contain either genotype 1 (Wa-like) or genotype 2 (DS-1-like) internal genes. However, reassortment events can lead to human strains containing dsRNA segments with other genotypes.

Although the mechanism by which RV infection elicits immunological protection is not fully understood, G/P-type-specific neutralizing antibodies have been shown to play an important role (Ward, 2003). Strains with G/P-type combinations of G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8] are the most prevalent causes of disease in humans worldwide, and thus, are targets of the two currently licensed RV vaccines (Santos and Hoshino, 2005). RotaTeq (Merck) contains five live-attenuated, reassortant viruses with human VP7 (G1, G2, G3 and G4) and VP4 (P[8]) genes in a predominantly bovine RV background (strain WC3) (Matthijnssens et al., 2010a; Ciarlet and Schodel, 2009; Heaton and Ciarlet, 2007). In contrast, Rotarix (GlaxoSmithKline) is a live-attenuated, G1P[8] human RV (strain 89-12) containing genotype 1 internal genes (Ward, 2003). Both vaccines have proven safe and effective at protecting against severe diarrheal disease in industrialized countries and Latin America (Ruiz-Palacios et al., 2006; Vesikari et al., 2006; Ward, 2003). However, the efficacy of RotaTeq and Rotarix in developing countries is expected to be reduced, which may be related to viral serotype diversity among other factors (Madhi et al., 2010; Tate et al., 2010). Additionally, the high monetary cost of these current vaccines may limit their availability in regions of the world where they are most needed. As a result, there is a global health initiative to develop new RV vaccines that can be manufactured on-site at a lower cost. Two vaccine candidates being considered are the live-attenuated human strains RV3 (G3P[6]) and 116E (G9P[11]).

RV3 and 116E were isolated from asymptomatic newborns (<28 days old) in hospital neonatal units in Australia (1977) and India (1985), respectively (Albert et al., 1987a; Glass et al., 2005). Follow-up studies showed that the RV3- or 116E-infected newborns did not experience episodes of severe diarrhea later in life when compared with uninfected individuals (Bhan et al., 1993; Bishop et al., 1983). This observation suggested that these attenuated strains might protect against subsequent, symptomatic RV infection, providing rationale for their development as vaccines. Clinical testing with cell culture-adapted RV3 and 116E demonstrates that they are safe, attenuated, and immunogenic in all age groups, and that they replicate well in the infant gut (Barnes et al., 1997; Barnes et al., 2002; Bhandari et al., 2006; Bhandari et al., 2009). Moreover, phase II trials show that RV3 partially protected infants against severe diarrhea during successive winter months (Barnes et al., 2002). Studies are ongoing to determine whether RV3 and 116E elicit broadly-protective immune responses against heterotypic strains, or whether they will be limited to preventing infections with G/P-type-matched strains. Because they are being considered as vaccines, there is also great interest in elucidating the molecular basis for the attenuated, neonatal phenotypes of RV3 and 116E. Towards this goal, a few dsRNA segments have been sequenced and analyzed for these viruses (Cunliffe et al., 1997; Das et al., 1993; Gentsch et al., 1993; Kirkwood et al., 1996; Palombo and Bishop, 1994b). Nonetheless, in the absence of complete RV3 and 116E genome sequences, it is impossible to fully identify attenuation and neonatal infection determinants.

In this study, we deduced the nucleotide sequences of the open-reading frames (ORFs) for each of the eleven dsRNA genome segments of cell culture-adapted RV3 and 116E viruses. The segments were classified into genotypes according to the nucleotide identity cut-off percentages established by the Rotavirus Classification Working Group (RCWG). The genetic relatedness of RV3 and 116E genome segments to those of other human and animal RVs was determined using phylogenetic analyses. By

performing amino acid alignments of the deduced proteins, we identified residues of RV3 or 116E that may contribute to their attenuation. Additionally, the three-dimensional locations of VP7 residues specific to RV3 or 116E in comparison to serotype-matched strains were mapped onto a high-resolution structure of the glycoprotein trimer. This analysis revealed changes that could influence the efficacy of RV3 or 116E as vaccines. Equally important, using amino acid alignments we found that the VP4 attachment proteins of P[6] strains isolated from neonates, such as RV3, differed at several positions compared with P[6] RVs isolated from older infants. While these changes do not correlate with disease outcome, several of them localize to the protein surface and may influence viral entry into cells of the neonatal gut. Together, the results presented in this study are important for the continued development of RV3- and 116E-based vaccines.

## Results

### Genotype classification of RV3 and 116E genes

The ORF nucleotide sequences for the eleven genome segments of cell culture-adapted RV3 and 116E strains were determined. The sequences deduced in this study are either identical or show a few changes from those that are already in GenBank for RV3 (VP4, VP6, and NSP4 genes) and 116E (VP4, VP6, VP7, NSP1, and NSP4 genes) (Table S1) (Cunliffe et al., 1997; Das et al., 1993; Gentsch et al., 1993; Kirkwood et al., 1996; Palombo and Bishop, 1994b). Genotypes were assigned for each genome segment based on the nucleotide percent identity cut-off values defined by the RCWG and by submission to RotaC (http://rotac.regatools.be) (Matthijnssens et al., 2008a; Matthijnssens et al., 2008b; Maes et al., 2009).

Our analyses show that RV3 can be classified as a G3P[6] strain, which is consistent with previous reports (Albert et al., 1987a; Kirkwood et al., 1996). Specifically, RV3 VP7 shares 97% nucleotide identity with the G3 human strain P (98% amino acid identity), and RV3 VP4 shares 98% nucleotide identity with the P[6] human strain ST3 (96% amino acid identity) (Tables 1 and 2). Also, like previous reports, our results show that 116E is a G9P[11] strain, with a VP4 that is very similar to those of several bovine RVs (Das et al., 1994; Das et al., 1993; Gentsch et al., 1993). In particular, 116E VP7 shares 89% nucleotide identity with the G9 human strain Wi61 (94% amino acid identity), while 116E VP4 shares 91% nucleotide identity with the P[11] bovine strain B223 (94% amino acid identity) ( Tables 1 and 2). Moreover, we found that the nine internal genes of RV3 and 116E show percent nucleotide identity values above the cut-offs when compared with the genotype 1 prototype strain Wa ( Table 3). Thus, RV3 and 116E have genome constellations of G3-P[6]-I1-R1-C1-M1-A1-N1-T1-E1-H1 and G9-P[11]-I1-R1-C1-M1-A1-N1-T1-E1-H1, respectively.

**Table 1**

**Sequence-based G-typing of RV3 and 116E VP7**

| | | RV3 | | 116E | |
|---|---|---|---|---|---|
| G-type | Strain | %NT[a] | %AA[b] | %NT | %AA |
| G1 | Wa | 75 | 83 | 75 | 79 |
| G2 | DS-1 | 73 | 75 | 74 | 76 |
| G3 | P | 97 | 98 | 79 | 85 |
| G4 | ST3 | 74 | 76 | 75 | 78 |
| G5 | IAL28 | 77 | 86 | 78 | 81 |
| G6 | Se584 | 77 | 86 | 77 | 83 |
| G8 | 69M | 75 | 83 | 75 | 82 |
| G9 | WI61 | 79 | 86 | 89 | 94 |
| G10 | A64 | 75 | 83 | 75 | 81 |
| G12 | L26 | 74 | 80 | 76 | 82 |

[a]abbreviation: percent nucleotide identity (%NT)
[b]abbreviation: percent amino acid identity (%AA)

**Table 2**

**Sequence-based P-typing of RV3 and 116E VP4**

| | | RV3 | | 116E | |
|---|---|---|---|---|---|
| P-type | Strain | %NT[a] | %AA[b] | %NT | %AA |
| P[1] | RF | 69 | 73 | 60 | 59 |
| P[2] | SA11 | 71 | 74 | 59 | 58 |
| P[4] | DS-1 | 74 | 76 | 60 | 58 |
| P[5] | UK | 66 | 68 | 59 | 58 |
| P[6] | ST3 | 98 | 96 | 59 | 56 |
| P[8] | Wa | 74 | 77 | 59 | 58 |
| P[9] | AU-1 | 64 | 66 | 59 | 55 |
| P[10] | 69M | 70 | 75 | 61 | 59 |
| P[11] | B223 | 58 | 56 | 91 | 94 |

[a]abbreviation: percent nucleotide identity (%NT)
[b]abbreviation: percent amino acid identity (%AA)

**Table 3**

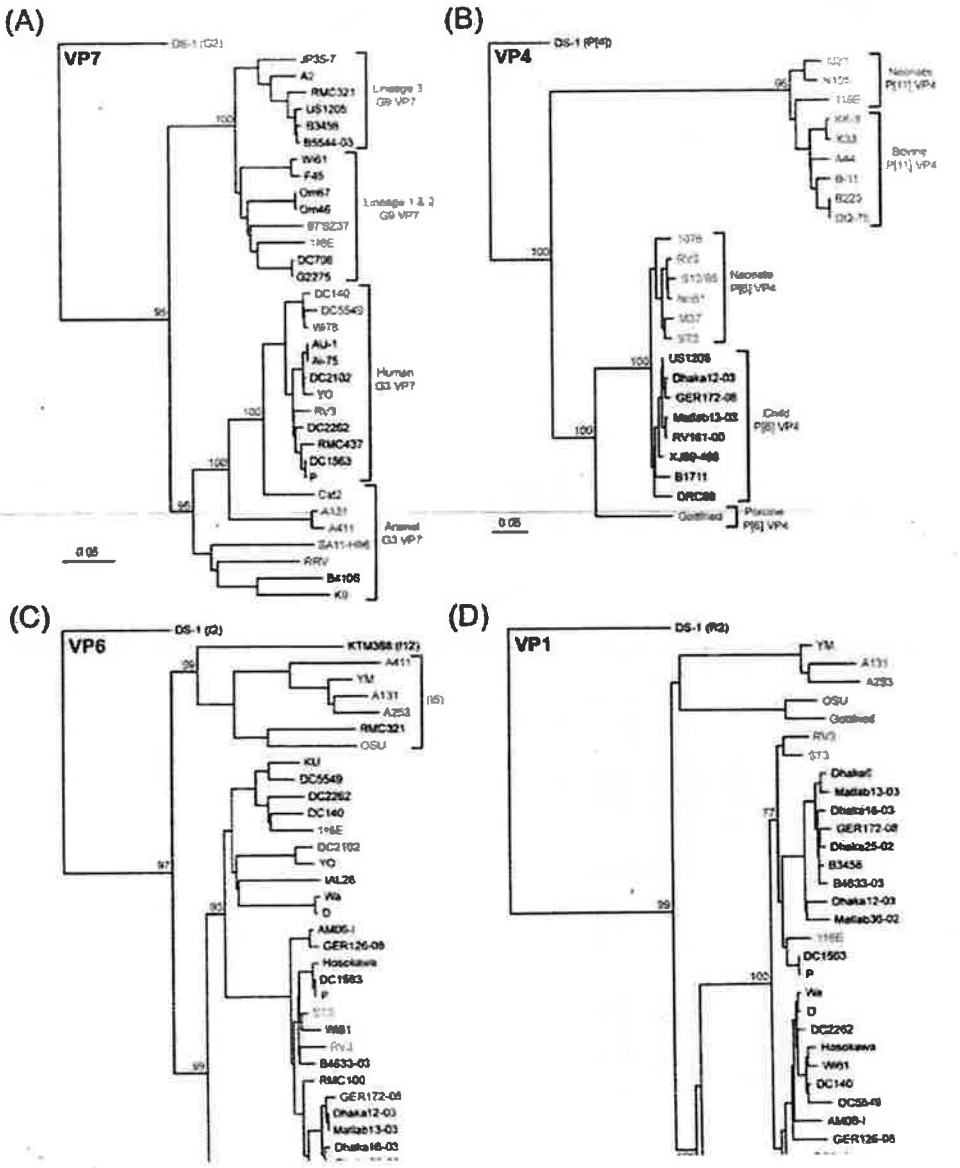
**Genotyping of RV3 and 116E Internal Genes**

| | | RV3 v. Wa | | 116E v. Wa | |
|---|---|---|---|---|---|
| Gene | % cut-off[a] | %NT[b] | %AA[c] | %NT | %AA |
| VP1 | 83 | 96 | 98 | 96 | 99 |
| VP2 | 84 | 94 | 97 | 94 | 98 |
| VP3 | 81 | 98 | 99 | 89 | 92 |
| VP6 | 85 | 90 | 98 | 91 | 98 |
| NSP1 | 79 | 85 | 83 | 89 | 88 |
| NSP2 | 85 | 91 | 95 | 92 | 96 |
| NSP3 | 85 | 97 | 97 | 89 | 90 |
| NSP4 | 85 | 98 | 96 | 96 | 97 |
| NSP5 | 91 | 93 | 93 | 95 | 96 |

[a]percent nucleotide identity cut-off values for genotyping
[b]abbreviation: percent nucleotide identity (%NT)
[c]abbreviation: percent amino acid identity (%AA)

### Phylogenetic relationship of RV3 and 116E to other strains

To further investigate the genetic relatedness of RV3 and 116E VP7 and VP4 genes with those of other G/P-type-matched strains, we constructed phylogenetic trees using the ORF sequences and the neighbor-joining method (Fig. 1A and B). Strain DS-1 (G2P[4]) was included as an out-group in the analyses. The results show that RV3 VP7 clustered tightly with human G3 VP7s and away from those of animal G3 strains (Fig. 1A). The VP7s of G9 strains have been previously defined into at least three phylogenetic lineages (1, 2, and 3) (Cao et al., 2008; Martinez-Laso et al., 2010). We found that 116E VP7, which is the only representative of lineage 2, clustered with lineage 1 VP7s and was distinct from lineage 3 VP7s (Fig. 1A). For VP4, we found that RV3 segregated with other human P[6] strains and away from the porcine P[6] strain Gottfried (Fig. 1B). Yet, interestingly, RV3 VP4 was part of a subcluster of P[6] VP4s belonging to human strains that were isolated from newborns (Fig. 1B). This neonatal P[6] VP4 lineage was separate from human RVs isolated from infants or children (>28 days old) and contained both symptomatic (strain 12/85) and asymptomatic (strains M37, 1076, NnB1, and ST3) P[6] strains (Fig. 1B). As reported previously, 116E VP4 showed a close phylogenetic relationship to VP4s of the human neonatal strains I321 (asymptomatic) and N155 (symptomatic), as well as to the P[11] VP4 proteins of several bovine RVs (Fig. 1B) (Gentsch et al., 1993; Glass et al., 2005). This result is consistent with the notion that 116E, I321, and N155 contain bovine RV VP4 genes.

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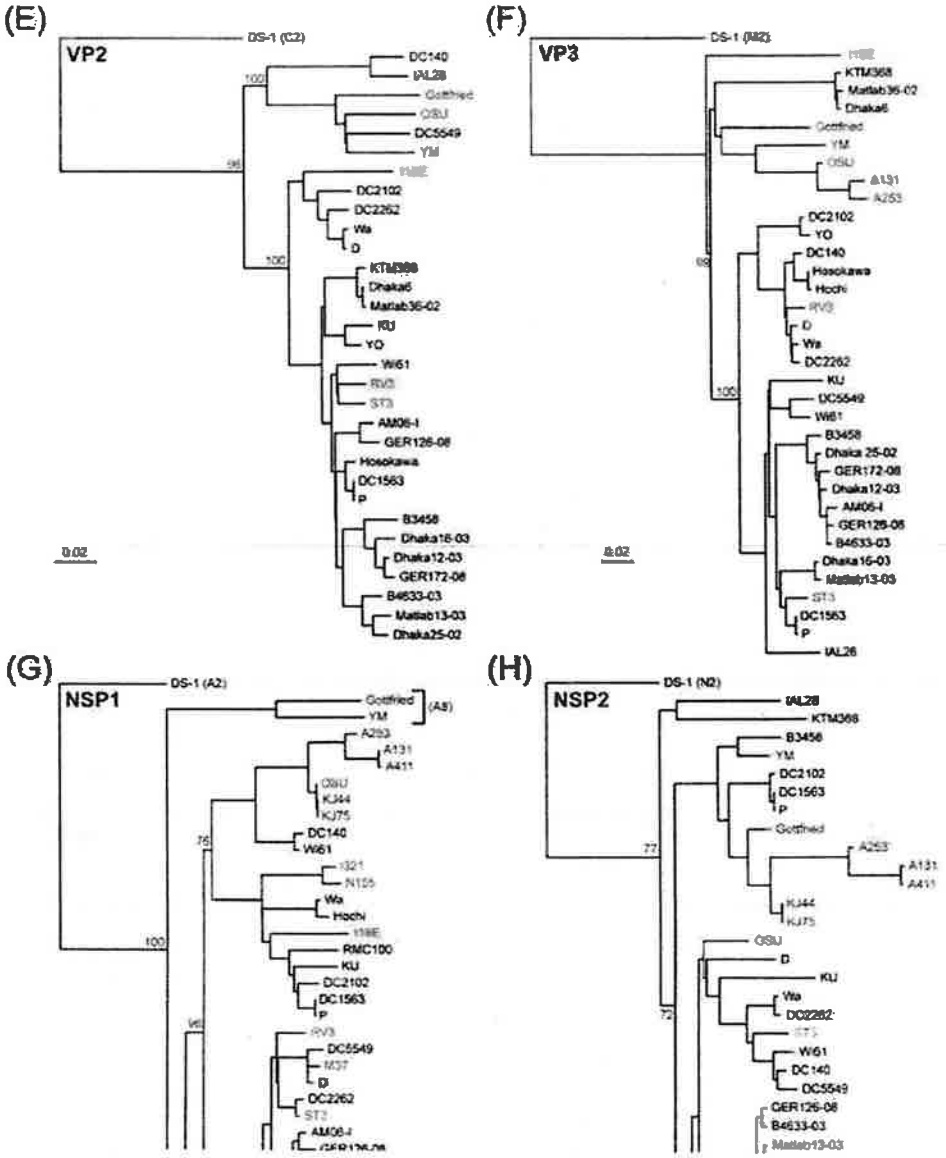


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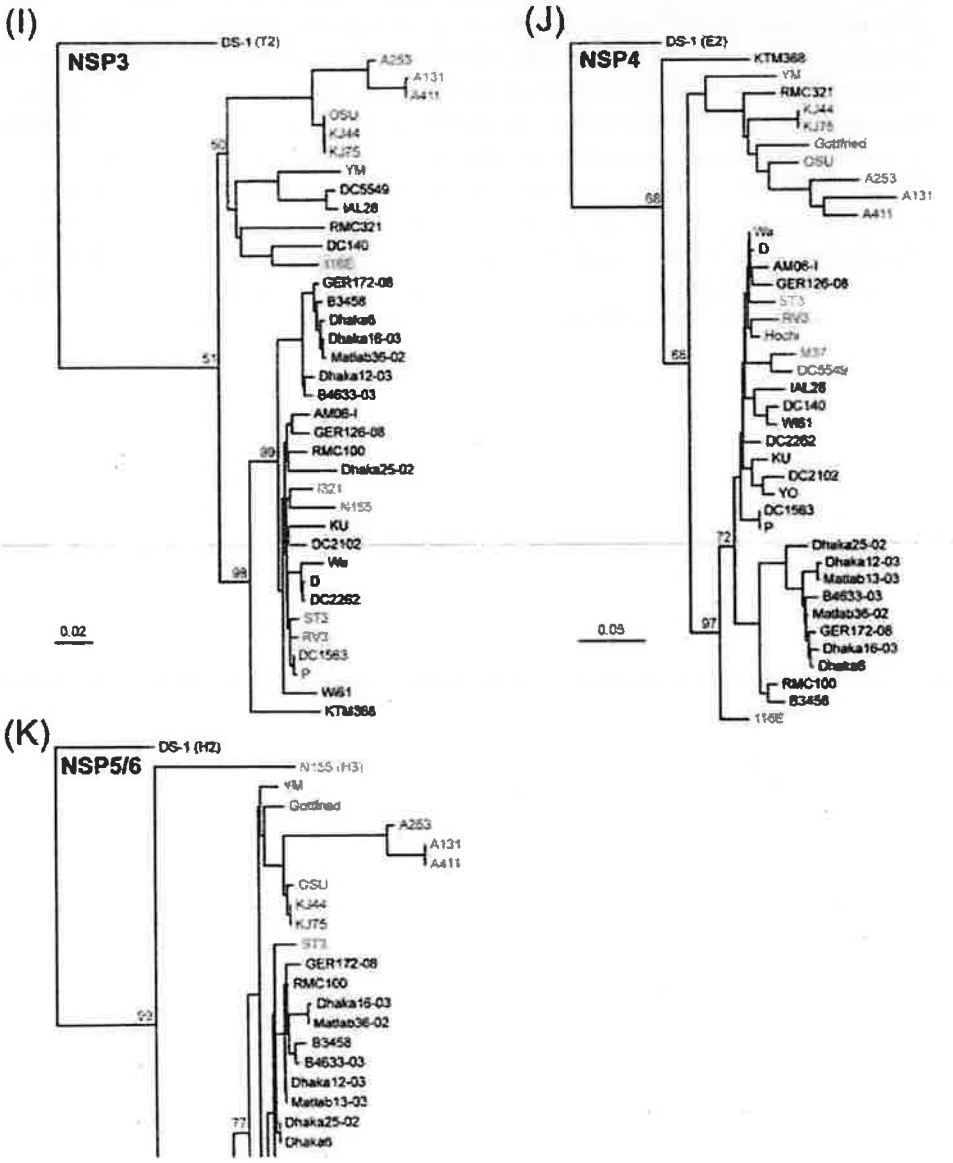


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Fig. 1

Phylogenetic relationships of RV3 and 116E genome segments to those of other RVs. The neighbor-joining trees were constructed using the individual ORF nucleotide sequences for each isolate and are out-group rooted to DS-1 for purposes of clarity. Horizontal branch lengths are drawn to scale (nucleotide substitutions per base), and bootstrap values are shown as percentages for key nodes. Strain names are colored accordingly: animal strains (green), human neonatal strains (red), and human strains isolated from older infants/children (black). Strains RV3 and 116E are highlighted in yellow.

We next sought to determine the phylogenetic relationships of the RV3 and 116E genotype 1 internal genes to those of other RVs. Although genotype 1 genes are predominantly found in human RVs that cause disease in young children (i.e., human Wa-like strains), several porcine and two bovine strains also contain dsRNA segments classified as genotype 1 (Matthijnssens et al., 2008a). These porcine RV-like genotype 1 genes generally cluster distantly from the human RV genotype 1 genes in phylogenetic trees, suggesting that they comprise distinct evolutionary lineages (Matthijnssens et al., 2008a). For VP6, the porcine RV lineage was separate enough to warrant its assignment as a different genotype I5 (Matthijnssens et al., 2008a; Matthijnssens et al., 2008b). In this study, we created neighbor-joining phylogenetic trees using the internal gene ORF sequences of human, porcine, and bovine RVs whose genomes contain several genotype 1 genes (Fig 1C-K). Figure 2 summarizes the genome constellations of the viruses analyzed. Strain DS-1 (genotype 2) was included in the trees as an out-group.

| Strain | Host | VP7 | VP4 | VP6 | VP1 | VP2 | VP3 | NSP1 | NSP2 | NSP3 | NSP4 | NSP5/6 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| M37 | neonate | G1 | P[6] | | | | | A1 | | | E1 | |
| Wa | infant/child | G1 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| KU | infant/child | G1 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Dhaka16-03 | infant/child | G1 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| D | infant/child | G1 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| AM06-I | infant/child | G1 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| DS-1 | infant/child | G2 | P[4] | I2 | R2 | C2 | M2 | A2 | N2 | T2 | E2 | H2 |
| RV3 | neonate | G3 | P[6] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| A131 | porcine | G3 | P[7] | I5 | R1 | C2* | M1 | A1 | N1 | T1 | E1 | H1 |
| A411 | porcine | G3 | P7 | I5 | | | | A1 | N1 | T1 | E1 | H1 |
| DC140 | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| DC2102 | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| DC2262 | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| DC1563 | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| DC5549 | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| P | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| YO | infant/child | G3 | P[8] | I1 | R1 | C1 | M1 | | | | E1 | |
| ST3 | neonate | G4 | P[6] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Gottfried | porcine | G4 | P[6] | I1 | R1 | C1 | M1 | A5 | N1 | | E1 | H1 |
| Hosokawa | infant/child | G4 | P[8] | I1 | R1 | C1 | M1 | | | | | |
| RMC100 | infant/child | G4 | P[8] | I1 | | | | A1 | N1 | T1 | E1 | H1 |
| Hochi | infant/child | G4 | P[8] | | | | M1 | A1 | | | E1 | |
| KJ44 | bovine | G5 | P[1] | | | | | A1 | N1 | T1 | E1 | H1 |
| KJ75 | bovine | G5 | P[5] | | | | | A1 | N1 | T1 | E1 | H1 |
| OSU | porcine | G5 | P[7] | I5 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| IAL28 | infant/child | G5 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| B3458 | infant/child | G9 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Wi61 | infant/child | G9 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| 116E | neonate | G9 | P[11] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| RMC321 | infant/child | G9 | P[19] | I5 | | | | A1 | N1 | T1 | E1 | H1 |
| I321 | neonate | G10 | P[11] | I2* | | | | A1 | N2* | T1 | E2* | |
| N155 | neonate | G10 | P[11] | I2* | R2* | C2* | M2* | A1 | N1 | T1 | E2* | H3 |
| A253 | porcine | G11 | P[7] | I5 | R1 | C2* | M1 | A1 | N1 | T1 | E1 | H1 |
| YM | porcine | G11 | P[7] | I5 | R1 | C1 | M1 | A8 | N1 | T1 | E1 | H1 |
| Matlab36-02 | infant/child | G11 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Dhaka6 | infant/child | G11 | P[25] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| KTM368 | infant/child | G11 | P[25] | I12 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Dhaka12-03 | infant/child | G12 | P[6] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Matlab13-03 | infant/child | G12 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T2* | E1 | H1 |
| GER172-08 | infant/child | G12 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| GER126-08 | infant/child | G12 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| B4633-03 | infant/child | G12 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |
| Dhaka25-02 | infant/child | G12 | P[8] | I1 | R1 | C1 | M1 | A1 | N1 | T1 | E1 | H1 |

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Fig. 2

Genome constellations of several human and animal RVs. The schematic illustrates the genotype of each genome segment for several RV strains. The strain name is listed to the left of the corresponding genome constellation, and the protein encoded by each gene is listed at the top. RV strain names are colored accordingly: animal strains (green), human neonatal strains (red), and human strains isolated from older infants/children (black). Strains RV3 and 116E are highlighted in yellow. All genotype 1 genes are shown as white boxes, non-genotype 1 genes are shown as grey boxes, and dotted boxes indicated genome segments in which no or only partial ORF sequences are available. Asterisks (*) indicate sequences that were omitted from the phylogenetic trees for purposes of clarity.

These results show that most of the RV3 and 116E internal genes are quite similar to those of prototypic human Wa-like strains and are more distantly related to porcine RV-like genes. Interestingly, seven of the nine RV3 internal genes (VP1, VP2, VP6, NSP1, NSP3, NSP4, and NSP5/6) clustered tightly with those of ST3, a G4P[6] strain that was also isolated from an asymptomatic neonate (England, 1975) (Chrystie et al., 1975; Wyatt et al., 1983) (Fig. 1C-E, G, I and J). RV3 VP3 and NSP2 genes did not cluster with ST3, but did show close relationships to genes of other human strains (Fig. 1F, H, and K). The 116E VP1, VP2, VP6, and NSP1-5/6 genes segregated phylogenetically with those of prototypic human Wa-like RVs and away from porcine RV-like genes (Fig 1C-E, G-K). However, 116E NSP4 formed a separate branch, located just off the main group of human RV genes (Fig. 1J). Most strikingly, 116E VP3 did not group with any other known human or animal genotype 1 genes (Fig. 1F). Using BLAST, we found that the VP3 gene of 116E is most closely related that of strain Wa; yet, these genes only share 89% nucleotide identity (Table 3). While it is not possible to determine the ancestral origin of 116E VP3, the branching pattern is consistent with a reassortment event. A similar pattern was seen with several genes from the G11 human strains Matlab36-02, KTM368, and Dhaka6 (Matthijnssens et al., 2010b). Together, these phylogenetic analyses indicate that all of the RV3 genome segments are most likely of human Wa-like RV origin. These results also suggests that 116E may be a multi-gene reassortant, containing a bovine RV VP4 gene and a VP3 gene of unknown ancestry in a human Wa-like RV background.

### Atypical residues of RV3 and 116E proteins

To gain insight into possible attenuation determinants for RV3 and 116E, we created alignments using the deduced amino acid sequences. We found that RV3 proteins exhibit several amino acid changes not yet documented in RVs whose sequences are available in GenBank (Table 4). Specifically, each internal gene protein had one to three amino acid differences when compared with other known RV strains; many of these changes occurred at invariable sites in the protein sequence (Table 4 and data not shown). Of particular interest are the two amino acid changes (Y85C and G162V) in NSP4, a viral nonstructural protein that can function as an enterotoxin (Estes and Kapikian, 2007). Though both changes are outside of the putative toxin domain (NSP4 residues ~114-135), the Y85C change is non-conservative and may influence the function of this protein (Estes and Kapikian, 2007). Neither of these changes are seen in a RV3 NSP4 sequence determined from the primary stool specimen, indicating have been acquired during cell culture passage (Kirkwood et al., 1996) (Table S1). At 92 amino acids, the length of the putative NSP6 protein of RV3 is identical to that of strain Wa, but contained three changes compared with known strains (Table 4).

**Table 4**

**Atypical Residues of RV3 Proteins**

| Structural Proteins | | Non-structural Proteins | |
|---|---|---|---|
| VP1 | I732V | NSP1 | L138V |
| | V741I | | C/Y/Q394W |
| VP2 | S606G | NSP2 | A243V |
| | M672T | | T244A |
| | | | D/E256N |
| VP3 | N139D | | |
| | N686S | NSP3 | T137S |
| VP6 | E/D86K | NSP4 | Y85C |
| | | | G162V |
| VP7[a,b] | S97A (7-1A, A) | | |
| | Q280R | NSP5 | E46G |
| VP4[c] | none | NSP6 | K27E |
| | | | S30L |
| | | | R63K |

[a]compared to human G3 RV sequences in GenBank

[b]VP7 antigenic domain or region as defined in (Matthijnssens et. al., 2010c) is indicated in parentheses next to associated residue

[c]compared to P[6] RV sequences in GenBank

Consistent with the phylogenetic analysis using nucleotide sequences, we found that RV3 VP7 is nearly identical at the amino acid level to other human RV G3 VP7 proteins. We did discover two residues of RV3 VP7 that are not seen in most other G3 proteins from human RVs for which sequences are available in GenBank (Table 4 and Fig. 3A). Specifically, RV3 VP7 has alanine and arginine at positions 97 and 280, respectively, while nearly every other human RV G3 VP7 protein shows serine and glutamine at these locations (Fig. 3A). By mapping these residues onto the three-dimensional structure of the VP7 trimer, we saw that the S97A change is located near antigenic domain 7-1A (classic antigenic region A) (Fig. 3B) (Aoki et al., 2009; Matthijnssens et al., 2010c). In contrast, the Q280R change is buried underneath the VP7 trimer, likely at the VP6 interface (data not shown). For RV3 VP4, all residues are represented in other human P[6] RV strains (Table 4).

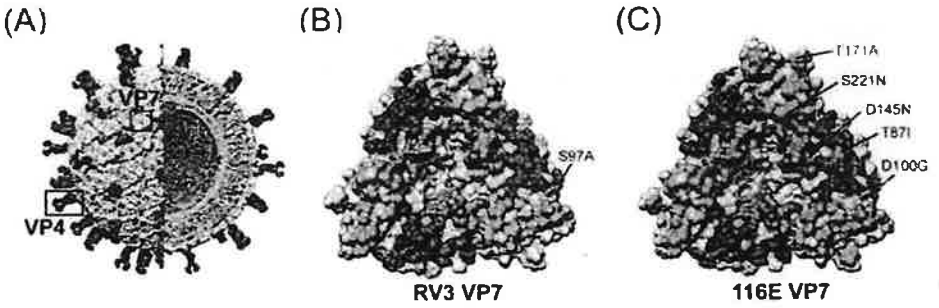


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Fig. 3

Surface-exposed VP7 amino acids unique to RV3 or 116E. (A) Architecture of a RV virion (modified with permission from B.V.V. Prasad), showing the positions of VP7 and VP4. (B and C) Three-dimensional locations of amino acid changes in RV3 or 116E. In both images, a surface representation of the VP7 trimer crystal structure (PDB 3FMG) is shown. Residues comprising the putative neutralization domains have been colored as follows: 7-1A (red), 7-1B (salmon), and 7-2 (purple). Amino acids unique to RV3 or 116E, not represented in any other G-type-matched strains, are shown in cyan and are labeled for a single monomer of the trimer.

The amino acid alignments revealed that many of the 116E proteins exhibit numerous residues not yet seen in other RVs whose sequences are in GenBank (Table 5). Of the 116E internal gene proteins, VP2, VP3, and NSP1 exhibit the largest number of changes (4, 9, and 10 residues, respectively) (Table 5). The changes in NSP1 are interesting in light of the attenuated phenotype of 116E, as this nonstructural protein can function as an interferon antagonist (Barro and Patton, 2005). Moreover, VP1, VP6, NSP3, and NSP5 each show a single residue differing for 116E compared with all other RV strains (Table 5). The 116E NSP6 protein is predicted to be 92 amino acids long, like that of RV3, and shows two changes compared with known strains (Table 5). We found no amino acid residues that were unique to 116E NSP2 and NSP4. The fact that 116E NSP4 did not show any amino acids changes was surprising, given its distant phylogenetic relationship to human RV genes at the nucleotide level.

**Table 5**

**Atypical Residues of 116E Proteins**

| Structural Proteins | | | | Non-structural Proteins | |
|---|---|---|---|---|---|
| VP1 | G95V | VP7[a,b] | L26V | NSP1 | D94N |
| | | | L41I | | N109T |
| VP2 | Q/L123R | | I43V | | Q203R |
| | Q180H | | L57V | | H237Y |
| | E197D | | T87I (7-1A, A) | | Q/K292R |
| | H850Y | | D100G (7-1A, A, B) | | K296E |
| | | | L133F (B) | | H319R |
| VP3 | D83N | | M142V | | I444V |
| | N139K | | D145N (7-2, B) | | R451T |
| | A184T | | T171A | | Y478S |
| | A395T | | D179N | | |
| | K/N480Q | | S221N (7-1B, B, C) | NSP2 | none |
| | K496R | | A278T | | |
| | K/T687I | | | NSP3 | S280A |
| | K704E | VP4[c] | S73K | | |
| | T807M | | N116S | NSP4 | none |
| | | | T118V | | |
| VP6 | A/V101S | | T136A | NSP5 | T/N113S |
| | | | R138K | | |
| | | | T148A | NSP6 | T49M |
| | | | Y156F | | R56L |
| | | | T181A | | |
| | | | G221R | | |
| | | | M226I | | |
| | | | I241V | | |
| | | | [illegible] | | |

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[a]compared to human G9 RV sequences in GenBank

[b]VP7 antigenic domain or region as defined in (Matthijnssens et. al., 2010c) is indicated in parentheses next to associated residue

[c]compared to P[11] RV sequences in GenBank

Amino acid alignments of 116E VP7 with other G9 sequences showed that its glycoprotein has several atypical residues. In particular, we found 14 amino acids in 116E VP7 (positions 26, 41, 43, 57, 68, 87, 100, 133, 142, 145, 171, 179, 221, and 278) that differ for the majority of G9 VP7s (Table 5). Most of these changes are buried, but T87I, D100G, D145N, T171A, and S221N are located on the surface of VP7 in proximity to potential sites of antibody binding (Table 5 and Fig. 3C) (Aoki et al., 2009; Matthijnssens et al., 2010c). Likewise, 116E VP4 contains 17 amino acid changes when compared to other human and animal P[11] proteins (Table 5).

### P[6] VP4 residues that correlate with neonatal infection

Phylogenetic analysis at the nucleotide level suggested that the P[6] VP4 genes of neonatal RVs, such as RV3, are genetically-divergent from the P[6] VP4 gene of strains isolated from infants and children (>28 days old). In agreement, using amino acid alignments, we discovered that the P[6] VP4 proteins of neonatal RVs differed at several positions (73, 78, 167, 169, 217, 456, 539, 544, 553, 616, 646, and 695) compared with those of non-neonatal strains (Fig. 4). While the correlation at each position was not absolute, the observation that P[6] VP4 proteins of RVs isolated from newborns generally vary from those of other P[6] human RVs was surprising. Importantly, because strains that cause symptomatic (strain 12/85) and asymptomatic (strains RV3, M37, 1076, NnB1, and ST3) infections are conserved at these sites, we predict that they do not contribute to virulence. Instead, we hypothesize that some or all of these amino acid changes confer P[6] strains with the enhanced capacity to infect newborns. By mapping these neonatal RV-specific VP4 differences onto the three-dimensional structure of the attachment protein, we found that six of them (S73, S78, L167, H169, T199, and V217) are located at the basal surface of VP8*, which is the trypsin-activated distal domain of VP4 (Fig. 5) (Dormitzer et al., 2004; Dormitzer et al., 2002). It is possible that these residues allow P[6] RVs to adhere more efficiently to cell surface receptors in the neonatal gut, thereby aiding in viral entry.

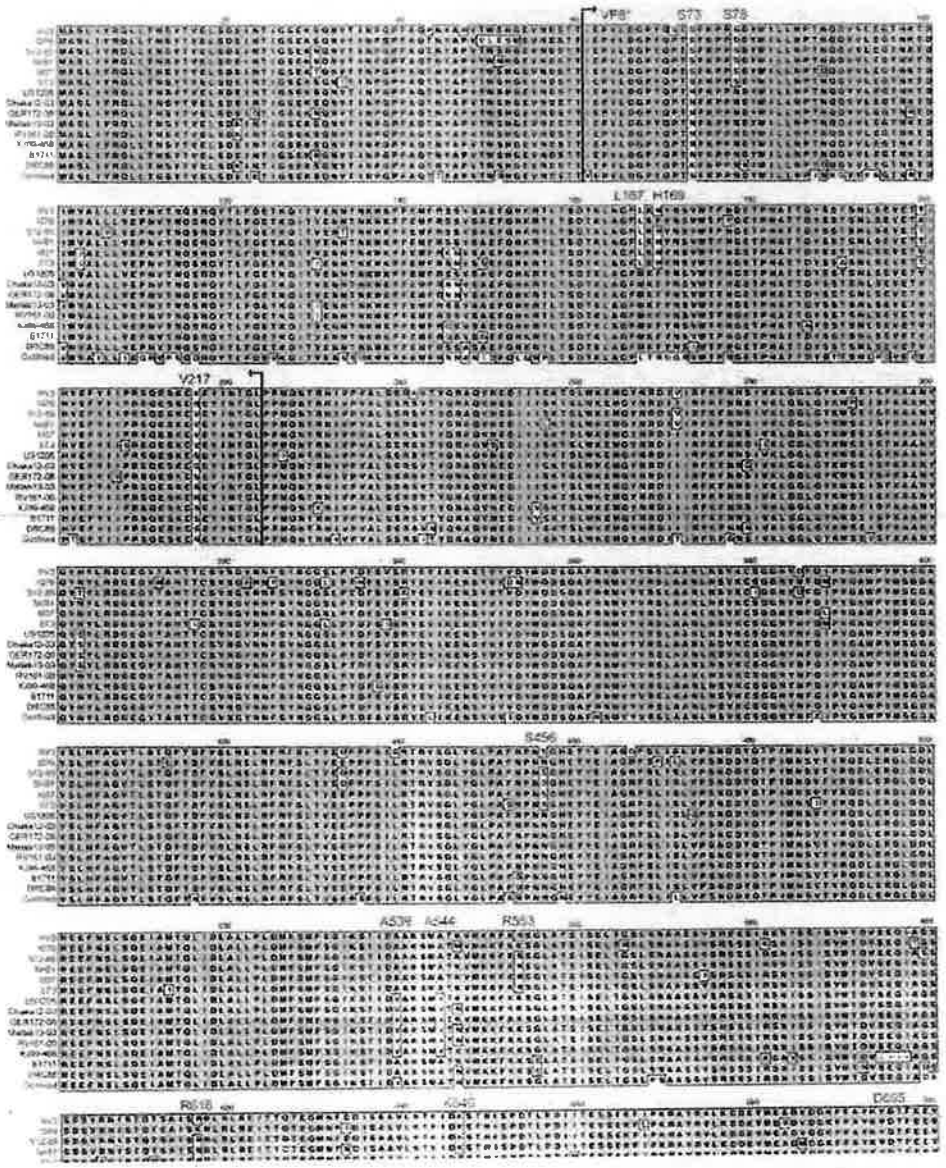


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Fig. 4

Alignment of P[6] VP4 showing residues that correlate with neonatal infection. The VP4 amino acid sequences of several representative P[6] strains are shown. The strain names are to the left of each sequence and are colored according to Fig. 1. Grey shading indicates conservation of amino acid identity. Residues associated with most P[6] strains isolated from neonates are labeled. Blue arrows show the region of VP4 comprising the VP8* core.

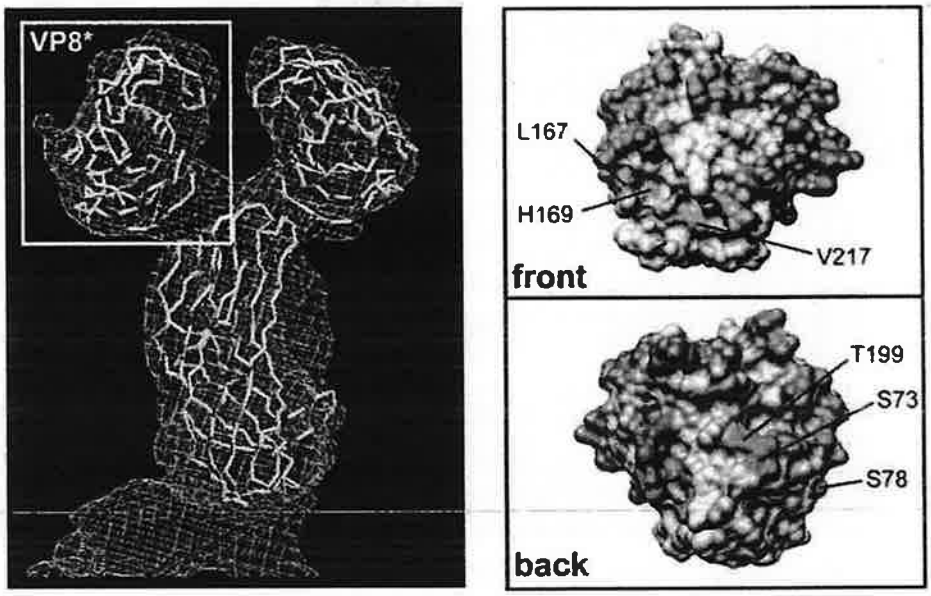


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Fig. 5

Location of surface-exposed P[6] VP8* residues that correlate with neonatal infection. The left image shows a surface representation of the VP4 crystal structure (PDB 1KQR). A white box defines the position of VP8*. The right images show the VP8* core from two different viewpoints (front or back). The front viewpoint is rotated 90° to the right compared with the image in the white box. The back viewpoint is rotated 180° to the left compared with the front. Residues comprising the putative neutralization domains of VP8* have been colored as follows: pink (8-1), salmon (8-2), purple (8-3) and green (8-4). Residues that correlate with the capacity of P[6] strains to infect neonates are shown in cyan.

## Discussion

In many developing countries, RV infections are a leading cause of illness and death among children less than 2 years of age (Parashar et al., 2006). It is unclear whether the currently available RV vaccines will be effective and affordable in these regions of the world (Tate et al, 2010). Consequently, new vaccines are being generated, several of which are based on live-attenuated strains isolated from newborn infants. Two neonatal RV strains, RV3 and 116E, were adapted to growth in culture by multiple passages in primary African green monkey kidney (AGMK) cells (Palombo and Bishop, 1994; Das et al., 1993). Derivatives of these cell culture adapted versions of RV3 and 116E have undergone several phases of clinical testing and were proven safe and immunogenic (Barnes et al., 1997; Barnes et al., 2002; Bhandari et al., 2006; Bhandari et al., 2009). Prior to this study, the genome sequences of RV3 and 116E had not been determined, making it difficult to fully identify factors contributing to their inherent attenuation. The results described in this report help close this gap in knowledge by revealing amino acid atypical residues of proteins encoded by these viruses. These changes are not only predicted to influence virulence, but also impact neonatal host infection and the efficacy of RV3- or 116E-based vaccines. Still, it is important to note that the RV3 and 116E strains sequenced in this study are not the

actual vaccine preparations. Also, the VP4, VP6, and NSP4 sequences of the original RV3 stool isolate that are available in GenBank show changes compared with the sequences we determined (Table S1) (Palombo et al., 1994; Kirkwood et al., 1996). We think it is possible that some of these changes resulted from adaptation to growth *in vitro*. For 116E there is no available sequence information of the original stool material. However, the 116E VP6, NSP1, and NSP4 sequences that we determined in this study exactly match those in GenBank for the culture-adapted strain (Table S1) (Cunliffe et al., 1997). For 116E VP7 and VP4, we found a few nucleotide and amino acid changes compared to the sequences in GenBank (Das et al., 1993; Gentsch et al., 1993) (Table S1). Because we passaged 116E six additional times in AGMK cells (see Material and Methods), it is possible that these differences could be attributed to evolution of the virus in culture. The manufacturers have not released the sequences of the RV3 or 116E vaccine preparations; thus, this study is the first to describe the complete genetic characteristics of these important cell culture-adapted strains.

### Why are strains RV3 and 116E attenuated?

RV infections of newborns are uncommonly documented, but are generally asymptomatic. Factors such as the prevalence of maternal antibodies and immature gut physiology likely contribute to the lack of diarrhea in neonates (Haffejee, 1991). However, some of the strains isolated from newborns also seem attenuated in older infants and children, demonstrating that they are phenotypically different from pathogenic RVs. The complete genome sequence of only one asymptomatic neonatal strain, ST3 (G4P[6]), has been reported to date, but partial genome sequences exist for M37 (G1P[6]) and I321 (G10P[11]) (Dunn et al., 1994; Heiman et al., 2008; Kirkwood and Palombo, 1997; Palombo and Bishop, 1994a; Rao et al., 1995). Strains M37 and I321 were originally considered as vaccine candidates, along with RV3 and 116E, prior to studies showing that they are poorly immunogenic or do not protect against RV disease (Bhandari et al., 2006; Perez-Schael et al., 1994; Vesikari et al., 1991). While the evolutionary origin of M37 is unknown, I321 is thought to have derived from an inter-species transmission of a bovine RV to a human, providing a basis for its lack of virulence (Sukumaran et al., 1992). On the contrary, the attenuating determinants of ST3, RV3, and 116E seem subtler, as the vast majority of their genes are of human RV origin.

The atypical G/P-type combinations seen in RV3 and 116E may contribute, at least in part, to their attenuated phenotypes. Specifically, RV3 is a G3P[6] strain and, although G3 strains readily circulate in the human population, they are usually combined with P[8] VP4 proteins (Albert et al., 1987a; Kirkwood et al., 1996). Human RVs with P[6] specificity are more rare, but can be seen with multiple G-types (Matthijnssens et al., 2009). Interestingly, many P[6] strains have been isolated from neonates with both symptomatic and asymptomatic infections, but there does not seem to be a clear correlation with residues of VP4 and clinical illness (Hoshino et al., 2003; Santos et al., 1994). Two RV3 internal genes (encoding VP6 and NSP4) had been sequenced previously, revealing that they are similar to common Wa-like human strains (Kirkwood et al., 1996; Palombo and Bishop, 1994b). Our results extend these findings and show that all of the internal RV3 genes are classified as genotype 1. Despite their phylogenetic similarities to pathogenic RV isolates, we found unique amino acid changes in every RV3 internal gene protein. We hypothesize that some of these point mutations contribute to the attenuation of this strain.

In contrast to RV3, which seems to have human RV-like VP7 and VP4 proteins, 116E is a G9 strain with a P[11] VP4 that is very similar to that of several bovine RVs (Das et al., 1994; Das et al., 1993; Gentsch et al., 1993). The only other known P[11] human strains were also isolated from neonates, suggesting that, like P[6] RVs, those with P[11]-specificity may have an enhanced capacity to replicate in the newborn gut. Previous sequence and RNA hybridization studies showed that 116E contains Wa-like internal genes (Cunliffe et al., 1997; Das et al., 1993). Our results are consistent with these earlier

ones, but also indicate that many of the internal genes/proteins of 116E are unusual compared with other genotype 1 genes/proteins. Most notably, the gene of the 116E RNA capping enzyme, VP3, is distantly related to human and animal RV genotype 1 genes at the nucleotide level and shows 9 amino acid changes not represented in any known RV sequence. It is possible that 116E picked up its VP3 gene by reassorting with an unidentified Wa-like RV ancestor. The changes in the other 116E proteins (e.g., the VP2 inner capsid) might reflect co-evolution driven by the requirement to maintain VP3 interactions during viral replication. Alternatively, 116E VP3 could have accumulated point mutations via genetic drift; however, the pressures that would have selected for such changes in this enzyme are not obvious. Based on the available data, we speculate that the ancestor of 116E may have been a human G9P[8] strain that acquired a bovine P[11] VP4 gene and a VP3 gene from an unknown RV during separate reassortment events. Because VP3 has been shown to be a virulence determinant, it is possible that this gene alone is responsible for the attenuation of 116E (Hoshino et al., 1995). However, we think it is more likely that the combination of changes in the 116E genome is responsible for its avirulent phenotype. Of particular interest are the amino acid changes at highly conserved positions of the interferon-antagonist NSP1 protein of 116E (Barro and Patton, 2005).

### Does VP4 confer some RVs an enhanced capacity to infect newborns?

A surprising result of this study was the apparent relationship between VP4 sequence and neonatal infection. The phylogenetic clustering pattern we found is in agreement with analysis done on the VP8* gene region of neonatal P[6] strains isolated in Brazil (Mascarenhas et al., 2007). Using amino acid alignments, we found that the VP4 proteins of neonatal P[6] RVs tend to differ at several positions compared with P[6] strains isolated from older infants for children. However, the correlation was not absolute; there are examples of P[6] strains isolated from children that show neonatal RV-like amino acids and vice-versa. Because P[6] strains that cause symptomatic (strain 12/85) and asymptomatic (strains RV3, M37, 1076, NnB1, and ST3) infections are conserved at these sites, they probably do not contribute to virulence (Santos et al., 1994). However, these amino acid changes may confer some P[6] strains with the enhanced capacity to infect newborns. We found that six of them (S73, S78, L167, H169, T199, and V217) are located at the basal surface of the VP8* core, which is exposed upon trypsin cleavage of the VP4 spike. The location of these changes outside putative neutralization domains suggests that do not merely allow P[6] strains to evade maternal antibodies. Instead, we hypothesize that the changes help these viruses adhere more efficiently to cell surface receptors in the neonatal gut. Interestingly, P[11] strains (including 116E, I321, and N155) also show serines at positions 73 and 78. Thus, these two sites might be of particular importance in determining whether a RV can establish an infection in a newborn. Treatment of RV3 (P[6]) or 116E (P[11]) with neuraminidase does not alter infectivity in cell culture, suggesting attachment is sialic-acid independent (Ciarlet et al., 2002). Likewise, the VP4 proteins of all known P[6] and P[11] strains do not conserve the sialic acid-binding residues of strain RRV (Matthijnssens et al., 2010c). These observations indicate that the VP4 amino acid changes identified in this study may confer binding to alternative carbohydrate molecules or to proteins present on the surface of neonatal enterocytes.

### Will RV3 and 116E protect against RV disease?

The most significant question that remains regarding monovalent vaccines, such as RV3 (G3P[6]) and 116E (G9P[11]), is whether they will be effective at protecting against disease brought on by heterologous serotype strains (G1, G2, G4, P[4], P[8], etc.). The clinical efficacy of RV3, even in communities where G1 and G2 strains dominated, provides indirect evidence of cross-protection with this vaccine candidate (Bishop et al., 1983). RV3 VP7 shows a single amino acid difference (S97A) located near epitope 7-1A when compared with common human G3 RVs; yet, we do not expect this conservative change to dramatically influence neutralization. In contrast, the VP7 protein of 116E is

quite divergent from most other human G9 VP7s and contains numerous amino changes located on the protein surface. Because of the number of changes, we think that 116E might be less effective at producing antibodies capable of protecting against circulating G9 strains. In support of this notion, guinea pig hyper-immune serum raised against 116E VP7 failed to robustly neutralize several human G9 RVs in plaque reduction assays (Cao et al., 2008). In fact, G9 strains with VP7 proteins belonging to phylogenetic lineage 1 may be more suitable for vaccines, as they more broadly cross-neutralize other G9 strains *in vitro* (Hoshino et al., 2004). However, studies in animal models have shown that CD4 and CD8 T cell responses can contribute to serotype-independent protection for RVs (Ward, 2003). If this is the case, vaccines that are based on human Wa-like strains, such as RV3 and 116E, may be quite successful. The findings from this study are expected to aid future research into the true protective efficacy of RV3 and 116E.

## Materials and Methods

### Viruses and RNA isolation

RV3 was amplified from the original stool specimen in primary AGMK cells (30 passages) and was triple-plaque purified during passages 19 to 23 (Palombo and Bishop, 1994). The virus was then grown in monkey kidney (MA104) cells for >15 passages. An aliquot this cell culture-adapted RV3 strain was generously provided to us by Carl Kirkwood (Melbourne Children's Research Institute). Our laboratory further amplified the virus (one passage) in MA104 cells and used the clarified infected cell culture supernatant for RNA extraction and sequencing.

116E was amplified from the original stool specimen in primary AGMK cells (2 passages), grown in MA104 cells (8 passages), and plaque purified twice in MA104 cells (Das et. al, 1993). An aliquot this cell culture-adapted 116E strain was sent to Taka Hoshino (National Institutes of Health) from Jon Gentsch (Centers for Disease Control). In the Hoshino laboratory, the virus was passaged six times in primary AGMK cells, and an aliquot of the cell culture supernatant was given to our laboratory for RNA extraction and sequencing.

For both viruses, RNA was extracted from the clarified supernatant using TRIzol-LS as described by the manufacturer's protocol (Invitrogen). RNA was denatured in 50% dimethyl sulfoxide for ten minutes at 94°C and then used as template for RT-PCR.

### RT-PCR and sequencing

Denatured RNA was used as template for RT-PCR to amplify cDNA fragments corresponding to regions of RV3 or 116E gene ORFs. For 116E genome segments 1, 2, and 3, SuperScript II RT and Accuprime *Pfx* Supermix were used according to the manufacturer's protocols (both Invitrogen). For 116E segments 4, 5, 6, 7, 8, 9, 10 and 11 and all eleven RV3 segments, the SuperScript One-Step system (Invitrogen) was used according to the manufacturer's protocol. Primers are listed in supplemental materials (Table S2).

The RT-PCR reactions were electrophoresed in a 1% agarose gel, and specific cDNA products were excised and purified using a QIAquick gel extraction kit (Qiagen). The purified cDNAs were then sequenced with an ABI Prism BigDye v3.1 terminator cycle sequencing kit (Applied Biosystems Group). The dye terminator was removed using Performa DTR (Edge Biosystems) and sequences were obtained with a 3730 DNA Analyzer (Applied Biosystems). The sequence files were assembled and verified using Sequencher 4.7 (Gene Codes Corporation). Nucleotide sequences generated in this study have been deposited into GenBank with the following accession numbers: FJ998270-FJ998280 (RV3) and FJ361201-FJ361211 (116E). Previously determined sequences for these two strains have the

following GenBank accession numbers: U16299 (RV3 VP4); U04741 (RV3 VP6); U42628 (RV3 NSP4); L14072 (116E VP7); L07934 (116E VP4); U85998 (116E VP6); U85999 (116E NSP1); and U78558 (116E NSP4)

### Phylogenetic analyses, amino acid alignments, and structure-based predictions

Phylogenetic trees were generated in MacVector 8.1.2 (Accelrys) using the neighbor-joining method (1000 bootstrap repetitions) and the Kimura-2 correction parameter. Amino acid alignments were constructed with MacVector 8.1.2. using ClustalW, BLOSUM Series, with the defaults set (open gap penalty of 10.0, extended gap penalty of 0.05, and delay divergence of 40%). Structural analysis of VP7 (PBD 3FMG), VP8* (PDB 1KQR), and VP5* (PDB 2B4H) was performed using UCSF Chimera-Molecular Molecular Modeling System (Petterson, 2004). GenBank accession numbers for all RV sequences used in this study are included in the supplemental materials (Table S3).

## Supplementary Material

**01**

Click here to view. (204K, doc)

**02**

Click here to view. (50K, doc)

**03**

Click here to view. (53K, xls)

## Acknowledgments

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## Footnotes



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# National Biodiversity Authority

राष्ट्रीय जैव विविधता प्राधिकरण

(Statutory body of Ministry of Environment, Forest and Climate Change, Government of India)


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18.02.2020

NBA/IPR-Gen/33/17-1/18-19/3882

To

Shri. O P Gupta, IAS
Controller General of Patents, Designs & Trade Marks
Intellectual Property India,
Patents/Designs/Trade Marks/Geographical Indications,
Boudhik Sampada Bhavan,
Antop Hill, S.M. Road,
Mumbai-400037

Sir,

Sub: Patent application number: 201917035818 – Requirement of Prior-approval from NBA- reg.

This has reference to patent application no.: 201917035818 titled "Heat stable liquid rotavirus vaccine" filed Inventprise, LLC and published by IPO. As you are aware, Section 6 of the Biological Diversity Act, 2002 mandates that any person applying for any Intellectual Property Right for an invention based on any research or information on a biological resource obtained from India, shall obtain prior approval of NBA.

In the patent application referenced above, the applicant has used human rotavirus strain 116E, originally isolated in New Delhi, India, for developing the claimed invention. However, the applicant has not obtained requisite approval under Section 6 of the Biological Diversity Act, 2002. Hence, it is requested that the applicant may be instructed to seek approval under section 6 and the patent shall not be granted until approval is obtained from National Biodiversity Authority. The applicant may apply online using the ABS e-filing portal, the link for which has been provided here – [http://absefiling.nic.in/NBA/login/auth]

Yours faithfully

J. Justin Mohan

(J. Justin Mohan)
Secretary, NBA

Copy to:

1. Inventprise, LLC, 18133, NE 68th Street, d150 Redmond, Washington 98052 USA
2. P. S. Davar. P. S. Davar & Co, N-220, Greater Kailash -1, New Delhi – 110048. E-mail: psdavar@psdavar.com

TRUE COPY

# Annexure 3

INTELLECTUAL PROPERTY INDIA
Patents/Designs/
Trade Marks/
Geographical Indications.

सत्यमेव जयते
Government of India
Office of The Controller General of
Patents, Designs & Trade Marks
Boudhik Sampada Bhavan
S.M. Road, Antop Hill
Mumbai-400 037 (India)

(Tel): 022-24132735
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(Fax): 022-24123322

(Email): cgoffice-mh@nic.in
(Website): www.ipindia.nic.in

No.CG/Office Circular (P)/2017/ 451

Date 23-5-2017

## OFFICE CIRCULAR

During the recent meetings with stakeholders at Mumbai and Delhi, certain issues have been raised regarding examination of patent applications involving the use of biological material. Stakeholders have submitted that unwarranted objections are raised by the Patent Office regarding requirement of approval from National Biodiversity Authority (NBA) and difficulties are faced by them because of delay in obtaining NBA permission.

In view of the submissions made by stakeholders, this issue has been considered and existing instructions/guidelines issued from time to time by various office orders/circulars are further streamlined by way of the following.

| Sl. No | Issue | Modified procedure to be followed |
|---|---|---|
| 1 | Where the invention does not relate to a biological resource defined under the Biological Diversity Act 2002, such as:<br>(a) Value-added product<br>(b) Bio-wastes<br>(c) Synthetically prepared biological material | (a) Value Added Product:<br>Section 2 of Biological Diversity Act 2002 explicitly excludes value added products from the purview of "Biological resources".<br>*As per* Biological Diversity Act, 2002:<br>*Section 2 (c) : "biological resources" means plants, animals and micro-organisms or parts thereof, their genetic material and by-products (excluding value added products) with actual or potential use or value, but does not include human genetic material;*<br>*Section 2 (p): "value added products" means products which may contain portions or extracts of plants and animals in unrecognizable and physically inseparable form.*<br>Examiners/Controllers shall verify from the disclosure in patent specification if the claimed invention resides in the biological resource or value added product. If the invention resides in a value added product, then they shall avoid |

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|---|---|---|
| | | raising objection with respect to NBA approval while issuing First Examination Report.<br>**(b) Bio-wastes:**<br>A bio-waste is generated after the economic use of the biological resource/material is exhausted. Therefore, a bio-waste may not be covered under the definition of the biological resource as envisaged in the Biodiversity Act 2002.<br>Hence, NBA approval may not be sought from the applicant when the invention merely uses such bio-wastes (for example: incinerator, gas burner, etc.)<br>**(c) Synthetically prepared biological material:**<br>NBA approval is required for IPRs which are based on research or information on the biological resource and ought not to be required if use is made of the synthetically prepared material like enzymes, pigments, gums, sucrose etc. which may be produced from a biological resource.<br>Therefore, Examiners/ Controllers shall verify as to whether the invention resides in synthetic material before issuing FER and shall not raise objections in FER when explicit declaration is made by the applicant to this effect supported by sufficient disclosure in the specification. |
| 2 | Where the biological resource/material used in invention is not obtained /sourced from India. | *Section 6 (1) of the Biological Diversity Act , 2002 states,*<br>*" No person shall apply for any intellectual property right, by whatever name called, in or outside India for any invention based on any research or information on a biological resource obtained from India without obtaining the previous approval of the National Biodiversity Authority before making such application.*<br>*Provided that if a person applies for a patent, permission of the National Biodiversity Authority may be obtained after the acceptance of the patent but before the sealing of the patent by the patent authority concerned; and,*<br>*Provided further that the National Biodiversity Authority shall dispose of the application for permission made to it within a period of ninety days from the date of receipt thereof."*<br>Thus, no approval from NBA is necessary when the invention is based on any research or information on a *biological resource not obtained from India.* |

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|---|---|---|
| | | Therefore, when an applicant makes unequivocal declaration in application for patent (Form 1) that the biological material used in the invention is neither obtained from India nor sourced from India, then Examiners/Controllers shall duly consider such declaration before issuing FER and shall avoid raising an objection with respect to the requirement of NBA approval. |
| 4 | Marking of applications in the module regarding requirement of NBA approvals. | While examining the applications involving use of biological resource, Examiners should mark these applications as "NBA approval application" in the examination module before sending the examination report to the Controller for approval. However, if the Controller is not satisfied with requirement regarding NBA approval, he shall unmark the application by giving reasons thereof. |
| 5 | Cases held up for grant of patents only due to non-submission of NBA permission. | Where the applicant has complied with all the objections, except submission of NBA approval, the Controller shall mark the application in the examination module by remark that "NBA approval pending, but in order for grant" and, the System Administrator shall put a tag on such cases so that these applications can be treated as if disposed of by the Controller. |

All Examiners/Controllers may note that any false declaration on behalf of the applicant makes him liable for revocation of patent under section 64 (1) (j)/ 64(1) (p) of the Patents Act 1970 (as amended). Further, as per provisions in section 55(1) of Biological Diversity Act 2002, if the applicant contravenes or attempts to contravene or abets the contravention of the provision of section 6 of the Biological Diversity Act 2002, he shall be liable for penal action under section 55(1) of the Act.

(O.P Gupta)

Controller General of Patents, Designs & Trade Marks

Copy to

1. Head of offices, Patent Office, Delhi, Kolkata, Chennai and Mumbai
2. System Administrator
3. All Examiners and Controllers (Patent- List)
4. Office order File

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| 60.18 | III 3(2) applicant who accessed the bio resource(s) and filed/ obtained patent without the prior approval of NBA (Contravention of Section 3 and 6 of BD Act) |
|---|---|
| | Part A: Filled by the NBA Secretariat |
| **File No** | INBA3202002159 (4228) 11.09.2020 |
| **Name and Address of Applicant** | M/s INVENTPRISE, LLC<br>18133 NE 68th St d150, Redmond,<br>Washington 226, USA<br><br>*Contact person:*<br>Mr Praneét Singh Davar<br>Patent Attorney<br>P.S.Davar& Co<br>N-220, N-Block Greater Kailash-1<br>New Delhi 110 048 |
| **Legal Status of Applicant** | Section 3(2) Entity |
| **Details of Fee Paid** | Rs. 500/-<br>Ref. no. - DUD5017583 |
| **Title of Patent Application** | Heat stable liquid rotavirus vaccine |

**Details of Patent Filings**

| Country | Application no. | Status | Date of grant |
|---|---|---|---|
| India | 201917035818 | Pending | -- |
| USA | 15/896,939 | Granted | (10.413.604) 19.09.2019 |
| Korea | 10-2019-7026145 | Pending | -- |
| China | 201880024988 | Pending | |
| Indonesia | PID201907114 | Pending | -- |
| Philippines | 1-2019-501856 | Pending | -- |
| Malaysia | PI2019004553 | Pending | -- |
| PCT | PCT/US18/018226 | pending | -- |

**Details of Biological Resources used in the Invention**

| Nature of the Biological Resource | Common Name | Scientific Name | Parts Used | Source of Access | Place of Access | Rare/ Endemic/ Endangered/ Threatened/ | NTC List (Yes/No) |
|---|---|---|---|---|---|---|---|
| Micro organisms | Virus | *Rotavirus* strain 116E | Others- Naturally attenuated Rota virus | Company | Bharat Biotech International Ltd, Genome Valley, Shampeerpet Hyderabad - 500 078 Telangana | Nil | Nil |

| **Details of TK if any** | No |
|---|---|

Remarks:

1. The applicant being a section 3(2) entity has accessed the biological resources from Bharat Biotech Pvt Ltd (in the year of 2016-2017) without prior approval of NBA and thereby contravened section 3 of the BD Act.
2. Since Patent has been granted in USA on 17.09.2019 (USA Patent Number 10,413,604),applicant obtained the patent without prior approval of NBA and thereby contravened section 3 & 6 of the BD Act. ***(Pg.no. 57)***
3. Therefore this application is placed before EC for examination

| Signatures of: | |
|---|---|
| NIL<br>Expert Consultant (if any) | |
| K. Satheesh / S. Shakthivel<br>Technical Staff (Contract) | |
| P. Jaishankar<br>Technical Assistant | |
| T. Narendran<br>Technical Officer (IPR) | |
| | J. Justin Mohan<br>Counter signed: Secretary, NBA |

| **Part B: To be checked by the Expert Committee** | | | |
|---|---|---|---|
| 1. | Whether Traditional Knowledge has been used | | No |
| 2. | Screening of the bioresources species: | | |
| | (a) | Whether Rare/Endemic/Endangered/Threatened | No |
| | (b) | Whether listed under Wildlife Act/CITES/BDA, etc | No |
| | (c) | Whether restricted/prohibited underEXIM policy/DGFT guidelines/rules | No |
| 3. | Whether the original file of the applicant was placed before the EC | | No |
| 4. | Whether the proposal is likely to have an adverse impact on environment/sustainability of use/ livelihoods/ national interest | | No |
| 5. | Any other item | | No |

**Recommendations of the Expert Committee on ABS** (*to be incorporated in the prescribed agreement format once approved by the Authority*):

1. EC observed that applicant being a section 3(2) entity has accessed the biological resources from Bharat Biotech Pvt Ltd without prior approval of NBA as required under section 3 of the BD Act. It was also observed that applicant obtained Patent in USA without prior approval of NBA as required under section 6 of the Act. Hence, the applicant had contravened section 3 and section 6 of the Act.
2. EC took note of the OM issued by the MoEFCC and also noted that Authority decided to determine highest benefit sharing component on such cases.

3. After deliberations, Expert Committee recommended to consider the application for approval, subject to the following higher benefit sharing Component and also apply in Form-I

(a)Where the applicant himself commercializes the process/product/ innovation, the monetary benefit sharing shall be 1% on the annual gross ex-factory sale minus government taxes.

(b) Where the applicant assigns/licenses the process/product/innovation to a third party for commercialization, the applicant shall pay to NBA 5.0% of the fee received (in any form including the license / assignee fee) and 5.0% of the royalty amount received annually from the assignee/licensee.

Signature of Chairman and Members (Present) of Committee on ABS

**P S Davar & Company**
Patent & Trademark Attorneys

Address : N 220, Greater Kailash 1
New Delhi 110048, India
Tel.: +91 11 41065143, 41053715, 29241034
Fax : +91 11 43601991
E-mail : psdavar@psdavar.com
sdavar@psdavar.com
Website : www.psdavar.com

No: PSD/PAT/301
NBA/IPR Appl/4172/20-21

Dated: 08/10/2020

**Via email only**
iprsection@nbaindia.org

**National Biodiversity Authority,**
Government of India,
5th Floor, TICEL Bio Park,
Taramani,
**Chennai-600 113**

**Attn:** Dr. Narendran T, Technical Officer (IPR)

**Sub:** Application in Form-III seeking approval for obtaining IPR on invention titled "Heat stable Liquid Rotavirus vaccine" (Patent Application No. 201917035818)

Dear Sir,

We write with reference to your email of 07/10/2020 and furnish herewith the requisite information as below.

Please be advised that no prior permission from NBA for access to biological resources and conduct of research which culminated into an invention was taken, as the Applicant was not aware of seeking such permission and further it has collaborated with Bharat Biotech International Ltd., Hyderabad, India who has also provided the biological resource to them.

As no prior permission was obtained, further following details are given below as required:

| Sl. No. | Biological resource(s) | | Exact Parts used | Quantity | Date of access of BR | Source of access (Wild/Cultivated/ trader and or etc.) | Exact Geographical location of the access of the biological resources. If procured from local market/ Trader/Institution/ supplier, give detailed contact address |
|---|---|---|---|---|---|---|---|
| | Common name | Scientific name | | | | | |
| | Rotavirus | Rotavirus strain 116E (serotype G9P[11]) | Entire virus | N/A | Experiments performed in the year 2016-2017 | Bharat Biotech International Ltd. | Genome Valley, Shameerpet Hyderabad-500078, TS India |

(a) Details of the research activities carried out with the accessed the biological resources. (100 words).

*The details of the research activity carried out with the biological resource have been distinctly described in the complete specification as filed with the Indian Patent Application No. 201917035818 which is available for public on the Indian Patent Office website.*

*The invention as detailed in the Indian Patent Application No. 201917035818 is directed to an oral vaccine composed of a micronized freeze-dried rotavirus particle emulsion with buffering excipients in a non-aqueous liquid. This IVT-06 formulation has imparted heat stability by protecting the virus at temperatures of 30°C and 40°C for at least twelve months. Extrapolations from the 12-month stability data indicate a shelf life of more than two years at*

*30°C, and six months at 50°C. in addition, for ease oof administration, the formulated dose has a volume of 0.5 mL.*

(b) Whether any Organization has collaborated in the R&D? If so, furnish the details and a copy of the agreement.

*The applicant has collaborated with Bharat Biotech International Ltd. The license agreement is confidential in nature for both the licensee and licensor.*

(c) Exact date of commencement of the research and when did this research culminate into an invention?

*On 14 February, 2017 a provisional Patent application for the subject invention has been filed with the US Patent and Trademark Office with the Patent Application No. 62/458,904 followed by a non-provisional Patent application no. 15/896,939 indicating the commencement and culmination of research.*

(d) Please intimate the rationale for not obtaining the prior approval of NBA for accessing the biological resources (Rotavirus strain) from India.

*Since the Applicant has obtained the biological resource from Bharat Biotech International Ltd., Hyderabad, India, it was not in the knowledge of the applicant that the Permission from the NBA was still required. Nonetheless, the Applicant has applied for permission from NBA in prescribed manner as soon as it was brought to the Applicant's notice by the Authority.*

(e) On examination of the patent details, it was found that you have filed patent applications in USA, Korea, China, Indonesia, Philippines and Malaysia. You are requested to submit the patent details in the format given below:

*We provide the corresponding Patent Application details as below:*

| Sl.no | Country name | Patent application number | Current Status of the application | Patent number (if granted) |
|---|---|---|---|---|
| 1 | USA | 15/896,939 | Granted | 10,413,604 |
| 2 | Korea | 10-2019-7026145 | Pending | |
| 3 | China | 201880024988 | Pending | |
| 4 | Indonesia | PID 201907114 | Pending | |
| 5 | Philippines | 1-2019-501865 | Pending | |
| 6 | Malaysia | PI2019004553 | Pending | |

We understand that with the above submissions, all the requirements have been met.

We kindly request you to grant the requisite permission for further smooth proceedings of the instant Patent Application.

Thanking you,

Sincerely,

Praneet Singh Davar
Patent Agent, (Regd No.: IN/PA-311)
of P S DAVAR & CO.,
APPLICANT'S AGENT

# National Biodiversity Authority

राष्ट्रीय जैव विविधता प्राधिकरण

(Statutory body of Ministry of Environment, Forest and Climate Change, Government of India)

**J. Justin Mohan, IFS**
Secretary
☎ +91 44 2254 1071
+91 44 2254 1074
secretary@nba.nic.in www.nbaindia.org

5th Floor, CSIR Road, TICEL Bio Park,
Taramani, Chennai - 600 113, Tamil Nadu, India.
5 वां तल, सीएसआईआर रोड, टाइसल बायो पार्क,
तरमणि, चेन्नई - 600113 तमिल नाडु, भारत.

NBA/IPR Appl/4228/20/20-21/3896 Date: 28-01-2021

To

Mr. Praneet Singh Davar
Patent Attorney
P.S.Davar & Co
N-220, N-Block Greater Kailash-1
New Delhi - 110 048
Email: psdavar@psdavar.com

Sir,

Sub: Application in Form-III (INBA3202002159 – 11.09.2020) – M/s. Inventprise, LLC - seeking approval for obtaining IPR (201917035818) on the invention entitled "Heat stable liquid rotavirus vaccine" – *reg.*

**********

With reference to your application in Form-III cited above, it is to inform that your application has been examined by the Expert Committee on Access Benefit Sharing (ABS) and observed that applicant being a section 3(2) entity has accessed the biological resources from Bharat Biotech Pvt Ltd without prior approval of NBA. It was also observed that applicant obtained Patent in USA without prior approval of NBA as required under section 6 of the Act. Hence, the applicant had contravened section 3 and section 6 of the Act.

2. After considering the aforesaid issues, Expert Committee recommended for approval of application in Form-III with higher benefit sharing component as applicant contravened section 6 of the Act, subject to filing of Form-I application by applicant.

3. Accordingly, your requested to submit application in Form-I through online portal (http://absefiling.nic.in), within 15 days from the date of receipt of this communication, for regularizing biological resources that have been accessed for developing the said Invention.

4 It may be noted that approval will be accorded for Form-III application upon approval of application in Form-I only.

Kindly acknowledge receipt.

Yours faithfully,

(J. Justin Mohan)
Secretary, NBA

प्रेषक / Despatcher
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
5वां तल, टाइसल बायोपार्क
5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तरमणि, चेन्नई / Taramani, Chennai - 600 113.

**Email** **P. Jaishankar**

**Execution of agreement for obtaining IPR underSection 6 of the Biological Diversity Act, 2002 – Reg**

**From :** iprsection@nbaindia.org Fri, Mar 26, 2021 10:50 AM

**Subject :** Execution of agreement for obtaining IPR underSection 6 of the Biological Diversity Act, 2002 – Reg 3 attachments

**To :** psdavar@psdavar.com

**Cc :** absdesk2@nbaindia.in, P. Jaishankar <techasstz@nba.nic.in>

NBA./IPR Appl/ 4228/20-21/4708 (only through email) Date:26.03-2021

To

Mr. Praneet Singh Davar
Patent Attorney
P.S.Davar & Co
N-220, N-Block Greater Kailash-1
New Delhi 110 048
Email: psdavar@psdavar.com

Sir,

**Sub:** Execution of agreement for obtaining IPR under Section 6 of the Biological Diversity Act, 2002 – Reg.
Ref: Form III application (INBA3202002159) dated 11.09.2020

**********

With reference to your application cited in reference, preferred under Section 6 of the Biological Diversity Act, 2002 read with Rule 18 of the Biological Diversity Rules, 2004 for obtaining IPR (**201917035818)** on the invention titled **"Heat Stable Liquid Rotavirus Vaccine"** mentioned therein, an agreement is enclosed herewith to enable you to **execute and send two copies of the Stamp Paper Agreements (In Indian Rs. 20/- Non Judicial Stamp Paper)** duly signed along with seal, at the bottom of every page of the agreement including schedules along with witness signature.

Further you are informed that, in pursuant to the coming into force of Nagoya Protocol on Access and Benefit Sharing, it is obligatory on each of the Party to the Protocol to provide at the time of access, a permit or equivalent document as evidence of Prior Informed Consent (PIC) and Mutually Agreed Terms (MAT) and make it available to the CBD Access and Benefit Sharing Clearing House. This permit or equivalent document will serve as an Internationally Recognized Certificate of Compliance (IRCC), which can be used as an evidence of access approval granted by the competent Authority as per the provisions of the Biological Diversity Act, 2002.

In view of the same, the format of permit or equivalent document is enclosed herewith. This format has columns that have an option to mark certain information as confidential in nature. It is requested that, the information which in your opinion are to be kept confidential need to be specified in this enclosed format enabling NBA to furnish only such non-confidential information with ABS-CH. This will help in strengthening the monitoring mechanism of the movement of biological resources and/or associated knowledge between the user and the provider countries and also enhance transparency about the utilization of biological resources. In case of non-receipt of

filled IRCC format along with the signed stamp paper agreements, it will be deemed that you do not require any specific information to be kept confidential by the NBA.

On receipt of the above said documents, the National Biodiversity Authority will grant approval in the form of a written agreement duly signed by the authorized officer of the Authority. **You are therefore requested to submit the signed agreement within 60 days of receipt of this communication and if no reply is received within the stipulated time, the application will be treated as closed, as per the procedure in vogue.**

**However, it is also informed to you that approval in this form III application will be granted only after clearance of the Form I applications**

Yours faithfully,
SD/-
(J.Justin Mohan IFS)
Secretary,
National Biodiversity Authority

Encl:

1) Copy of the Model Agreement
2) IRCC Form

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**ABS agreement-4228.DOCX**
30 KB

**IRCC Form.doc**
40 KB

**Stamp Paper Agreement Preperation Guide.pdf**
147 KB

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## AGREEMENT FOR ACCESS AND BENEFIT SHARING

***(Form-III – For filing applications for obtaining any Intellectual Property Right)***

***(Under the Biological Diversity Act, 2002 and Rules, 2004 and Guidelines on ABS Regulations, 2014)***

This Agreement is made and entered on this ..... day of .....2021 at Chennai, India

**Between**

**National Biodiversity Authority,** a statutory body established under the Biological Diversity Act, 2002, having its head office at 5th Floor, TICEL Bio Park, Taramani, Chennai-600 113, Tamil Nadu, India (hereafter "**NBA**"), acting through and represented by the Secretary, NBA/authorized signatory of NBA, being the person authorised to execute this Agreement.

AND

M/s Inventprise, LLC, registered/incorporated in USA having its registered office at 18133 NE 68th St d150, Redmond, Washington 226, USA, (hereafter the "**Applicant**"), acting through and represented by The Director, Inventprise, LLC being the person authorised to execute this Agreement on behalf of the Applicant as specified in Annex C.

*Hereafter, referred to as the "Parties" and individually as a "Party".*

**WHEREAS** the NBA is the authority established under the Biological Diversity Act, 2002 (hereafter "**the Act**") authorised to grant approval for the purpose set forth herein and to determine terms and conditions to secure fair and equitable sharing of benefits arising out of the use of biological resources, knowledge and practices associated with their use;

**WHEREAS** the Applicant has submitted an application in Form III (Appl.no. 4228 dated 11.09.2020) under the Biological Diversity Rules, 2004 (hereafter the "**Rules, 2004**") to seek prior approval from NBA;

**WHEREAS** under the Rules and the guidelines on access to biological resources and/or associated knowledge and benefit sharing regulations, 2014 made under the Act, the approval shall be in the form of a written agreement duly executed between the Parties (hereafter the "**Agreement**");

**AND** the Parties have entered into this Agreement for access and benefit sharing according to the terms and conditions set out below.

**NOW the Parties agree as follows:**

1. **Definition:** For the purpose of this Agreement, the expression "***Effective Date***" shall mean the date on which both the parties sign this Agreement. In case the parties sign on different dates, the effective date shall be the date signed by NBA;

2. **Terms and Conditions of the Agreement**

**2.1 Grant of approval**

The NBA hereby grants approval for filing applications for obtaining Intellectual Property Right ("**IPR**") over the invention as described in **Annex B, *only*** in the countries mentioned in **Annex D** subject to such other terms and conditions set forth in this Agreement.

**2.2 Scope and extent**

The approval is limited to the extent and for the purpose for which it is accorded under the appropriate Annexures.

**2.3 Period**

**2.3.1** ***Period of Agreement*** –This Agreement shall remain in force from the effective date of this Agreement till the subsistence of the IPR for which approval was granted.

**2.3.2** Notwithstanding the above, this Agreement shall remain in force until the applicant fulfils all the obligations as required under this Agreement.

**2.4 Transfer to third party or by operation of law**

In the event that the IPR of the Applicant is transferred by way of an assignment, licensing or by operation of law (including in cases of death or bankruptcy or dissolution of a company), all rights and obligations under this Agreement shall be binding upon the assignee or licensee or legal representative or the person to whom the IPR devolves as the case may be.

In the case of above eventuality, the legal representative or the assignee or licensee or the person to whom the IPR has devolved shall intimate and submit such relevant documents to NBA within **sixty days** of the happening of such event. Upon receiving such intimation, NBA may amend the agreement under clause 13 of this Agreement so as to ensure fair and equitable benefit sharing.

3. **Obligations of the Applicant**

3.1. The Applicant shall share benefits as stipulated under Schedule A.

3.2 The permission granted to the Applicant is limited to that granted by the NBA in Annex-B of Schedule B of this Agreement. All other activities of the Applicant, which require NBA's prior approval, will need to be applied separately in the concerned Form under Rules, 2004. Further, the Applicant shall intimate to the NBA in the event of seeking IPR in other territories and thereafter the Agreement's annex will be suitably amended.

3.3 The Applicant shall abide by all the terms and conditions of the Agreement and other related legislations in force including any clearances required from the concerned authorities, such as the Chief Wildlife Warden in protected areas and forest authorities in other forest areas.

3.4 The Applicant shall, in the event of any material changes in the management or the shareholding of the Applicant that alters the control structure of the Applicant including changes brought by a transfer of business units, acquisition, merger, demerger or any other kind of corporate restructuring, intimate and submit all related documents to NBA within **90 days** from the completion of that event. Subsequent to the said intimation, NBA shall decide whether this Agreement shall be amended as per clause 13 or a fresh approval is required. NBA's decision in this regard shall be final.

3.5 The Applicant shall have India as its first source of supply and/or cultivation of biological resources for the commercialization of IPR as the case may be.

3.6 The Applicant shall in the event of any breach of this Agreement pay such compensation commensurate with the damage incurred to the Republic of India or to the benefit claimers as decided by the appropriate forum.

3.7 The Applicant shall keep all the relevant records that serve as a proof of the monetary benefits shared by the Applicant with NBA or the concerned benefit claimers as the case may be, together with supporting documents. This may be submitted to NBA as specified from time to time and such records shall be retained for at least three (3) years after the termination of this Agreement.

3.8 NBA shall have the right to regulate /monitor the activities approved under this Agreement, by itself or through any appropriate agency as it may deem fit.

3.9 Whenever the Applicant requires to access biological resources for commercial utilization of the IPR for which approval is granted under this Agreement, the Applicant shall take prior approval of NBA under Form I of the Rules, 2004 or the respective form of the concerned State biodiversity rules.

3.10 The Applicant shall notify in writing to the NBA about the grant of IPR and the assignment or licensing of such IPR, if any, in each of the countries/territories as specified in Annex D, within **60 days** from the date of grant of the said IPR.

3.11 The Applicant shall, in case of any modification or improvement or commercialization of the invention/ product/process of the IPR, intimate to NBA within **45 days** of the happening of such event. Based on such intimation, NBA may decide to review the earlier approval and its decision shall be final.

3.12 The Applicant, in the event of decision to withdraw or abandon the patent application, shall intimate to NBA within 45 days of the happening of such event.

3.13 *Status Reports*

**3.13.1** The Applicant shall submit a status report for each reporting year not later than two months of the end of each reporting year in the prescribed format of NBA.

**3.13.2** During the subsistence of this Agreement, the Applicant shall submit separate status reports in relation to each of the countries/territories mentioned in Annex D for each reporting year in the prescribed format of NBA. This shall be submitted not later two months of the end of each reporting year.

**3.13.3** Non-submission of the status reports within the stipulated time period in relation to any of the countries/territories mentioned in Annex D will be construed as a breach for which penalty may be imposed by NBA under clause 6 of this Agreement.

**3.13.4** The Applicant shall submit a copy of Form 27 of the Indian Patent Rules, 2015 within one month of submitting the same to the Patent Office.

**4. Fair and Equitable Benefit Sharing**

**4.1** The Applicant shall share benefits as per Schedule A in monetary mode.

**4.2** The Applicant shall make the payment preferably by way of demand draft or any other approved mode of payment and the same shall be drawn in the name of "**National Biodiversity Fund**".

**5. Written Notice**

**5.1** Any communication including serving notices under this Agreement, shall be in writing and communicated by Registered post with acknowledgement due or e-mail or fax in the address mentioned hereunder.

**If to NBA**:

The Secretary, NBA, 5th Floor, TICEL Bio Park, Taramani, Chennai-600 113, Tamil Nadu, India. secretary@nba.nic.in

**If to the Applicant**

M/s Inventprise, LLC, 18133 NE 68th St d150, Redmond, Washington 226, USA. Email: info@ventprise.com

**Copy to Attorney**

Mr. Praneet Singh Davar, Patent Attorney, P.S.Davar & Co N-220, N-Block Greater Kailash-1. New Delhi 110 048. Email: psdavar@psdavar.com

5.2 Notice is deemed to have been given if duly communicated in accordance with the Indian Contract Act, 1872 and the Information Technology Act, 2000 and related Indian legislations.

5.3 Any change in the address/email address/fax of the Parties shall be notified to the other Party within **15 days** of such change by way of a notice.

**6. Procedure for imposing penalty in case of breach.**

6.1 If NBA has prima facie evidence to the effect that the Applicant has committed a breach of any of the terms of this Agreement, NBA shall send a written notice to the Applicant communicating the default or details of the breach within **30 days** of the discovery of that event, giving an opportunity to be heard to the Applicant.

6.2 The Applicant shall within **30 days** from the date of serving of such notice respond in writing to NBA.

6.3 Upon receiving such explanation from the Applicant, NBA shall take into account the explanation and decide if there is a breach committed by Applicant or not. In the event that the NBA does not receive such explanation from the Applicant, NBA shall send final notice to the Applicant. If the Applicant responds within 30 days, NBA shall be taken into account the explanation and decide on the breach. If the Applicant does not respond within 30 days, the Applicant will be deemed to be in breach of this Agreement.

6.4 In the event that the Applicant does not respond to the final opportunity given by NBA or in the event that NBA decides that there is a breach of this Agreement, NBA has the power to issue any order executable under section 53 of the Act including imposition of penalty of a sum which may extend to one lakh rupees as determined by NBA from time to time and in addition direct the Applicant to pay such compensation commensurate with the damage incurred by the Republic of India or the benefit claimers.

6.5 Penalties imposed by NBA under this clause shall be in addition to any recovery of any monetary benefits due, compliance with directions or orders issued by NBA and without prejudice to any other rights under this Agreement.

6.6 Notwithstanding any of the clauses above, in addition to imposition of penalty, if the breach or default committed by the Applicant amounts to violation of any of the provisions of the Act, appropriate legal proceedings shall be initiated under Section 61 of the Act.

**7. Termination and Revocation**

7.1 Subject to clause 2.3, the Agreement shall stand automatically terminated on the completion of the period agreed to between the Parties including the period of

extension agreed to, if any. On termination, the Applicant shall comply with obligation under clause 7.3.

**7.2** During the subsistence of this Agreement, the Applicant shall have an option to initiate termination of this Agreement by sending a request to NBA in the form of a notice stating valid reasons for the same. On receipt of the same, it shall be the discretion of NBA to accept the reasons specified by the Applicant or not. In the event of its decision to terminate, NBA shall intimate to the applicant by way of a notice within **90 days** of making the decision. On receipt of such a notice from NBA, the applicant shall comply with clause 8.3.

**7.3** Upon termination of the Agreement, the Applicant shall pay all outstanding dues including the benefit sharing amount and submit status report dues, if any, due until then by the Applicant within 45 days of the date of termination of this Agreement.

**7.4** NBA may withdraw the approval granted and revoke this Agreement in case of occurrence of any of the conditions mentioned in Rule 15 of the Rules, 2004 or if the applicant performs activities contrary to any restriction or prohibition imposed by NBA or under the Act and Rules, 2004.

## 8. Liabilities and Indemnification

**8.1** NBA shall not be liable for any loss or damage whatsoever caused to the Applicant due to revocation of approval for access and/or termination of this Agreement on any grounds whatsoever.

**8.2** The Applicant shall be solely responsible for any claims by third parties arising from the Applicant's acts or omissions in the course of performing this Agreement and under no circumstances shall the NBA be held responsible or liable for any claims by such third parties.

**8.3** The Applicant shall pay such sum for breach committed by the Applicant as determined by NBA under clause 6 of this Agreement which is in addition to the compensation commensurate with the damage incurred by the Republic of India or the benefit claimers that the Applicant is liable to pay as decided by the appropriate forum.

**8.4** The Applicant shall indemnify and save NBA and its employees, members and officers, from and against all claims, demands, losses, damages, costs (including attorney fees), actions, suits or other proceedings, all in any manner based upon, arising out of, related to, occasioned by or attributable to, any acts or conduct of the Applicant, its employees or agents, (whether by reason of negligence or otherwise) in the performance by or on behalf of the Applicant of the provisions of this Agreement or any activity undertaken or purported to be undertaken under the authority or pursuant to the terms of this Agreement.

## 9. Confidentiality

9.1 Upon request from the Applicant, NBA shall keep as confidential that information which is desired to be kept as confidential by the Applicant.

9.2 Notwithstanding the above, confidential information may be disclosed by NBA to the extent required by any law or regulation or order of any authority established by law having jurisdiction over any of the Parties or in the opinion of NBA such disclosure becomes necessary to deal with any emergency situations, or national or public interest .

**10. Arbitration**

**10.1** In case any dispute or difference arises out of the interpretation of any clauses of the Agreement, either of the Parties may give the other Party a notice clearly identifying and providing details of the dispute. On receipt of such notice by the other Party, the Parties shall try to settle such dispute/difference amicably between them by negotiating in good faith within **30 days** of the receipt of such notice.

**10.2** If the dispute or difference is not resolved by such negotiations within the period mentioned, the dispute or difference shall be referred to the sole arbitrator appointed by NBA.

**10.3** The arbitration shall be governed by the Arbitration and Conciliation Act, 1996 and the rules framed thereunder. The place of arbitration shall be Chennai, India.

**10.4** The award of the Arbitrator shall be final, conclusive and binding on the Parties. The Arbitrator shall be competent to decide whether any matter or dispute or difference referred to him falls within the purview of arbitration.

**11. Governing Law and Jurisdiction**

**11.1** This Agreement is governed by and is to be construed in accordance with the laws of India without regard to the principles of conflicts of laws subject to the provisions of arbitration clauses to this Agreement.

**11.2** In the event of a dispute or difference not settled through arbitration as specified in clause 11, the Parties shall irrevocably and unconditionally submit to the appropriate court of jurisdiction in Chennai.

**11.3** As regards all other aspects and the terms and conditions not provided for this in this Agreement, they shall be governed by the provisions of the Act read with Rules and Regulations made thereunder.

**11.4** This Agreement shall not in any way constitute or be presumed to constitute a partnership or a joint venture or a joint enterprise in any way or for any purpose between the Parties hereto or make the parties in any way liable as partners of or as agents for one another.

**12. Severability**

**12.1** If any part of this Agreement is declared or held improper or unjustifiable or invalid by a Court of Law for any reason, the deficiency or invalidity of that part shall not affect the validity of the remainder which will continue in full force and effect and be construed as if the Agreement had been executed without the invalid portion.

**12.2** However, the remainder of the Agreement shall not come into force unless the remainder is consistent with the declaration or order or judgment of the Court.

**13. Amendment**

No amendment to this Agreement shall be valid or binding upon the Parties, unless agreed upon by the Parties, in writing, and signed on behalf of each Party by their duly and legally authorized persons and such amendment shall be made as a supplementary agreement along with Annexes, as applicable.

**14. Entirety of Agreement:** This Agreement constitutes the culmination of all prior negotiations, understanding, representations and commitments and sets down the complete terms and conditions of Agreement between the parties as to the subject matter.

**15. Annex and Schedules**

a. The Schedules and their Annexes attached to this Agreement or Schedule that may be added subsequently by way of an amendment under the provisions of this Agreement shall form an integral part of this Agreement and shall be binding on the Parties.

b. This Agreement has been executed in duplicate, each of which shall be deemed to be original; one shall be retained by the NBA and other by the Applicant and both shall constitute one and the same instrument.

**IN WITNESS WHEREOF** the parties hereto have signed in this Agreement on the day month and the year aforesaid in this Agreement.

| | |
|---|---|
| ..... | ..... |
| (S/d with date) | (S/d with date) |
| Signed by the Authorized person of the Authority | Signed by the Applicants |
| **For National Biodiversity Authority** | **For the Applicant** |
| **Witnesses** | **Witnesses** |
| 1. Signature | 1. Signature |
| Name | Name |
| Address | Address |
| 2. Signature | 2. Signature |
| Name | Name |
| Address | Address |

**NBA application no. 4228**
**SCHEDULE A – BENEFIT SHARING COMPONENT**

(i) Where the applicant himself commercializes the process/product/innovation, the monetary benefit sharing shall be **1.0%** on the annual gross ex-factory sale minus government taxes.

(ii) Where the applicant assigns/licenses the process/product/ innovation to a third party for commercialization, the applicant shall pay to NBA **5.0%** of the fee received (in any form including license/ assignee fee) and **5.0%** of the royalty amount received annually from the assignee/ licensee.

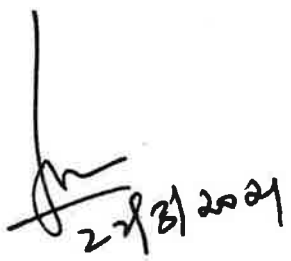
**SCHEDULE B – ANNEXES TO BE ATTACHED**

**ANNEX A** - Details of biological resources and/or knowledge associated thereto and geographical locations

**ANNEX B** - Title, Details of the invention and the patent application number in case patent has been filed

**ANNEX C** – Original Authorisation signed by the Applicant (*if any*) for signing the Agreement and/or filing IPR

**ANNEX D** - Name of the countries/territories where IPR over the invention is sought to be taken



**PERMIT OR ITS EQUIVALENT CONSTITUTING AN INTERNATIONALLY RECOGNIZED CERTIFICATE OF COMPLIANCE (IRCC)**

Internationally Recognised Certificate of Compliance (**IRCC**) is a globally recognised compliance certificate that serves as an evidence of the decision by the Parties to grant permit to the Applicant. The permit issued by the National Biodiversity Authority (*the competent national authority under the Nagoya Protocol*) will facilitate generation of IRCC and will be published online in the Access and Benefit Sharing Clearing House (ABSCH) (https://absch.cbd.int/)

By procuring an IRCC, the Applicant can globally demonstrate their legal compliance with the domestic Access and Benefit Sharing (ABS) legislation (in the present case with the Biological Diversity Act, 2002 and Rules, 2004). Applicant can also keep certain information confidential, as the IRCC document is publicly available. For this purpose, the Applicant shall fill in the following details as given in the table below:

| S.No | Particulars | Details about the nature of information (Please mention YES or NO in the box) |
|---|---|---|
| 1 | Name of the Applicant | *Do you require your name to be kept confidential?* ☐ |
| 2 | Subject matter of approval | *Do you require the biological resources/ knowledge for which the approval was given to be kept confidential?* ☐ |
| 3 | Keywords that describe the subject matter of approval | *Do you require the keywords that describes or indicates the biological resources/ knowledge for which the approval was given to be kept confidential?* ☐ |
| 4 | Type of activity to be undertaken using the subject matter of approval | *Do you require the activity (research/commercial utilisation/bio-survey and bio-utilisation/IPR/transfer of biological resources/knowledge) to be carried out using the approved biological resources/knowledge to be kept confidential?* ☐ |

**Applicants Signature**

*Disclaimer: Please note that the above format does not constitute an access permit in itself and only validates the permit.*

राष्ट्रीय जैव विविधता प्राधिकरण
NATIONAL BIODIVERSITY AUTHORITY
5th Floor, TICEL Bio Park, CSIR Road, Taramani, Chennai – 600 113, Tamil Nadu, India
५ फ्लोर टाइसल बायोपार्क,सीएसआईआर रोड, तारामनी, चेन्नै - ६०० ११३, तमिलनाडु, भारत

Phone : 044- 2254 2777
Fax : 044-2254 1200

Email : toipr@nba.nic.in
Website : www.nbaindia.org

-- F.no NBA/IPR/4228/20/22-23/252 *(Through email only)* Date 12/10/22

To,
Mr Praneet Singh Davar,
Patent Attorney,
P.S.Davar & Co,
N-220, N-Block Greater Kailash-1,
New Delhi -110 048.
Email- psdavar@psdavar.com

Sir,

Sub: Non- receipt of executed agreement based on your application No. 4228.

Ref: Our Communication dated: 26.03.2021, 29.04.2021.
Your Communication dated: 26.04.2021.

This has reference to this office email dated 26.03.2021 and 26.04.2021. wherein you are requested to send two copies of Stamp paper agreements (Indian Patent No 201917035818,) On perusal of your application foreign filings were found (details enclosed). without statutory prior approval from NBA. Till date this office had not received the agreements.

In this regard, you are requested to submit two copies of the original Stamp Paper Agreements duly signed with seal within 15 days from the date of receipt of this communication for further process failing which, further necessary action shall be initiated as per the provisions of the BD Act, 2002 without further communication to you.

Kindly acknowledge the receipt of this communication.

Regards,
12/10/2022
Dr. M. Sundar Rajan,
Consultant- Legal Affairs, NBA.

Enclosed details of foreign patent filing

12/10/22
प्रेषक / Despatcher
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
5वां तल, टायसल बायोपार्क
5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तरमणि, चेन्नई / Taramani, Chennai - 600 113.

**FORM-3**
**THE PATENTS ACT, 1970**
**(39 of 1970)**
**&**
**The Patents Rules, 2003**
**STATEMENT AND UNDERTAKING UNDER SECTION 8**
**[See section 8, rule 12]**

We, **INVENTPRISE, LLC**, an American Company, of **18133 NE 68th St., d150 Redmond, Washington 98052, USA**, hereby declare:

(i) that we who have made this application No. **201917035818** dated **05.09.2019** have made for the same/substantially same invention, application for patent in the other countries, the particulars of which are given below:

Application Number **201917035818** Dated **05.09.2019**

| Name of the country | Date of Application | Application No. | Status of the Application | Publication No. | Date of Publication | Patent No. | Date of grant |
|---|---|---|---|---|---|---|---|
| PCT | 14.02.2018 | PCT/US2018/18226 | PUBLISHED | WO/2018/152237 | 23.08.2018 | | |
| United States of America | 14.02.2017 | 62/458,904 | Expired | | | | |
| United States of America | 14.02.2018 | 15/896,939 | GRANTED | 20180228889 | 16.08.2018 | 10,413,604 | 17.09.2019 |
| United States of America | 16.09.2019 | 16/571,702 | PENDING | 20200009242 | 09.01.2020 | | |
| China | 14.10.2019 | 201880024988.1 | | | | | |
| Indonesia | 11.09.2019 | PID 201907114 | | | | | |
| Korea | 05.09.2019 | 10-2019-0111117 | | | | | |
| Malaysia | 07.08.2019 | PI 2019004553 | | | | | |
| Philippines | 09.08.2019 | 1-2019-501856 | | | | | |

ii) that the rights in the application(s) has/have been assigned to NIL.

iii) that we undertake that up to the date of grant of the patent by the Controller, we would keep him informed in writing the details regarding corresponding applications for patents filed outside India within six months from the date of filing of such application.

Dated this 5th day of June, 2021

(Praneet Singh Davar)
(Patent Agent No. IN/PA-311)
Of P. S. Davar and Company
Applicant's Agent

To,
The Controller of Patents,
The Patent Office

RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>

# Non- receipt of executed agreement based on your application No. 4228.

**NBA_IPR SECTION** <iprsection@nbaindia.org> Mon, Oct 17, 2022 at 1:15 PM
To: psdavar@psdavar.com
Cc: RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>, Sundar Rajan <sundar@nbaindia.org>, Vimal <absdesk2@nbaindia.in>

**F.no NBA/IPR/4228/20/22-23** (***Through email only***) **Date 17/10/2022**

To,
Mr Praneet Singh Davar,
Patent Attorney,
P.S.Davar & Co,
N-220, N-Block Greater Kailash-1,
New Delhi -110 048.
Email- psdavar@psdavar.com

Sir,

Sub: Non- receipt of executed agreement based on your application No. 4228.

Ref: Our Communication dated: 26.03.2021, 29.04.2021.
Your Communication dated: 26.04.2021.

This has reference to this office email dated 26.03.2021 and 26.04.2021. wherein you are requested to send two copies of Stamp paper agreements (Indian Patent No 201917035818,) On perusal of your application foreign filings were found (details enclosed). without statutory prior approval from NBA. Till date this office had not received the agreements.

In this regard, you are requested to submit two copies of the original Stamp Paper Agreements duly signed with seal within 15 days from the date of receipt of this communication for further process failing which, further necessary action shall be initiated as per the provisions of the BD Act, 2002 without further communication to you.

**IPR Section**
**National Biodiversity Authority,**
**Government of India,**
**5th Floor, TICEL Bio Park,**
**Taramani, Chennai-600 113.**
**Tel+91-44-2254 1075/2254 2777**

**2 attachments**

**4228 letter to applicant.pdf**
211K

**4228 Foreign filings.pdf**
403K

(9)

NBA

RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>

# Non- receipt of executed agreement based on your application No. 4228.

**sb@psdavar.co.in** <sb@psdavar.co.in> Sat, Nov 5, 2022 at 11:45 AM
To: iprsection@nbaindia.org
Cc: rajivgandhi@nbaindia.org, sundar@nbaindia.org, absdesk2@nbaindia.in, psdavar@psdavar.co.in

Dear Sir,

Kindly refer to our mail below.

We may here advise that our clients are not interested in proceeding further in the matter and wishes to abandon the instant application.

Therefore, please treat the instant application as abandoned.

Best regards,

Dr. Sudipta Banerjee

P.S. Davar and Company

Patent & Trademark Attorneys

Founding Partner P.S. Davar

---

Office Address: Delhi: N -220, Greater Kailash – 1, New Delhi 110048, India

Kolkata: DD-30, Andromeda, 5th Floor, Salt Lake Sector-1, Kolkata, India

Tel: +91 11 41065143, 41053715, 29241034

Fax: +91 11 43601991

Website: https://psdavar.com/



[Quoted text hidden]

**2 attachments**

**4228 letter to applicant.pdf**
211K

**4228 Foreign filings.pdf**
403K

10


राष्ट्रीय जैव विविधता प्राधिकरण
NATIONAL BIODIVERSITY AUTHORITY
5th Floor, TICEL Bio Park, CSIR Road, Taramani, Chennai – 600 113. Tamil Nadu. India
५ फ्लोर टाईसल बायोपार्क,सीएसआईआर रोड, तारामनी, चेन्नै - ६०० ११३. तमिलनाडु, भारत

Phone : 044- 2254 2777
Fax : 044-2254 1200

Email : toipr@nba.nic.in
Website : www.nbaindia.org


**F.no NBA/IPR Appl/4228/20/20-21/2933** ***(Through email only)*** **Date: 9 / 11/2022.**

To,
Mr. Praneet Singh Davar,
Patent Attorney,
P.S Davar & Co,
N-220, N- Block Greater Kailash-1,
New Delhi- 110 048.
Email- info@inventprise.com, psdavar@psdavar.com sb@psdavar.co.in,

Sir/ Madam,

**Sub:** Non receipt of executed agreement based on your application No 4228.

**Ref:** (i) Our Communications dated 17.10.2022.
(ii) Your Email Dated 05.11.2022.

This has reference to your application filed in Form – III (No.4228) submitted on 20.06.2020 for seeking approval of NBA for obtaining IPR on your invention (Indian Patent No 201917035818).

We received an email communication dated 05.11.2022 stating that you are not interested in pursuing the Form – III application further. On verification of your patent application foreign filings found (details enclosed) without statutory prior approval from NBA. Hence, your application in Form – III cannot be closed.

In this regard, you are requested to submit two copies of the original Stamp Paper Agreements duly signed with seal within 15 days from the date of receipt of this communication for further process failing which, further necessary action shall be initiated as per the provisions of the BD Act, 2002 without further communication to you. Kindly acknowledge receipt.

09/11/2022

Dr. M. Sundar Rajan,
Consultant- Legal Affairs, NBA.

Enclosed details of foreign patent filing

प्रेषक / Despatcher
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
5वां तल, टायसल बायोपार्क
5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तारामनी, चेन्नै / Taramani, Chennai - 600 113.

RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>

# Non receipt of executed agreement based on your application No 4228.

**NBA_IPR SECTION** <iprsection@nbaindia.org> Wed, Nov 9, 2022 at 5:15 PM
To: info@inventprise.com, psdavar@psdavar.com, sb@psdavar.co.in
Cc: RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>, Sundar Rajan <sundar@nbaindia.org>, Vimal <absdesk2@nbaindia.in>

**F.no NBA/IPR Appl/4228/20/20-21** **(*Through email only*)** **Date: 09/11/2022.**

To,
Mr. Praneet Singh Davar,
Patent Attorney,
P.S Davar & Co,
N-220, N- Block Greater Kailash-1,
New Delhi- 110 048.
Email- info@inventprise.com, psdavar@psdavar.com sb@psdavar.co.in,

Sir/ Madam,

**Sub:** Non receipt of executed agreement based on your application No 4228.

**Ref:** (i) Our Communications dated 17.10.2022.
(ii) Your Email Dated 05.11.2022.

This has reference to your application filed in Form – III (No.4228) submitted on 20.06.2020 for seeking approval of NBA for obtaining IPR on your invention (Indian Patent No 201917035818).

We received an email communication dated 05.11.2022 stating that you are not interested in pursuing the Form – III application further. On verification of your patent application foreign filings found (details enclosed) without statutory prior approval from NBA. Hence, your application in Form – III cannot be closed.

In this regard, you are requested to submit two copies of the original Stamp Paper Agreements duly signed with seal within 15 days from the date of receipt of this communication for further process failing which, further necessary action shall be initiated as per the provisions of the BD Act, 2002 without further communication to you. Kindly acknowledge receipt.

Enclosed details of foreign patent filing.

**IPR Section**
**National Biodiversity Authority,**
**Government of India,**
**5th Floor, TICEL Bio Park,**
**Taramani, Chennai-600 113.**
**Tel+91-44-2254 1075/2254 2777**

**3 attachments**

**4228 letter to applicant.pdf**
220K

**4228 Foreign filings..pdf**
78K

**4228 Foreign filings details.pdf**
88K

(11)

NBA

RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>

# Non receipt of executed agreement based on your application No 4228.

**sb@psdavar.co.in** <sb@psdavar.co.in> Thu, Nov 17, 2022 at 3:42 PM
To: NBA_IPR SECTION <iprsection@nbaindia.org>, info@inventprise.com, psdavar@psdavar.com
Cc: RAJIVGANDHI MUNUSAMY <rajivgandhi@nbaindia.org>, Sundar Rajan <sundar@nbaindia.org>, Vimal <absdesk2@nbaindia.in>

Dear Sir,

This has reference to your mail dated 09.11.2022.

We would like to inform you that we have already referred the matter to our clients for seeking their instructions.

In the meanwhile, we humbly request you to give us some more time to procure their instructions, as they are based in a foreign jurisdiction.

Please do not pass any adverse order without giving us an opportunity to be heard in the matter.

Best regards,

Dr. Sudipta Banerjee

P.S. Davar and Company

Patent & Trademark Attorneys

Founding Partner P.S. Davar

Office Address: Delhi: N -220, Greater Kailash – 1, New Delhi 110048, India

Kolkata: DD-30, Andromeda, 5th Floor, Salt Lake Sector-1, Kolkata, India

Tel: +91 11 41065143, 41053715, 29241034

Fax: +91 11 43601991

Website: https://psdavar.com/

[Quoted text hidden]

12

राष्ट्रीय जैव विविधता प्राधिकरण
NATIONAL BIODIVERSITY AUTHORITY
5th Floor, TICEL Bio Park, CSIR Road, Taramani, Chennai – 600 113, Tamil Nadu, India
५ फ्लोर टाईसल बायोपार्क,सीएसआईआर रोड, तारामनी, चेन्नै – ६०० ११३, तमिलनाडु, भारत

Phone : 044- 2254 2777
Fax : 044-2254 1200

Email : toipr@nba.nic.in
Website : www.nbaindia.org

F.no NBA/IPR Appl/4228/20/22-23 /4266 *(Through email only)* Date: 22/07/2023.

**Final reminder**

To,
Mr. Praneet Singh Davar,
Patent Attorney,
P.S Davar & Co,
N-220, N- Block Greater Kailash-1,
New Delhi- 110 048.
Email- info@inventprise.com, psdavar@psdavar.com sb@psdavar.co.in,

Sir/ Madam,

**Sub:** Non receipt of executed agreement based on your application No 4228.

**Ref:** (i) Our Communications dated 07.07.2021, 17.10.2022 05.11.2022 and 09.11.2022.
(ii) Your Email Dated 05.11.2022 and 17.11. 2022.

This has reference to this office email dated 02.07.2021 wherein you are requested to submit two copies of original stamp paper agreements for the Indian Patent No 201917035818. The same was reminded on 17.10.2022, 05.11.2022 and 09.11.2022. Vide email dated 17.11.2022 wherein you were requested some time to submitting stamp paper agreements. Despite giving sufficient time till date this office has not received the stamp paper agreements.

In this regard, you are requested to submit two copies of the original Stamp Paper Agreements duly signed with seal within 15 days from the date of receipt of this communication for further process failing which, further necessary action shall be initiated as per the provisions of the BD Act, 2002 without further communication to you. Kindly acknowledge receipt.

O/L

22/7/23

Dr. M. Sundar Rajan,
Consultant- Legal Affairs, NBA.

8/24/23

प्रेषक / Despatcher
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
5वां तल, टायसल बायोपार्क
5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तरमणि, चेन्नई / Taramani, Chennai - 600 113.

(13)

**Email** **Rajiv Gandhi M**

**Non receipt of executed agreement based on your application No 4228.**

**From :** sb@psdavar.co.in Sat, Feb 25, 2023 12:40 PM

**Subject :** Non receipt of executed agreement based on your application No 4228. 1 attachment

**To :** iprsection@nbaindia.org

**Cc :** Rajiv Gandhi M <techbs7-nba@govcontractor.in>, Dr Sundarajan <legal1-nba@nic.in>, psdavar@psdavar.co.in, psdavar1@psdavar.co.in

Dated: 25.02.2023

**To,**
**The National Biodiversity Authority**
**5th Floor, TICEL Bio Oark, CSIR Road,**
**Taramani, Chennai 600113**
**Tamil Nadu**

**Reg**:

1. Your letter, dated 22.02.2023, vide reference no., NBA/IPR Apl/4228/20/22-23/4266.
2. Application no. 4228 in the name of Inventprise Inc. (formerly, Inventprise LLC.) (hereinafter referred to as "the Applicant")

**Kind Attention**: Dr. M. Sundar Rajan, Consultant, Legal Affairs, NBA.

Dear Sir,

We write with reference to the captioned matter and further to our various correspondences addressed to your good offices in this regard.

At the outset, we would like to bring to your attention, our correspondence of 17.11.2022. We may advise that we did not seek time to submit stamp paper agreements to you. In fact we had informed you that we require some time to seek instructions from our client who is based in a foreign jurisdiction.

We once again submit that Indian Patent Application No. **201917035818**, dated **05.09.2019**, titled, "**Heat Stable Liquid Rotavirus Vaccine**", in the name of, **Inventprise Inc.**, does not fall within the purview of the Biological Diversity Act, 2000.

In this respect, once again reliance is placed on *inter alia*, our written submissions dated 23.04.2021.

Thus, it is humbly requested that an No Objection Certificate be granted to the Applicant qua application no. 4228. Alternatively, a Hearing may kindly be granted in the matter before any order is passed in this respect.

Further, we would like to bring to your notice that this matter is now the subject matter of proceedings pending with the National Green Tribunal, Chennai. Thus, as the same is subjudice, any action that you may take in this regard shall be unilateral and not binding upon the Applicant.

Thus, in view of the aforesaid facts and circumstances, we once again request that no final order be passed in the matter.

Sincerely,
Dr. Sudipta Banerjee

P.S. Davar and Company
Patent & Trademark Attorneys
Founding Partner P.S. Davar

Office Address: Delhi: N -220, Greater Kailash – 1, New Delhi 110048, India
Kolkata: DD-30, Andromeda, 5th Floor, Salt Lake Sector-1, Kolkata, India
Tel: +91 11 41065143, 41053715, 29241034
Fax: +91 11 43601991

Website: https://psdavar.com/



**From:** NBA_IPR SECTION <iprsection@nbaindia.org>
**Sent:** Friday, February 24, 2023 5:17 PM
**To:** info@inventprise.com; psdavar@psdavar.com; sb@psdavar.co.in
**Cc:** techbs7-nba@govcontractor.in; Dr Sundarajan <legal1-nba@nic.in>
**Subject:** Non receipt of executed agreement based on your application No 4228.

**F.no NBA/IPR Appl/4228/20/22-23** **(*Through email only*)** **Date: 23/02/2023.**

(14)


राष्ट्रीय जैव विविधता प्राधिकरण
**NATIONAL BIODIVERSITY AUTHORITY**
5th Floor, TICEL Bio Park, CSIR Road, Taramani, Chennai – 600 113, Tamil Nadu, India
५ फ्लोर टाइसल बायोपार्क,सीएसआईआर रोड, तारामनी, चैन्नै – ६०० ११३, तमिलनाडु, भारत

Phone : 044- 2254 2777
Fax : 044-2254 1200

Email : toipr@nba.nic.in
Website : www.nbaindia.org


**F.no NBA/IPR Appl/4228/20/22-23/4343** ***(Through email only)*** **Date:02/03/2023.**

To,
Mr. Praneet Singh Davar,
Patent Attorney,
P.S Davar & Co,
N-220, N- Block Greater Kailash-1,
New Delhi- 110 048.
Email- info@inventprise.com, psdavar@psdavar.com sb@psdavar.co.in,

Sir/ Madam,

**Sub:** Non receipt of executed agreement based on your application No 4228.

**Ref:** (i) Our Communications dated 02.07.2021, 17.10.2022, 09.11.2022 and 24.02.2023.
(ii) Your Email Dated 26.04.2021, 05.11.2022, 17.11. 2022 and.25.02.2023.

This has reference to your email dated 25.02.2023 wherein you had stated that the invention 'Heat Stable liquid rotavirus vaccine' (Indian Patent No **201917035818**) does not fall within the purview of the Biological Diversity Act 2002, and the subject matter is pending with the National Green Tribunal, Chennai. Please be informed that we had sent a communication dated 02.07.2021 that your invention requires prior approval from NBA. Thereafter, reminders were sent on 17.10.2022, 09.11.2022 and 24.02.2023 to execute the agreement. Further, please furnish the exact details of the case pending before the NGT, Chennai to examine the applicability of the BD Act.

You are requested to submit the above mentioned details within 15 days from the date of receipt of this communication. Kindly acknowledge receipt.

o/c

Dr. M. Sundar Rajan,
Consultant- Legal Affairs, NBA

Enclosure: NBA letter dated 02.07.2021.

प्रेषक / Sender
राष्ट्रीय जैव विविधता प्राधिकरण
National Biodiversity Authority
5वा तल, तयमल बायोपार्क
5th Floor, TICEL Biopark
सीएसआईआर रोड / CSIR Road,
तरमणि, चेन्नई / Taramani, Chennai - 600 113.

(19)

**Email** **Rajiv Gandhi M**

**Non receipt of executed agreement based on your application No 4228.**

**From :** iprsection@nbaindia.org Mon, Mar 06, 2023 10:19 AM

**Subject :** Non receipt of executed agreement based on your application No 4228. 2 attachments

**To :** info@inventprise.com, psdavar@psdavar.com, sb@psdavar.co.in

**Cc :** Vimal Raj T <techbs9-nba@govcontractor.in>, Dr Sundarajan <legal1-nba@nic.in>, Rajiv Gandhi M <techbs7-nba@govcontractor.in>

**F.no NBA/IPR Appl/4228/20/22-23** **(*Through email and Post*)** **Date: 06/03/2023.**

To,
Mr. Praneet Singh Davar,
Patent Attorney,
P.S Davar & Co,
N-220, N- Block Greater Kailash-1,
New Delhi- 110 048.
Email- info@inventprise.com, psdavar@psdavar.com sb@psdavar.co.in,

Sir/ Madam,

**Sub:** Non receipt of executed agreement based on your application No 4228.
**Ref:** (i) Our Communications dated 02.07.2021, 17.10.2022, 09.11.2022 and 24.02.2023.
(ii) Your Email Dated 26.04.2021, 05.11.2022, 17.11.2022 and 25.02.2023.

This has reference to your email dated 25.02.2023 wherein you had stated that the invention 'Heat Stable liquid rotavirus vaccine' (Indian Patent No **201917035818**) does not fall within the purview of the Biological Diversity Act 2002, and the subject matter is pending with the National Green Tribunal, Chennai. Please be informed that we had sent a communication dated 02.07.2021 that your invention requires prior approval from NBA. Thereafter, reminders were sent on 17.10.2022, 09.11.2022 and 24.02.2023 to execute the agreement. Further, please furnish the exact details of the case pending before the NGT, Chennai to examine the applicability of the BD Act.

You are requested to submit the above mentioned details within 15 days from the date of receipt of this communication. Kindly acknowledge receipt.

Enclosure: NBA letter dated 02.07.2021.

--
**IPR Section**
**National Biodiversity Authority,**
**Government of India,**
**5th Floor, TICEL Bio Park,**
**Taramani, Chennai-600 113.**
**Tel+91-44-2254 1075/2254 2777**

NBA_IPR SECTION <iprsection@nbaindia.org>

# Non receipt of executed agreement based on your application No 4228.

**sb@psdavar.co.in** <sb@psdavar.co.in> Tue, Mar 21, 2023 at 4:48 PM
To: NBA_IPR SECTION <iprsection@nbaindia.org>
Cc: Vimal Raj T <techbs9-nba@govcontractor.in>, Dr Sundarajan <legal1-nba@nic.in>, techbs7-nba@govcontractor.in, psdavar@psdavar.co.in

-

**Kind Attention**: Dr. M. Sundar Rajan, Consultant, Legal Affairs, NBA.

Dear Sir,

We write with reference to the captioned matter and further to our various correspondences addressed to your good offices in this regard.

We once again submit that Indian Patent Application No. **201917035818**, dated **05.09.2019**, titled, **"Heat Stable Liquid Rotavirus Vaccine"**, in the name of, **Inventprise Inc.**, does not fall within the purview of the Biological Diversity Act, 2000 and thus, any action taken by you qua the subject patent application, is wholly without jurisdiction. In this respect, once again reliance is placed on *inter alia*, our written submissions dated 23.04.2021.

Thus, it is humbly requested that an No Objection Certificate be granted to the Applicant qua application no. 4228. Alternatively, a Hearing may kindly be granted in the matter before any order is passed in this respect.

Further, as advised vide our correspondence of 25.02.2023, this matter is now the subject matter of proceedings pending with the National Green Tribunal, Chennai (hereinafter referred to as "NGT". The matter, as filed with the NGT, is under objection / defects at the present moment. A copy of the final appeal, once defects have been duly addressed, shall be provided to you in due course. Thus, as the subject matter is subjudice, any action that you may take in this regard shall be unilateral and not binding upon the Applicant.

Thus, in view of the aforesaid facts and circumstances, we once again request that no final order be passed in the matter.

Best regards,

Dr. Sudipta Banerjee

P.S. Davar and Company

Patent & Trademark Attorneys

Founding Partner P.S. Davar

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## Application Details

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|---|---|
| APPLICATION NUMBER | 201917035818 |
| APPLICATION TYPE | PCT NATIONAL PHASE APPLICATION |
| DATE OF FILING | 05/09/2019 |
| APPLICANT NAME | **INVENTPRISE, INC.** |
| TITLE OF INVENTION | HEAT STABLE LIQUID ROTAVIRUS VACCINE |
| FIELD OF INVENTION | PHARMACEUTICALS |
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## Application Status

APPLICATION STATUS

# Granted Application, Patent Number :491743

E-Register | Order(s)/Decision(s) | View Documents

➡ Filed ➡ RQ Filed ➡ Published ➡ Under Examination

➡ Disposed

In case of any discrepancy in status, kindly contact ipo-helpdesk@nic.in