SOME INTELLECTUAL PROPERTY CLAIMS RELATED TO PATHOGENS THAT CAN CAUSE PUBLIC HEALTH EMERGENCIES[1]

Chetali Rao and Sangeeta Shashikant, Third World Network

1. INTRODUCTION

Throughout the COVID-19 pandemic, the mantra "No one is safe until everyone is safe" echoed persistently, with promises of equitable access made by leaders in the global north. However, as diagnostics, vaccines, and treatments emerged, the disparity became glaringly evident. Developed nations, comprising only 16% of the world's population, swiftly secured medical supplies, leaving developing countries, representing 84% of the global populace, grappling for affordable access. Meanwhile, entities, particularly the pharmaceutical industry, reaped substantial profits from intellectual property monopolies.

This inequity, though starkly highlighted by COVID-19, is not a new phenomenon during public health emergencies. Medical products developed from shared biological materials and genetic sequence data (GSD) typically remain beyond the reach of affected developing nations. Public and private entities in developed countries, often beneficiaries of significant public funds, make extensive patent claims linked to shared biological materials and GSD. These claims can curtail further research and development as well as local production in developing nations. Conversely, developed countries secure priority supply agreements with developers and manufacturers of essential products, ensuring their access to critical supplies during emergencies.

One of the most prominent and widely reported cases exemplifying this struggle occurred during the severe outbreak of avian influenza in 2007 when Southeast Asian nations grappled to secure timely access to vaccines. Despite these vaccines being developed using virus strains shared by these nations, they found themselves at a disadvantage amidst a global shortage. Commercial activities associated with shared viruses were underway, yet the benefits were reaped by only a select few, highlighting a stark division between developed and developing countries.[2] Pharmaceutical companies and numerous developed countries had already inked lucrative contracts for the supply of large vaccine quantities. Evidence also emerged of numerous patent applications, filed by both public and private entities in developed countries including WHO-designated laboratories over the shared virus samples and GSD.[3]

A similar pattern of inequitable access emerged as the H1N1 pandemic unfolded in 2009 with developing countries especially in Latin America bearing the brunt of the disparity. [4] This persistent

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[1] This paper is a working document and will be updated and edited before publication.

[2] Shashikant, S., "Winners and losers in the sharing of avian flu viruses", published by SUNS #6249 Thursday 10 May 2007, available at https://www.twn.my/title2/intellectual_property/info.service/twn.ipr.info.050705.htm

[3] Hammond, E.,"Some Intellectual Property Issues Related to H5N1 Influenza Viruses, Research and Vaccines", Intellectual Property Series 12, available at https://www.twn.my/title2/IPR/pdf/ipr12.pdf

[4] Chan, C.K., "Equitable Access to Pandemic Flu Vaccine", available at https://twn.my/title2/intellectual_property/info.service/2010/ipr.info.100311.htm; Shashikant, S., "Virus-Benefit

inequity eventually led to the adoption of a Pandemic Influenza Preparedness Framework (PIP Framework) that treated the sharing of influenza virus of pandemic potential (IVPP) on an equal footing with fair and equitable benefit sharing arising from the use of IVPP.

More recently, the MSF Access Campaign released a report titled "Ensuring Access to New Treatments for Ebola Virus Disease,"[5] shedding light on shocking inequities. On one hand, are the African nations affected by Ebola, which collaborated in developing treatments, and yet more than two years after their approval, access to the treatments remained elusive. On the other hand, the US government has secured an emergency stockpile of Ebola treatments, encompassing nearly all currently available options. Moreover, US-based entities maintain significant patent claims linked to shared Ebola material and GSD.

Equity considerations have now taken centre stage for developing countries within ongoing intergovernmental negotiations regarding a new pandemic instrument, as well as within the Working Group on the International Health Regulations (IHR), which is contemplating amendments to the IHR. In these discussions, intellectual property has emerged as a key point of contention between developed and developing nations, particularly in the context of the Pandemic Access and Benefit Sharing (PABS) system.

The Africa Group and the Group of Equity have emphasized in their comprehensive PABS proposal that intellectual property rights should not be sought or asserted over any shared biological material, including the GSD, *"or parts thereof, in any form, including any modified form or for any use"*.

This proposal of developing countries is not reflected in the design elements of a PABS system circulated on 14th February by the Chair/Facilitators of the sub-group on PABS.[6] Instead, it states *"[i]ntellectual property rights may not be sought on biological materials and GSD"* provided to the WHO coordinated laboratories or databases. This text reflects the suggestion contained in the European Union PABS proposal which does not allow IP claims over the biological materials and sequences in the form received but also states that "[s]amples or sequence data may otherwise be the subject of intellectual property rights, provided that the criteria relating to such rights are met".[7]

This paper aims to provide insights into the prevailing patenting trends surrounding pathogens that have the potential to instigate public health emergencies, including pandemics. Such trends can inform on the elements that are needed for an effective and accountable PABS system.

Sharing Working Group set up, pandemic flu response to be reviewed" available at https://twn.my/title2/intellectual_property/info.service/2010/ipr.info.100103.htm

[5] Available at https://www.msfaccess.org/ensuring-access-new-treatments-ebola-virus-disease

[6] "Attempts to side-line Africa and Equity Group proposal on the PABS System", Third World Network, available at https://www.twn.my/title2/health.info/2024/hi240205.htm

[7] Shashikant, S., "The European Union's ABS Proposal for the pandemic instrument: Backwards in International Solidarity & Excerbates Inequity" available at https://www.twn.my/title2/intellectual_property/info.service/2024/ip240101.htm

2. PATENT LANDSCAPE AND TRENDS IN PATENT CLAIMS RELATED TO PATHOGENS THAT CAN CAUSE PUBLIC HEALTH EMERGENCIES

2.1 METHODOLOGY

A very simple methodology has been used for this paper. To identify the patent landscape, searches were conducted on WIPO's PATENTSCOPE database using the following methodology:

a. Search using specific International Patent Classification (IPC) classes (where specific IPC classes are available for the virus family); or
b. Search using keyword; or
c. Search using keyword and specific IPC class.

The patent landscape search results for each viral disease is displayed below in Section 2.2. It depicts PCT applications by year (data collated from 2015 onwards), the category of patent claims, the main country of origin for the PCT applications and the leading patent applicants.

Section 2.3 of this paper contains summaries of selected patent applications. Its purpose is to provide an understanding of the diverse range of patent claims filed concerning pathogens and their corresponding GSD. To retrieve relevant patent applications, various searches were done, including by using specific keywords in the patent application text, sequence searches and forward-backward citations.

In Section 2.3, each entry showcases an international patent application number. These applications undergo processing per national patent laws. Upon granting, the patent holder is conferred exclusive rights for a period of 20 years from the filing date, over the approved patent claims. Given the territorial nature of patents—restricted to the jurisdiction where they are granted—the status of each application and nature of claims may vary across countries.

2.2 PATENT LANDSCAPE

Patent search based on the abovementioned methodology yielded a significant volume of patent applications covering a broad spectrum of patent claims including claims over native sequences and on parts or modified versions of the sequences to produce products like vaccines, antibodies or therapeutics. In addition, claims have been filed on vaccine compositions, antiviral drugs, antibodies and diagnostics kits. Further, many platform technologies like adjuvants, assembly systems also constitute a part of the pandemic preparedness and patent claims have also been filed on such platforms.

The patent applicants primarily hail from developed nations, with a notable presence from the United States (US) and the European Union (EU), representing a blend of public and private entities in addition to academic institutions. Significantly, the US government itself is prominently featured as an applicant for numerous patent applications.

A. EBOLA VIRUS

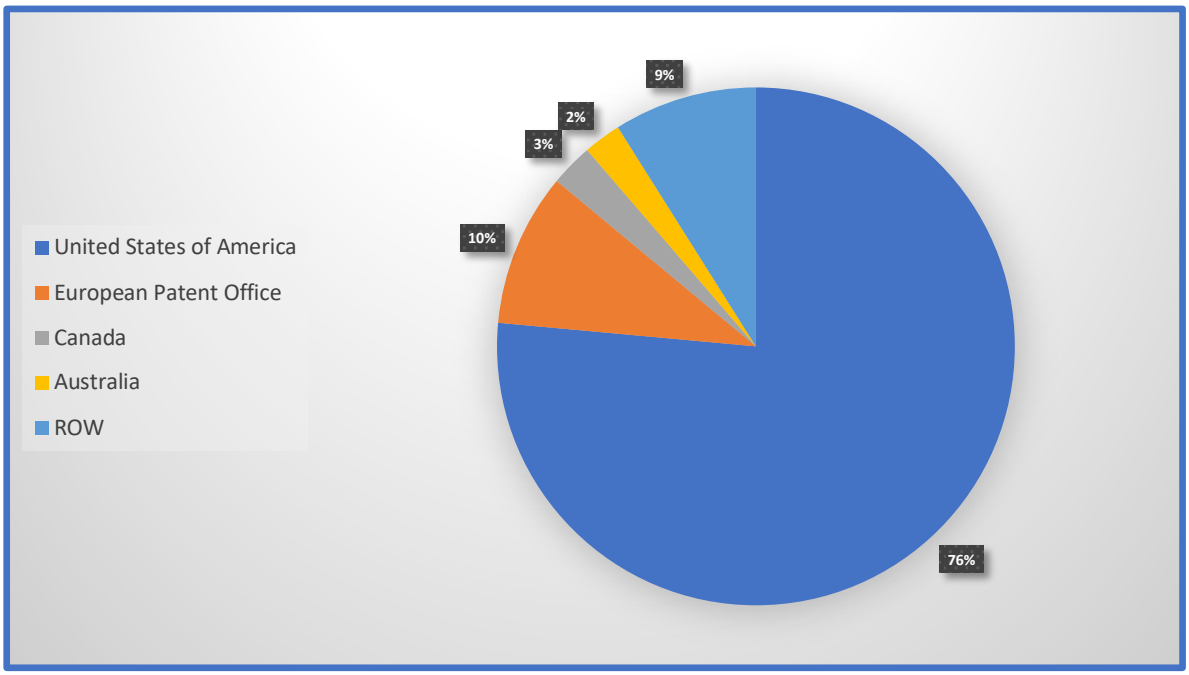
PCT PATENT APPLICATIONS FOR EBOLA WITH TERMS "EBOLA VIRUS*" OR "EBOLAVIRUS*" OR "EBOLA" OR "EBOV" OR "FILOVIRIDA*" APPEARING IN PATENT CLAIMS
SOURCE: WIPO PATENTSCOPE

A total of 2335 international patent applications related to Ebola were found with the majority of the applications originating from the US (76%) and the EU (10%). The applications generally cover the following claims:

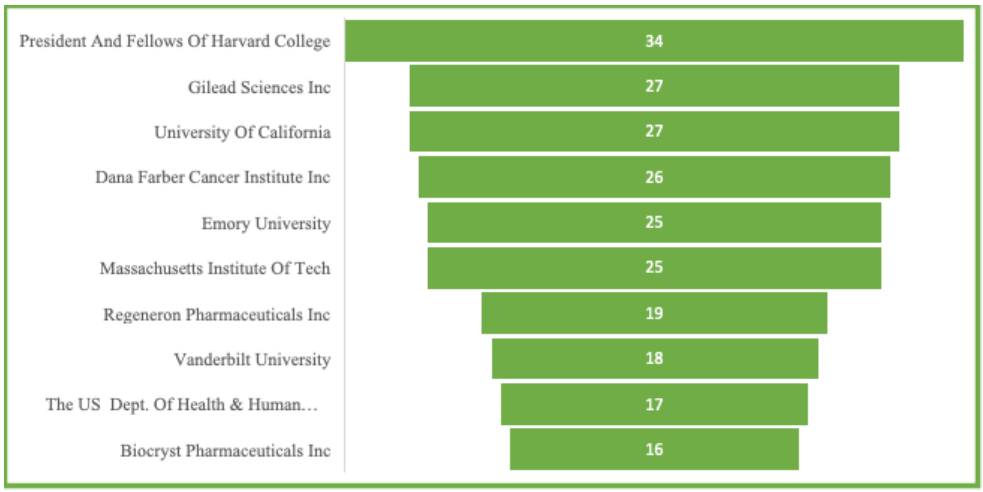
1. **Sequences and Production Methods**: Claims related to the native sequence, the nucleotide or amino acid sequences of Ebola virus glycoproteins, as well as methods for their production are included in patent applications.
2. **Vaccine Compositions and Platforms**: Claims related to the development, formulation, and production of Ebola vaccines including live-attenuated vaccines, preparation of virus-like particles and their use in immunogenic compositions, production of whole cell-based vaccines, vaccines containing modified Ebola viruses, chimeric vaccines, mRNA vaccines and nucleic acid vaccines.
3. **Antibodies**: Claims related to antibodies targeting Ebola virus antigens. These antibodies may be monoclonal or polyclonal and may target various epitopes on the virus.
4. **Recombinant Proteins**: Recombinant proteins derived from Ebola virus proteins or engineered to elicit an immune response against Ebola are included in patent claims.
5. **Chimeric Glycoproteins**: These are engineered proteins that combine elements from different sources, potentially enhancing their effectiveness as vaccine antigens or therapeutic agents against Ebola.
6. **Adjuvants and Formulation Technologies**: Adjuvants and formulation technologies play a crucial role in enhancing the immune response to vaccines and improving their stability and efficacy. Patent applications include claims related to novel adjuvants or formulations specifically designed for Ebola vaccines.

PCT Applications By Year	
2015	79
2016	194
2017	119
2018	105
2019	127
2020	113
2021	266
2022	259
2023	217
2024	15

Applications filed by Origin



Top Applicants



B. NIPAH VIRUS (NIV)[8]

PCT PATENT APPLICATIONS FOR NIPAH VIRUS WITH THE TERM "NIPAH OR NIPAH VIRUS" APPEARING IN PATENT CLAIMS
SOURCE: WIPO PATENTSCOPE

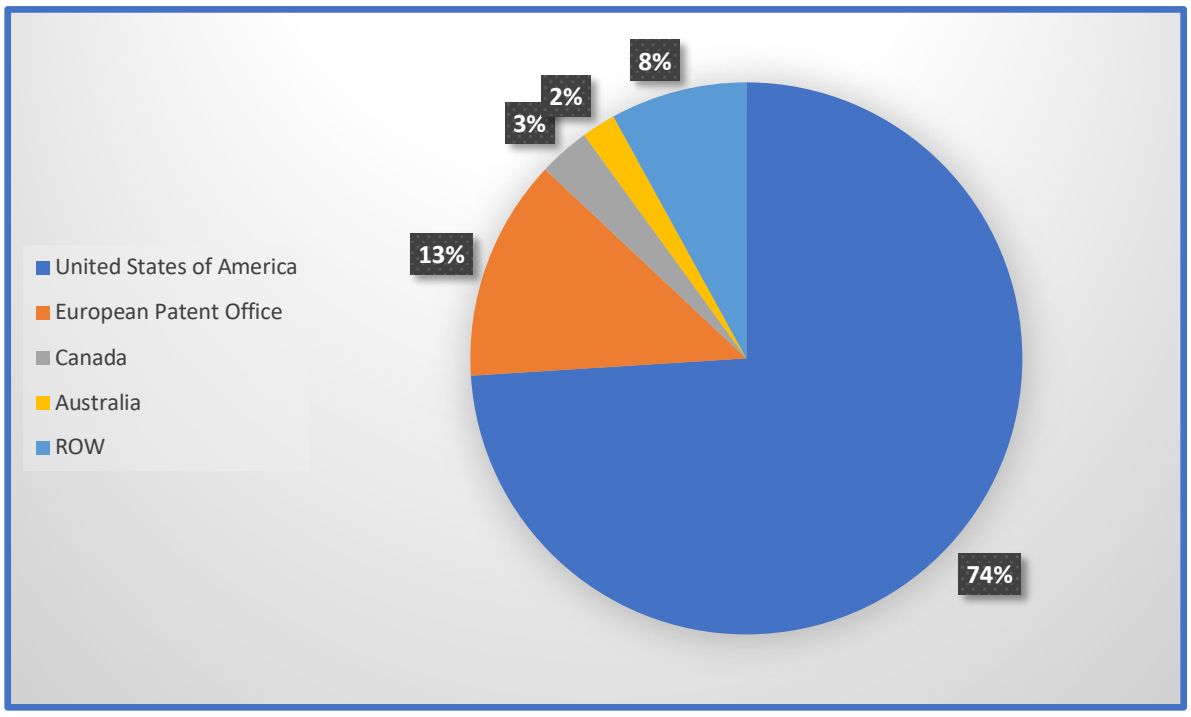
Based on the search 432 international applications claim Nipah Virus for animals or humans with 74% of the applications originating from the US and 13% from Europe. The applications encompass a wide array of claims:

1. **Sequences and Production Methods**: Patent applications encompass claims related to the nucleotide or amino acid sequences of NiV proteins, artificial nucleic acid sequences and polypeptides as well as methods for their production. These sequences and methods are essential for the development and manufacture of diagnostic tests, vaccines, and therapeutics targeting NiV infections.
2. **Vaccine Compositions and Platforms**: Claims within the patent applications relate to various vaccine platforms designed to prevent NiV infections including bivalent vaccines, non-replicating vectors, ribonucleic acid vaccines (NAVs), nano-structure based vaccines, CAdV vector vaccines. Each platform offers unique advantages in terms of immunogenicity, safety, and scalability. Additionally, claims have also been filed on replicating vectors, Hendra and Nipah Virus G Glycoprotein immunogenic compositions.
3. **Diagnostics and detection:** Claims filed on diagnostics encompass high throughput virus quantification, kits for detecting NiV like PT-PCR kits and detection reagents and the broad use of CRISPR technologies for virus diagnostics.
4. **Antibodies:** Claims related to antibodies include antibodies targeting Niv antigens, neutralizing, recombinant antibody and humanized antibodies, novel Niv glycoproteins and preparation of soluble forms of F and G glycoprotein of NiV among others.
5. **Antiviral drugs and therapeutic compositions:** Patent application claims encompass small molecule for the treatment of viral diseases in general including those for NiV. These include phospholipid, nucleoside and carbanucleoside analogues.
6. **Adjuvants and Formulation Technology**: Adjuvants play a crucial role in enhancing the immune response to vaccines. Patent application claims include novel adjuvants, oil based adjuvant systems or formulation technologies specifically designed to improve the efficacy and stability of NiV vaccines.

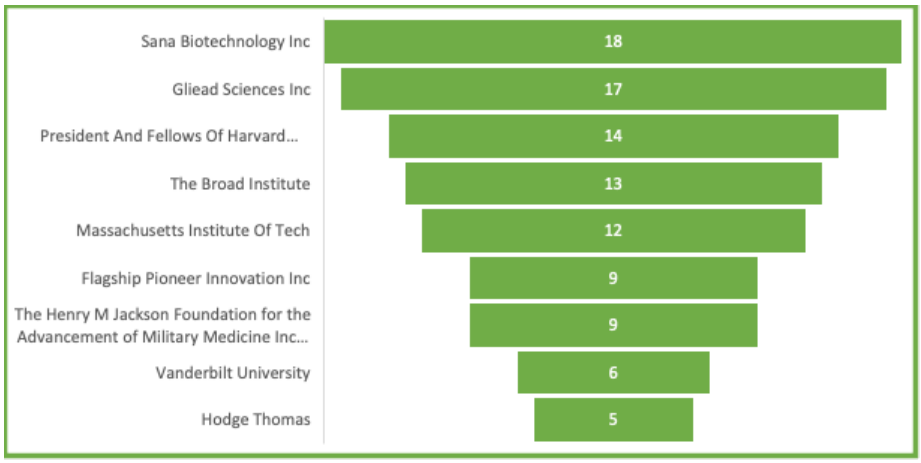
[8] Nipah Virus belongs to the family of Paramyxoviridae which is under PCT Classification A61K39/155 (Paramyxoviridae, E.G. Parainfluenza Virus). However, a Patentscope search for Nipah in Title, Abstract and Claims and IPC Class A61K39/155 resulted in 1182 patent applications, which contained numerous applications related to other members of paramyxovirus family like mumps, newcastle, fowl among others. Hence only a specific keyword-based search was done.

PCT APPLICATIONS BY YEAR	
2015	16
2016	08
2017	20
2018	17
2019	26
2020	22
2021	58
2022	58
2023	87
2024	7

Applications filed by Origin



Top Applicants



The top applicants' data illustrated above was obtained from the WIPO Patentscope. However, a search in other databases revealed that applications in the area of NiV have also been filed by government departments like the US Department of Health, Academy of Military Medical Sciences, various academic institutes including the Regents of University of California, The Board of Regents of University of Texas System, Icahn School of Medicine at Mount Sinai, Penn State Research Foundation, Board of Trustees of University of Illinois, Institut Pasteur, and other private organizations like CureVac, Moderntax Inc, Doma Pharmaceuticals and Zoetis Services LLC among others.

C. ZIKA VIRUS [9]

PCT PATENT APPLICATIONS FOR ZIKA VIRUS WITH TERMS "ZIKA VIRUS*" OR "ZIKA*" IN CLAIMS
SOURCE: WIPO PATENTSCOPE

A total of 1269 patent applications related to Zika virus were found with most of the applications originating from the US (85%). The PCT applications generally cover the following claims:

1. **Vaccine compositions:** Claims within the patent applications relate to live-attenuated vaccines, Zika virus-like particle (VLPs) based vaccines and their preparations including their use in immunogenic compositions, production of whole cell-based vaccines, vaccines containing modified Zika viruses, chimeric flavivirus vaccines, nucleic acid vaccines and inactivated virus compositions and Zika vaccine platforms.
2. **Antibodies**: Claims related to antibodies encompass antibodies targeting Zika virus antigens, neutralizing, recombinant antibody and humanized antibodies, novel antibodies specifically binding to Zika virus epitopes, nucleic acid antibody constructs, use of antibodies for finding

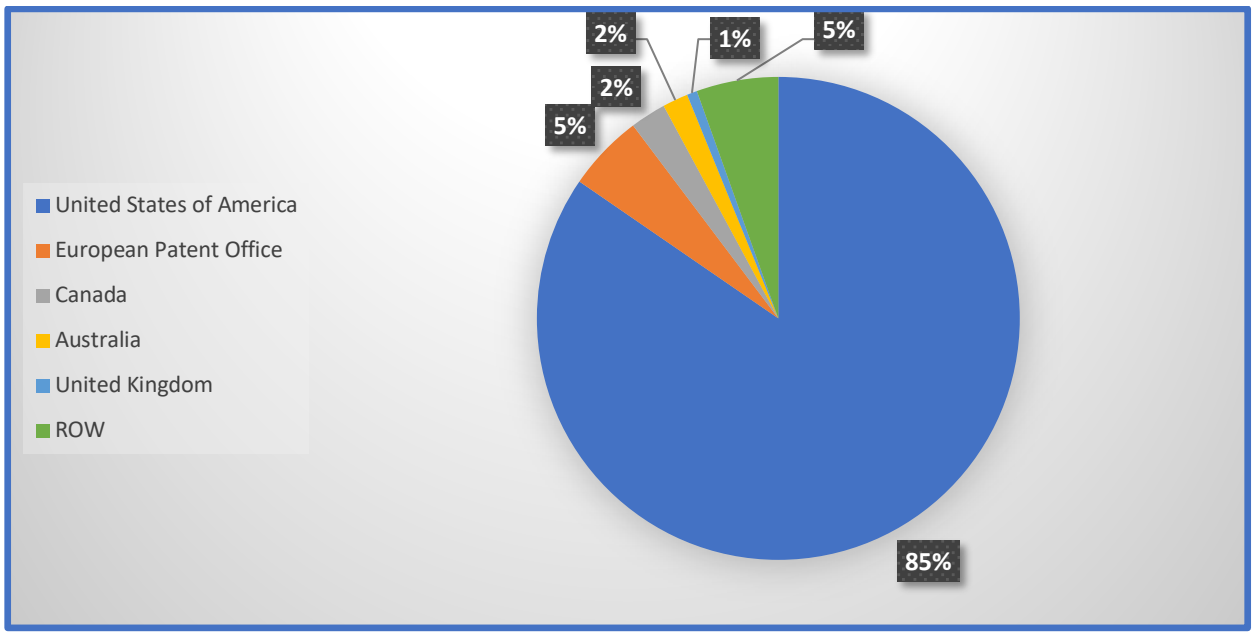
[9] Zika Virus belongs to family of Flaviviruses. IPC Class C07K14/18 (Togaviridae) consists of Togaviridae, e.g. Flavivirus, Pestivirus, Yellow Fever Virus, Hepatitis C Virus, Japanese Encephalitis Virus. A Patentscope search for only IPC Class C07K14/18 resulted in 2010 Patent Applications., which contained numerous applications related to Hepatitis C Virus. Hence only a specific keyword-based search was done)

exposure response and RNA-coded bispecific antibodies, antibodies that bind Zika virus envelope protein and Zika viral antigen constructs and method of production and detection of antibodies among others.

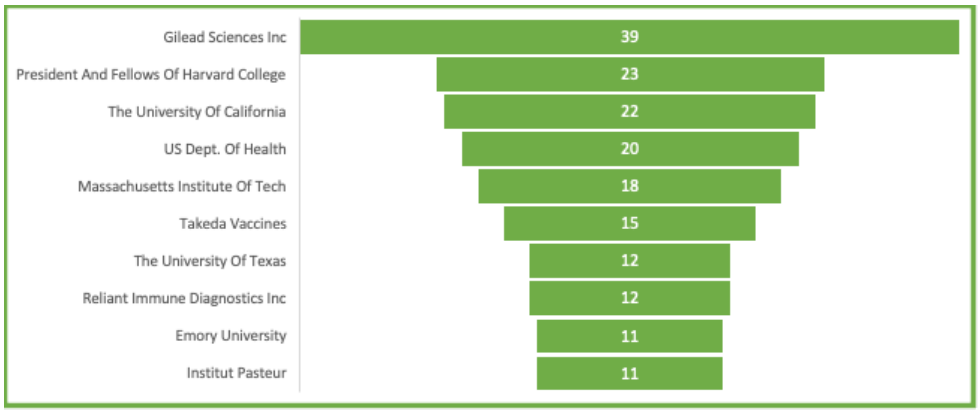
3. **Antiviral drugs and therapeutic compositions:** Patent application claims encompass small molecule inhibitors of Zika virus and other antiviral agents and therapeutic compositions example those containing protease inhibitors and Zika protein blockers among others.
4. **Diagnostics:** Patent claims have been filed on detection systems, immunochromatography analysis device for detecting Zika virus, immunoassays, serological tests and assays, high throughput nucleic acid testing among others.
5. **Chimeric glycoproteins and adjuvants/formulations:** Claims on chimeric glycoproteins, adjuvants or other formulations have also been filed.
6. **Sequences:** Patent claims have been filed on genomic sequences encoding for an attenuated mutant Zika virus, amino acid sequences of recombinant flaviviral protein among others

PCT APPLICATIONS BY YEAR	
2015	5
2016	20
2017	129
2018	180
2019	156
2020	113
2021	225
2022	224
2023	175
2024	14

Applications filed by Origin



Top Applicants



The applicant data presented above was sourced from the WIPO Patentscope Database. Nevertheless, further exploration across other databases uncovered additional applications in the realm of Zika Virus attributed to various private and academic institutions. These include but are not limited to: The Regents of the University of Michigan, The Regents of the University of California, The Trustees of the University of Pennsylvania, and Takeda Vaccines.

D. LASSA VIRUS (LASV)

PCT PATENT APPLICATIONS FOR LASSA VIRUS WITH TERMS "LASSA FEVER" OR "LASSA" OR "LASSA VIRUS" APPEARING IN PATENT CLAIMS

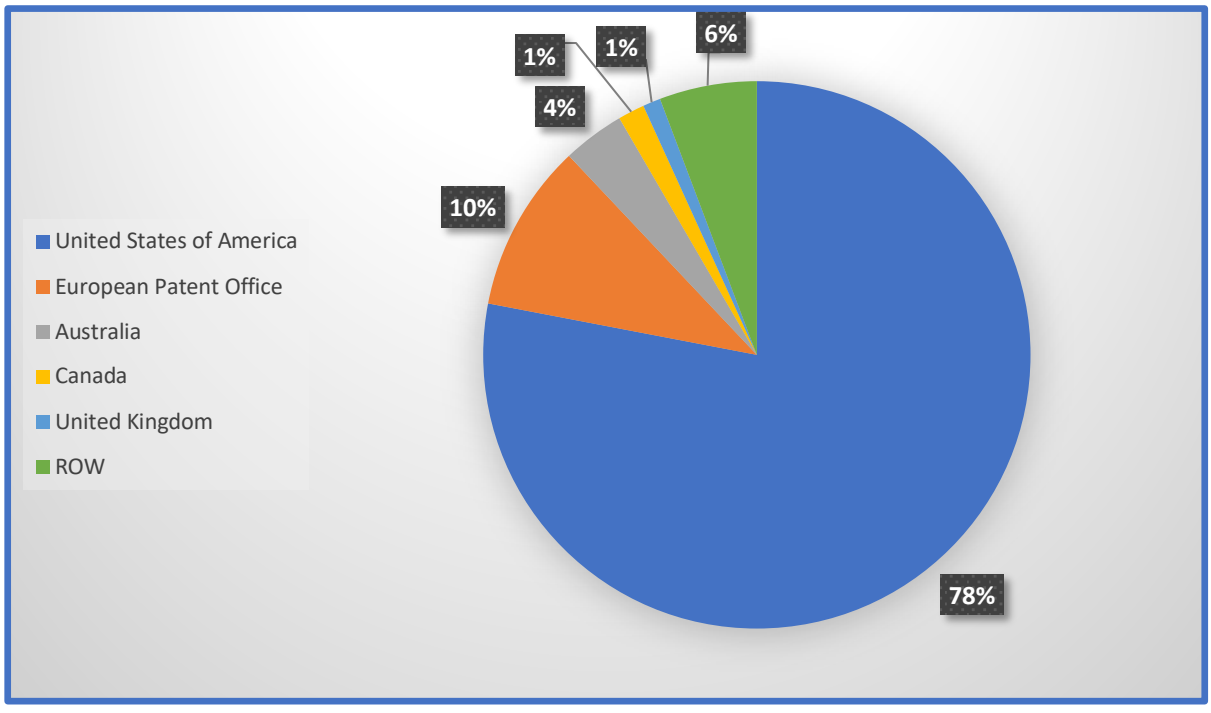
A search yielded a total of 784 patent applications pertaining to LASV, with the bulk originating from the US (78%) and some from the EU (10%). These applications exhibit a broad scope, aiming to encompass the Arenavirus family. Typically, the applications encompass the following claims:

1. **Vaccine Compositions -** Claims within the patent applications relate to live-attenuated vaccines, preparation of virus-like particles and their use in immunogenic compositions, the use of viral particles for vaccine production, mRNA vaccines and nucleic acid vaccines.
2. **Antibodies**: Claims include those related to antibodies targeting LASV antigens.These antibodies may be monoclonal or polyclonal and may target various epitopes on the virus, Additionally, claims are also filed on production of antibodies, use of antibodies for finding exposure response and RNA-Coded Bispecific Antibodies.
3. **Antiviral Drugs and Therapeutic Compositions:** Patent application claims encompass small molecule inhibitors of Lassa virus and other antiviral drugs and therapeutic compositions that help in the treatment of Arenaviridea viruses.

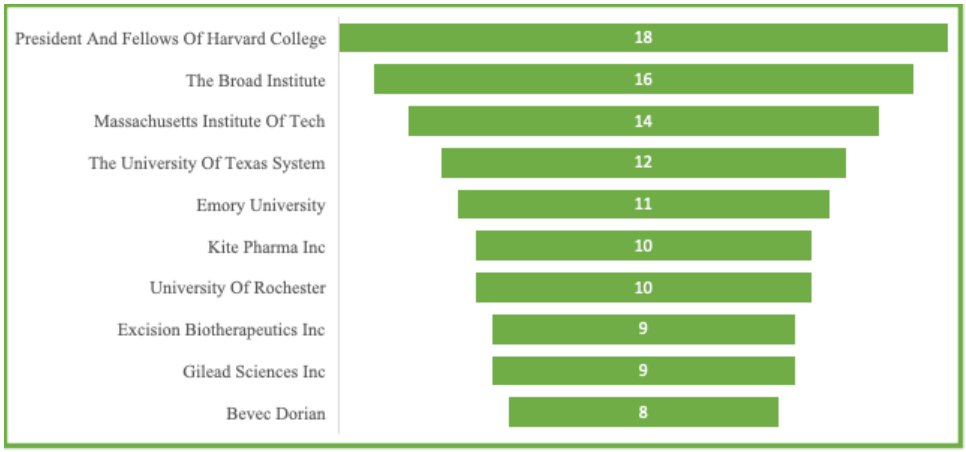
4. **Diagnostics:** Patent claims have been filed on detection systems, including high throughput screening, methods of determination of target sequences, nucleic acid amplification assays for pathogens and broad use of CRISPR technologies for diagnosis of viruses.

PCT APPLICATIONS BY YEAR	
2015	23
2016	36
2017	38
2018	34
2019	45
2020	39
2021	89
2022	93
2023	83
2024	4

Applications filed by Origin



Top Applicants



The leading applicants' data depicted above was sourced from the WIPO Patentscope Database. However, further investigation across other databases also unveiled additional applications concerning LASV, submitted by private and academic institutions, – Curevac, Siga Technologies Inc, Kineta Four LLC,[10] Tulane University, Chemimage Corp and Biocryst Pharmaceuticals.

[10]Kineta, Inc. is a clinical-stage biotechnology company committed to developing disruptive life science technologies. It has a focused pipeline of investigational drugs in oncology, neuroscience and biodefense and collaborates with a broad array of private, government and industry partners. Kineta had secured a $1.8 million funding boost from Wellcome Trust on Positive Phase 1a Clinical Study Results with LHF-535

2.3 . SUMMARIES OF SELECTED PATENTS

1. PCT Application No: WO2010048615
Title: Human Ebola Virus Species and Compositions and Methods Thereof
Applicant: The United States of America as Represented by the Secretary Department of Health and Human Services
Published: 29.04.2010

The present invention is based upon the isolation and identification of a **new human Ebola virus species - EboBun**. EboBun was isolated from patients suffering from hemorrhagic fever in an outbreak in Uganda. The isolated EboBun virus was deposited with the Centers for Disease Control and Prevention ("CDC") on Nov. 26, 2007 and accorded an accession number 20070629.

Patent Claims:
The patent application directly claims the attenuated hEbola virus. Attenuated viruses are weakened or modified versions of the wild-type virus that are less virulent and therefore safer for use in vaccines or therapeutic applications. Attenuated viruses can stimulate an immune response without causing severe disease. The application also claims an isolated antibody or an antigen-binding fragment which immuno specifically binds to the hEbola virus claimed in the patent application. These antibodies can be used for diagnostic purposes, such as detecting the presence of the virus in patient samples, or for therapeutic purposes, such as passive immunization or neutralizing the virus. The claims include a method for detecting the presence or absence of Ebola Bundibugyo. This method may involve various techniques, such as nucleic acid amplification, immunoassays, or other diagnostic assays capable of detecting the viral antigen or genetic material. The patent application also claims a vaccine formulation comprising an effective amount of the hEbola virus.

2. PCT Application No: WO2000000617
Title: Ebola Virion Proteins Expressed From Venezuelan Equine Encephalitis (Vee) Virus Replicons
Applicant: U.S. Medical Research Institute of Infectious Diseases
Published: 06.01.2000

The application describes the development and evaluation of a vaccine candidate against Ebola virus using VEE virus replicon technology, which holds promise for the development of vaccines against other infectious diseases as well. The VEE virus replicon (Vrep) is a modified version of the Venezuelan equine encephalitis (VEE) virus genome where the structural protein genes are replaced with genes encoding antigens of interest, such as those from the Ebola virus. In this case, the genes encoding Ebola virus antigens, including GP (glycoprotein), NP (nucleoprotein), VP40, VP35, VP30, and VP24, were inserted into the VEE virus replicon vector. This allows for the production of replicon particles expressing Ebola virus antigens.

Patent Claims:
The patent claims a DNA fragment which encodes a glycoprotein (GP) Ebola protein. The Ebola virus DNA fragments have been prepared by using a part of sequences of the Zaire Ebola 1976 strain. It also claims a recombinant construct comprising a vector and one of the Ebola virus DNA fragments. It also claims an immunogenic composition containing recombinant virus replicon particles that are designed to express the GP Ebola peptide, thereby triggering an immune response against the Ebola virus.

The Ebola virus genes used in the study were obtained from the Zaire strain of Ebola virus, which was originally isolated from a patient during the 1976 outbreak (Mayinga strain). The GP and NP genes from the Zaire strain of Ebola virus were previously sequenced and deposited in GenBank under accession number L11365. Sanchez et al. (1993, supra).

3. PCT Application: WO2005023837
Title: Ebola peptides and immunogenic compositions containing same
Applicant: United States of America as Represented by the Secretary of the Army
Published: 17.03.2005

Patent Claims:
The patent claims an isolated glycoprotein (GP) Ebola peptide comprising the sequence specified in SEQ ID NO:29, which is an isolated peptide fragment. The isolated peptide fragments have been prepared by using a part of the Zaire Ebola 1976 strain. It also claims an immunogenic composition comprising recombinant virus replicon particles expressing the peptide of the SEQ ID NO:29, thereby triggering an immune response against the Ebola virus.

4. PCT Application: WO2015034903
Title: Hendra and Nipah Virus G Glycoprotein Immunogenic Compositions
Applicant: Zoetis Services Llc
Published: 12.3.2015

Patent Claims:
The patent application claims an immunogenic composition comprising Hendra and/or Nipah virus G protein, adjuvants and excipients to produce neutralizing antibodies. It also claims a method of producing a neutralizing antibody response against a Hendra and/or Nipah virus by administering the immunogenic composition in an amount and duration effective to produce the neutralizing antibody response. The neutralizing antibody response reduces Hendra and/or Nipah virus reproduction and also reduces Hendra and/or Nipah virus shedding. The HeV immunogenic and vaccine compositions contain the Hendra virus G glycoprotein which consists of amino acids 73 to 604 (part of sequences) of the native Hendra G glycoprotein. The application does not claim the native sequence but uses a part of the native sequence to produce immunogenic and vaccine compositions.

5. PCT Application: WO2021209984
Title: Decoy Transcripts for Treatment of ssRNA Viral Replication
Applicant: Tel HaShomer Medical Research Infrastructure and Services Ltd
Published date: 21.10.2021

The patent application describes the use of a parasitic pseudo-viral transcript, also referred to as a "decoy transcript" to combat viral infections. The decoy transcript is described as a harmless entity that lacks the ability to replicate independently in the absence of the wild-type virus (WV) from which it derives. However, it contains all the necessary sequences required for efficient replication and packaging within the host cell. The primary purpose of the decoy transcript is to act as a competitive parasite within the host cell's replication and encapsulation machinery. By competing with the wild-type virus for these essential resources, the decoy transcript aims to disrupt the replication and spread of the WV.

Patent Claims:
The patent application claims a viral decoy transcript derived from a ssRNA virus, a composition comprising the decoy transcript and a method of treating/reducing/attenuating the spread of viral infection by providing the composition containing the decoy transcript. The decoy transcript claimed in the patent application is derived from many viral sequences - including the native Ebola Virus Sequence deposited in GenBank.

6. PCT Application: WO2016123019
Title: Human Antibodies to Ebola Virus Glycoprotein
Applicant: Regeneron Pharmaceuticals Inc.
Published: 04.08.2016

Patent claims:
The patent claims covers isolated antibody that binds to Ebola virus glycoprotein, pharmaceutical compositions containing the antibodies, production methods, and their use in combination with other antivirals or vaccines. It is notable that the patent application does not claim any novelty regarding the sequence of the Ebola but rather synthesized it from the sequence information available in "no strings" attached databases like GenBank.

Challenge of Access
Regeneron Pharmaceuticals, developed a monoclonal antibody (Inmazeb REGN-EB3) using genetic sequence data of a 2014 West African Strain. For the production of this monoclonal antibody - humanized mice were exposed to synthesized pieces of an Ebola virus. The strain C15 was isolated in a clinical sample of a 28-year-old woman from Guinea in Africa. The samples from the patient were taken and sequenced by the Bernard Nocht Institute in Germany and uploaded in the GenBank database which is a part of the US-EU-Japanese government-funded International Nucleotide Sequence Database Collaboration (INSDC)[11] that allows anonymous access, with "no-strings" attached.

The transfer of a physical virus sample by the Nocht Institute to other laboratories, including laboratories in the United States would be subject to a binding material transfer agreement (MTA) that references the CBD and Nagoya Protocol.[12] The MTA requires recipients of the C15 Ebola virus to negotiate a benefit-sharing agreement with Guinea, its country of origin, if they use the virus commercially or to generate intellectual property.

However, in this case, Regeneron utilized sequence information of the Ebola virus strain C15, downloaded the sequence information from GenBank and used it to synthesize portions of the Ebola virus for the development of Inmazeb. Since the sequence information was obtained from GenBank, and accessible without any obligation, Regeneron had no obligation to share benefits with Africa or other regions where the virus originated, and no benefit-sharing agreement appears to exist in this case.

Instead, access remains a challenge for affected African nations, very much dependent on *ad hoc* donations of the U.S. government or the benevolence of Regeneron. The U.S. appears to have access to the treatment, estimated to be at the cost of US$6,900 per treatment course. At this prohibitive price,

[11] Edward Hammond , "Ebola : Company avoids benefit-sharing obligation by using sequences", TWN Briefing Paper No 99, May 2019 available at https://www.twn.my/title2/briefing_papers/No99.pdf?utm_medium=email&utm_source=sendpress&utm_campaign
[12] Edward Hammond , "Ebola : Company avoids benefit-sharing obligation by using sequences", TWN Briefing Paper No 99, May 2019 available at https://www.twn.my/title2/briefing_papers/No99.pdf?utm_medium=email&utm_source=sendpress&utm_campaign

MSF has argued that "the ambitions for the size of the UN/WHO stockpile would likely need to be considerably reduced", adding that the access situation "leave WHO and others in a challenging position when responding to future outbreaks if the U.S. government is not willing to share these doses in a timely and appropriate manner".[13]

MSF also notes that Regeneron holds broad patents in the U.S. and other countries that cover the antibodies themselves, their production methods, antibodies which bind to the same epitope as the antibodies covered by the patent, and their use in combination with other antivirals or vaccines. To date, Regeneron has not engaged in any licensing or technology transfer agreements with entities in endemic countries.[14]

7. PCT Application No: WO2016077789
Title: Neutralizing Antibodies to Ebola Virus Glycoprotein and Their Use
Applicants: Institute for Research in Biomedicine IRB, Humabs Biomed SA, US Department of Health and Human Services, US Department of Army
Published: 19.05.2016

Patent Claims:
The patent application claims an isolated monoclonal antibody comprising of heavy and light chain. The monoclonal antibody or antigen-binding fragment specifically binds to Ebola virus glycoprotein. The patent application also claims nucleic acid molecule, pharmaceutical compositions, method of detecting an ebolavirus infection in a subject, method of preventing or treating an Ebola virus infection and method of generating therapeutic antibodies against the Ebola glycoprotein or antigen-binding fragment that specifically binds to Ebola virus glycoprotein. It is notable that the patent application does not claim the sequence of Ebola. However, it makes use of the Zaire Ebola sequence as part of the process to produce an isolated antibody and then claims the isolated antibody.

Challenge of Access :
EBANGA™ (Ansuvimab-zykl) is a Zaire ebolavirus glycoprotein (EBOV GP)-directed human monoclonal antibody isolated from a human survivor of the 1995 Ebola outbreak in Kikwit, a city in the DRC[15]. Nancy Sullivan, Ph.D., Chief of the Biodefense Research Section at the NIAID,VRC and her team, alongside scientists from VIR Biotechnology's Humabs BioMed S.A. subsidiary, discovered that the survivor retained antibodies against Ebola 11 years after infection. The team isolated the antibodies, tested the most favourable ones in both laboratory and nonhuman primate studies, and selected ansuvimab as the most promising among the set for clinical trial.

In December 2018, US-based biotechnology company Ridgeback Biotherapeutics received a license (originally non-exclusive was converted in 2021 into an exclusive license) for EBANGA™ from the National Institute of Allergy and Infectious Diseases (NIAID) for intellectual property associated with the monoclonal antibody. EBANGA™ was granted orphan drug designation and breakthrough therapy designation by the US Food and Drug Administration (FDA) for Ebola treatment in May 2019 and

[13] "Ensuring Access to New Treatments for Ebola Virus Disease", MSF Access Campaign, available at https://www.msfaccess.org/ensuring-access-new-treatments-ebola-virus-disease
[14] "Ensuring Access to New Treatments for Ebola Virus Disease", MSF Access Campaign, available at https://www.msfaccess.org/ensuring-access-new-treatments-ebola-virus-disease
[15] Corti D, Misasi J, Mulangu S, et al. Protective monotherapy against lethal Ebola virus infection by a potently neutralizing antibody. *Science.* 2016;351(6279):1339–1342. doi: 10.1126/science.aad5224 available at https://pubmed.ncbi.nlm.nih.gov/26917593/

September 2019 respectively[16]. In April 2020, Ridgeback secured a $10.9m contract from the US Biomedical Advanced Research and Development Authority (BARDA) for the development of EBANGA™ for the treatment of Ebola virus disease[17]. On December 21, 2020, the FDA approved Ridgeback Biotherapeutics' EBANGA™ indicated for treatment of infection caused by Zaire ebolavirus in adult and paediatric patients. The therapy's development has been wholly or partially funded by the proceeds from the US Department of Health and Human Services (HHS), as well as the Office of the Assistant Secretary for Preparedness and Response (ASPR) and BARDA. Access for affected African countries remains uncertain and a major concern.[18]

8. PCT Application: WO2016112188
Title: Methods and Compositions for Ebola Virus Vaccination
Applicant: Etubics Corporation
Published: 14.07.2016

The patent application discloses methods for generating immune response to Ebola virus antigens using adenovirus vectors. The application also provides nucleic acid sequences that encode one or more target antigens of interest, or fragments or variants.

Patent Claims:
The patent application claims a composition comprising a replication defective adenovirus comprising a nucleic acid sequence encoding an Ebola virus antigen, where the Ebola virus antigen encoding sequence has 70%-100% sequence identity to a sequence (selected from a group of sequences) where the sequences are from native Ebola Virus. The patent application also claims a method of generating an immune response against an Ebola virus antigen in a human, the method comprising administering to the human the compositions of the application as well as a method of treatment.

9. PCT Application: WO2023049794
Title: Rapid Acting Vaccine Against Nipah Virus
Applicant: Board Of Regents, The University Of Texas System
Published:30.03.2023

The use of recombinant vesicular stomatitis virus (rVSV) as a vaccine vector for various pathogenic viruses, including Ebola, Lassa, and Nipah, is indeed an area of active research and development. The characteristics of rVSV, such as its ability to propagate vigorously and its potential for industrial-scale manufacture of vaccine preparations, make it a promising candidate for vaccine development against a range of infectious diseases. In this case, a non-human primate African green monkey (AGM) was vaccinated with rVSV vectors expressing antigens from Nipah virus and subsequently challenged with Nipah virus strains to assess vaccine efficacy and immune response.

As challenge material for vaccinating the AGMs, the scientists utilized a viral isolate, designated as SPB200401066[19]. The patent application states: *"The NiVB (Bangladesh Strain) challenge material*

[16] Lee A. Ansuvimab: First Approval. Drugs. 2021 Apr;81(5):595-598. doi: 10.1007/s40265-021-01483-4. Epub 2021 Mar 22. PMID: 33751449; PMCID: PMC7983082. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7983082/
[17] https://www.clinicaltrialsarena.com/projects/ebanga-ansuvimab-zykl/
[18] Ensuring Access to New Treatments for Ebola Virus Disease", MSF Access Campaign, available at https://www.msfaccess.org/ensuring-access-new-treatments-ebola-virus-disease
[19] Harcourt BH, Lowe L, Tamin A, Liu X, Bankamp B, Bowden N, Rollin PE, Comer JA, Ksiazek TG, Hossain MJ, Gurley ES, Breiman RF, Bellini WJ, Rota PA. Genetic characterization of Nipah virus, Bangladesh, 2004. Emerg Infect Dis. 2005 Oct;11(10):1594-7. doi: 10.3201/eid1110.050513. PMID: 16318702; PMCID: PMC3366751. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3366751/

used in the study (200401066) originated from a fatal human case during an outbreak in Rajbari, Bangladesh in 2004. The challenge material was passaged twice onto Vero E6 cells and supernatants were collected and stored at -80°C as ~ 1 ml aliquots. Four distinct mutations of sufficient frequency were found between the P2 stock of NiVB and the reference genome (GenBank Accession number AY988601.1)"

Scientists at the University of Texas are developing a rapid-acting vaccine[20] supported by the US Army Medical Research Acquisition Activity contract W81XWH1910028 (to T.W.G.) and the US Department of Health and Human Services, NIH Grant UC7AI094660 for biosafety level-4 operations support of the Galveston National Laboratory.

Patent Claims:
The patent application claims composition or vaccine comprising a rVSV viral vector that expresses a Nipah Virus protein. It also claims methods of making compositions or vaccines comprising a rVSV viral vector that expresses a Nipah Virus protein antigen.

10. PCT Application No: WO2023133077
Title: Nipah Henipavirus Virus Replicon Particles and Their Use
Applicant: The United States of America, as represented by the Secretary, Department of Health and Human Services
Published: 13.07.2023

The patent application relates to NiV virus replicon particles (VRPs) and their potential use in inducing immune responses to Nipah virus (NiV) and/or Hendra virus. The application also discloses a production system including a NiV-derived VRP where the fusion protein (F) gene has been deleted (NiVΔF). Additionally, it involves a cell line engineered to constitutively express NiV F protein, which facilitates the generation of high-titer replicon particles, specifically NiVΔF VRP. In this application hamsters were vaccinated intranasally (IN) with a single dose of NiVΔF VRP. Similar to the previous application the hamsters were subsequently challenged with wildtype NiV strain Malaysia. The study likely assessed the effectiveness of the VRPs in inducing protective immunity against NiV infection. The patent application suggests that the administration of the disclosed VRPs may induce an immune response to more than one strain of NiV, including strains Malaysia and Bangladesh.

***Patent Claims**:*
The patent application claims NiV virus replicon particles (VRPs) that can be utilized to elicit an immune response against NiV and/or Hendra virus. The Nipah henipavirus virus replicon particle comprises a recombinant Nipah henipavirus genome, in which the nucleic acid sequence encoding the F protein of the Nipah virus sequence is deleted so that the functional mature F protein cannot be produced from the recombinant Nipah henipavirus genome. The Nipah henipavirus genome to which the deletion is carried out to produce a recombinant genome is from the Nipah Malaysia strain.

Origin of 200401066:
[Excerpts (NV was isolated from 2 oropharyngeal swabs (SPB200401066, SPB200406506), 1 cerebrospinal fluid (SPB200401617), and 1 urine specimen (SPB200405758) from human patients, and isolation was confirmed by reverse transcription polymerase chain reaction (RT-PCR). Two isolates were from Rajbari, and 1 was from Faridpur; the fourth isolate, from the Rajshahi district (100 km from Rajbari), was not linked to the other 2 outbreaks. The complete genomic sequence of the first viral isolate (SPB200401066) from Rajbari was derived and submitted to GenBank (accession no. AY988601) as NV-Bangladesh (NV-B)]

[20] https://www.utmb.edu/news/article/utmb-news/2022/03/18/scientists-develop-nipah-virus-vaccine-that-may-give-life-saving-protection-in-just-three-days

Additionally, methods for inducing an immune response in a subject involves administering an immunogenic composition containing an effective amount of the VRPs along with a pharmaceutically acceptable carrier. The use of wildtype NiV Malaysia strain as challenge material forms an essential part of the application.

11. PCT Application: WO2006115843
Title: Nipah Virus Vaccines
Applicant: Merial Inc. (Current Owner: Boehringer Ingelheim Animal Health USA Inc)
Published: 02.11.2006

Patent Claims:
The patent application describes the production of a recombinant vaccine that immunizes pigs against Nipah virus. The applications claims an avipox expression vector comprising of a polynucleotide that encodes a Nipah virus glycoprotein.
As described in the application the polynucleotide comprises nucleotide base sequence of nucleotide 8943 to nucleotide 10751 of the native Nipah Virus Malaysia strain. The application thus uses a part of the native sequence to produce immunogenic and vaccine compositions.

12. PCT Application: WO2018115507
Title: Henipavirus Vaccine
Applicant: Curevac Ag
Published: 28.6.2018

Patent Claims*:*
The patent application claims an artificial nucleic acid and polypeptides suitable for use in treatment or prophylaxis of an infection with Henipavirus, particularly Hendra virus and/or Nipah virus or a disorder related to such an infection. The claimed artificial nucleic acid sequence encoding a protein or peptide, or a fragment or variant, is derived from Nipah virus glycoprotein. The Nipah virus strains are from Malaysia, Bangladesh and India. The Nipah Virus proteins were downloaded from the Nipah virus sequences uploaded in GenBank database**.** The application also claims Hendra virus and/or Nipah virus vaccine and compositions comprising the artificial nucleic acid, polypeptides, and a method of treating or preventing a disorder or a disease by using the said compositions and vaccines.

13. PCT Application: WO2017109222
Title: Recombinant Zika Vaccines
Applicant: Themis Bioscience Gmbh
Published: 29.06.2017

Patent Claims:
The patent application claims an immunogenic composition. The composition is a vaccine that is designed to trigger an immune response against the Zika virus and contains a Zika virus antigen. The Zika virus antigen of the application is encoded by at least one nucleic acid sequence encoding at least one E-protein of a Zika virus or a functional fragment. These sequences are identified by Sequence ID numbers 1 to 13 and 67 to 87 and are independently derived from Zika virus strains - including the Brazilian strains-ZKV2015 and Haitian strain - Haiti/1225/2014 among others. The application also claims a method for producing a recombinant chimeric virus.

14. PCT Application: WO2020226831
Title: Inactivated Virus Compositions and Zika Vaccine Formulations
Applicant: Takeda Vaccines Inc
Published: 12.11.2020

Patent Claims:
The patent application claims a liquid inactivated virus composition comprising an inactivated whole Zika virus along with suitable excipients. The Zika virus used for the preparation of the said vaccine as claimed was derived from the Puerto Rico strain PRVABC59 of the genomic sequence corresponding to SEQ ID NO: 2. [This Puerto Rico strain PRVABC59 strain was isolated in 2015 from a human serum specimen in Puerto Rico and was deposited by the Center for Disease Control and Prevention].

15. PCT Application: WO2018009604
Title: Chimeric Dengue/zika Viruses Live-Attenuated Zika Virus Vaccines
Applicant: The United States of America, As Represented by the Secretary, Department of Health and Human Services
Published: 11.01.2018

Patent Claims
The patent application claims a nucleic acid chimera containing two nucleotides. The two nucleotides are respectively from a Dengue genome and a portion of the signal sequence from the Zika virus genome. As claimed the Zika virus genome for preparing the said chimera can be from the SPH2015 (Brazilian strain), PRVABC59 (Puerto Rico strain) or R103451 (Honduras strain). [The Puerto Rico strain PRVABC59 as claimed was isolated in 2015 from a human serum specimen in Puerto Rico and was deposited by the Center for Disease Control and Prevention. The Brazilian Strain ZikaSPH2015 (GenBank Accession No: KU321639.1) was isolated in São Paulo state, Brazil, in 2015, from a patient who received a blood transfusion from an asymptomatic donor at the time of donation].[21]

16. PCT Application: WO2018115525
Title: Lassa Virus Vaccine
Applicant: Curevac Ag
Published: 28.06.2018

Patent Claims:
This patent application claims mRNAs usable as vaccines against Lassa virus (LASV) infections. Further, it also claims (pharmaceutical) compositions and vaccines comprising said mRNAs and their use for treatment or prophylaxis of a Lassa virus infection. The present invention further features a kit comprising the mRNAs, (pharmaceutical) compositions or vaccines and a method for treatment or prophylaxis of Lassa virus infections using said mRNAs, pharmaceutical) compositions or vaccines. The mRNA usable as a vaccine comprises a coding region which encodes peptide or protein derived from Lassa virus from clade I, II, III and/or IV or lineage I, II, III and/or IV. These include strains from Nigeria, Guinea, Liberia, and Sierra Leone. Most claims are directed towards mRNA.

[21] Cunha MS, Esposito DL, Rocco IM, Maeda AY, Vasami FG, Nogueira JS, de Souza RP, Suzuki A, Addas-Carvalho M, Barjas-Castro Mde L, Resende MR, Stucchi RS, Boin Ide F, Katz G, Angerami RN, da Fonseca BA. First Complete Genome Sequence of Zika Virus (Flaviviridae, Flavivirus) from an Autochthonous Transmission in Brazil. Genome Announc. 2016 Mar 3;4(2):e00032-16. doi: 10.1128/genomeA.00032-16. PMID: 26941134; PMCID: PMC4777745. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4777745/

17. PCT Application: WO2011034953
Title: Lassa Virus-Like Particles and Methods of Production Thereof
Applicant: The Administrators of the Tulane Educational Fund
Published: 24.03.2011

This application describes virus-like particle (VLP) compositions for prevention against Lassa virus. The VLPs of this application comprise the Lassa virus (LASV) Z matrix protein, glycoproteins (GPs)-I and -2, and nucleoprotein (NP). The description discloses that the source of the samples used in the invention were from the Nigerian and Sierra Leone strains. The serum samples from approximately 100 volunteer blood donors from the Northwestern district of Bombali, Sierra Leone were analyzed for LASV-specific antigen, IgG and IgM antibodies. Additionally, a panel of archived human sera from patients that had been admitted to the KGH, Sierra Leone from January 2008-April 2010 as suspected Lassa fever cases were also chosen for conducting the studies.

Patent Claims:
The application claims the production of a nucleic acid construct for producing arenavirus like particles. The nucleic acid construct comprises at least one sequence that encodes a protein derived from LASV. The Z, NP, GPC, GP1 and/or GP2 proteins encoded by the construct are derived from LASV.

The Tulane University Health Sciences Center; Autoimmune Technologies, LLC; Corgenix Medical Corporation; Vybion, Inc.,; United States Army Medical Research Institute of Infectious Diseases (USAMRIID) have developed a vaccine candidate using the above GPC, NP, Z Matrix which is in preclinical stage. [22]

18. US Application: US10821143 (WO2015077714)
Title: Chimeric VSV virus compositions and methods of use thereof for treatment of cancer
Applicant: Yale University
Published: 03.11.2020

Patent Claims:
This patent application claims a method of treating cancer by administering to a subject with cancer a pharmaceutical composition comprising an effective amount of a chimeric vesicular stomatitis virus (VSV). The chimeric VSV virus comprises a VSV background with one or more heterologous viral glycoproteins in place of the VSV G-protein. The heterologous viral glycoproteins is a Lassa virus glycoprotein precursor (GPC) or a fragment derived from the Lassa virus Josiah strain. The Lassa virus Josiah strain is from Sierre Leone.

3. ANALYSIS OF PATENTING TRENDS

3.1 Broad patent claims covering pathogen material and associated GSD

This study delving into patent applications concerning pathogens capable of precipitating health emergencies reveals a broad spectrum of claims encompassing both the pathogen materials and their GSD. **Section 2 of this paper sheds light on the appropriation of native sequences and virus samples, wherein patents are sought over either portions of or modified versions of these**

[22] https://www.thelancet.com/cms/10.1016/S2214-109X(18)30346-2/attachment/efb6b1dd-e55b-4f00-9587-25f97eea6175/mmc1.pdf

sequences. Patent applications also may not claim native sequences per se but native sequences may be modified and patent claims made over artificial sequences i.e. modified sequences. Moreover, the scope of the patent claims frequently covers products like antibodies, vaccine compositions and other medical products, generated by the use of virus samples from patients.

The majority of the patent claims originate from both public and private entities as well as academic institutions in developed nations, notably the United States, positioning them to own the majority of "inventions" derived from these pathogens and GSD. This is particularly noteworthy considering that the primary countries affected by the pathogens under scrutiny in this study are predominantly developing nations. The claimed "inventions", once commercialized can lead to monopolisation and patent thickets; impeding scientific progress and hindering developing countries' efforts to combat public health threats.

In the context of the ongoing WHO negotiations, developed countries are insisting on the rapid sharing of biological materials and GSD, however such sharing bears the risk that the shared materials and data are appropriated by entities in developed countries through the use of the patent system. The design elements proposed by the Chair and the Facilitators lack safeguards against such exploitation.

It remains unclear if recipients of the biological material such as WHO-designated laboratories and those accessing GSD through "public databases" will be subject to legally binding terms and conditions including on IP to prevent appropriation of shared biological materials and GSD.

In addition, the IP text proposed by the Chair and the Facilitators as part of the design elements- "[i]ntellectual property rights may not be sought on biological materials and GSD" - is wholly inadequate given the broad spectrum of patent claims, described in Section 2 of this paper.

On the contrary, the proposition put forth by developing countries better captures the range of patent claims that should not be avoided, to prevent the exploitation of the PABS system. The proposal presented by the Africa Group and Group of Equity is: ***"no IP claims should be sought on WHO PABS biological material, including its GSD, or parts thereof, in any form including any modified form or for any use"***. This provision also reflects a critical effort by developing countries to remove monopolies that can hinder further R&D as well as barriers to the diversification of the production of medical products.

3.2 Genetic Sequence Data & Operationalizing Fair and Equitable Benefit Sharing

The Convention on Biological Diversity (CBD) acknowledges the inherent sovereign rights of states over their genetic resources. Additionally, it upholds their entitlement to fair and equitable benefit-sharing, established through mutually agreed terms stemming from the utilization of said resources. There is also agreement among CBD Parties that "benefits from the use of digital sequence information on genetic resources should be shared fairly and equitably"[23]

Evidence from Section 2 of the paper shows that both, the physical material of a pathogen and/or its GSD are important in the development of vaccines, diagnostics and therapeutics, with rapid affordable access being essential to contain and respond to public health emergencies including a pandemic. For pathogens in the scope of this paper, GSD was accessed through GenBank a "no-strings" attached public

[23] See CBD/COP/DEC/15/9 available at https://www.cbd.int/doc/decisions/cop-15/cop-15-dec-09-en.pdf

database. **In a few examples in Section 2, scientists were able to obtain the necessary biological material by accessing the GSD of the viral isolate from open databases like GenBank, without directly obtaining a sample from the countries like Bangladesh, Malaysia and in Africa.**

Databases like GenBank raise serious concerns including ethical considerations over the appropriation of shared GSD through the patent system (apparent in Section 2) and the impact on equitable access during a public health emergency as operationalization of benefit-sharing is challenging in the absence of user information, and data user agreement containing legally binding terms and conditions for the use of GSD. The ramifications for equitable access are starkly demonstrated by the unfortunate scenario of affected African countries being unable to access Ebola treatments, despite these treatments being developed through the utilization of GSD sourced from GenBank (See summaries no. 6 and 7 in Section 2.3).