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WIPO PATENT SEARCH REPORT ON PANDEMIC INFLUENZA PREPAREDNESS (PIP)-RELATED PATENTS AND PATENT APPLICATIONS

prepared by the International Bureau

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Executive Summary

In view of the emergence and circulation of highly pathogenic H5N1 avian influenza strains, the recent appearance of H1N1 influenza as a pandemic, and possibly of other pandemic strains, numerous activities are being conducted to improve the ability of the global community to respond to influenza. These include the establishment of surveillance networks, the development of diagnostic reagents and kits, and the development of vaccines to prevent infection and therapeutics to treat infection.

Within this context, Member States of the World Health Organization (WHO) currently negotiate a framework on "Sharing of Influenza Viruses and Access to Vaccines and Other Benefits" in an Open-Ended Working Group (OEWG) for Member States on Pandemic Influenza Preparedness (PIP). To assist this group formulate an appropriate intellectual property approach within the framework, they requested the Director-General of WHO to seek information from the World Intellectual Property Organization (WIPO) on PIP-related patents, including patent applications, in connection with the H5N1 and H1N1 pandemic virus. Recognizing that the phrase "in connection with" is rather ambiguous when searching patents, technical consultations between WIPO and WHO clarified referring to it as (a) patents or patent applications claiming inventions comprising the virus, a component, or a derivative of the virus, for diagnostic, therapeutic or prophylactic purposes, and (b) where the patent was applied for after the date at which it became clear that that strain of virus could be of pandemic potential (post 1995 for H5N1 and post-March 2009 for H1N1).

The adopted **search strategy and methodology** included a rigorous search for issued patents and patent applications (hereinafter referred to as "patents/applications") under the European Patent Office (EPO), the United States Patent and Trademark Office (USPTO), and the Patent Cooperation Treaty (PCT, covering 142 Contracting States), based on a broad-based keyword search of "H5N1" or "H1N1" anywhere in the patent/application. The H5N1 results were corroborated with a complementary strategy based on searches using published H5N1 amino acid sequences.

The **initial search** yielded 2119 documents for H5N1 and 81 for H1N1. Important to note is that this number of documents does not represent the number of relevant patents. This aggregate number of documents is inconsequential as it corresponds to an initial, intentionally broad keyword search designed to capture a large pool of documents. The 2119 and 81 documents, respectively, were then condensed to one representative document per **patent family**. This generated a list of 1024 documents for H5N1 and 76 for H1N1. That consolidated list of patent families also does not represent the number of patents/applications that claim any part of H5N1 or H1N1 pandemic virus. Indeed, most patent families fell outside the specific objective of the study and claimed, for example, monoclonal antibodies (mAbs), a composition of foods for preventing influenza virus diseases, or a rescue vehicle for the transport of infectious patients. A limited portfolio search of main assignees was also conducted yielding an additional patent.

Claims of one family representative of each of the identified patent family were then analyzed and **scored for relevancy**. This involved the reading of the claims and in many cases analysis of the entire patent/application. As with any such scoring, there is an element of interpretation and judgment. This scoring resulted in three groups:

- Twenty-seven (H5N1) and four (H1N1) patent families were scored as **relevant and clearly within the scope of the request** (including one patent found through the portfolio and BLAST searches; see below), defined as claiming sequences *per se,* or essential derivatives thereof. This includes patents claiming the virus, an isolated antigen from the virus, an isolated fragment of an antigen from the virus, or an isolated oligo- or poly-nucleotide sequence corresponding to the RNA sequence of the virus. In this category the invention is either derived from H5N1 or H1N1 sequences, or claim certain antigens or nucleotide sequences in isolation.

- Thirty-five (H5N1) and eight (H1N1) patent families were scored as **relevant but, subject to interpretation**, claiming sequences as one part or element of claimed invention. In this "subject to interpretation" are those patent families where sequences of H5N1 or H1N1 are only one element of the invention, for example an H5N1 vaccine that articulates a section of the viral genome and where the invention was primarily about a novel concept (novel method of making vaccines, novel adjuvant, vector etc.) and the claims included the use of an H5N1 or H1N1 peptide, nucleic acid or antigen in the invention, rather than as an isolated component.

- The majority of the patent families, or 964 for H5N1 and 64 for H1N1 did **not fall within the scope of the study**. In this category are included those applications and patents where it was not clear that a derivative of H5N1 or H1N1 sequence is claimed (but H5N1 or H1N1 may still have been included in the disclosure), inventions wherein viral sequences are articulated as possible embodiments (but are not integral *per se* to the invention such as adenoviral vectors expressing H5N1 antigens), plant-derived remedies, and mAbs. Although making mAbs requires using the virus, the compositions claimed in the applications or patent are in most cases not a derivative *per se* of the virus, and hence do not fall within the scope of the search.

A corroborative "BLAST" search based on published amino acid sequences of prevalent and well-characterized H5N1 strains yielded two additional patents not previously identified. One of these patents was categorized as relevant and clearly within the scope of the request. The BLAST search thus validated our H5N1 keyword search in that the results were highly congruent with the patent/application results. A limited portfolio search of main assignees yielded an additional patent. This approach illustrates the added value of combining iterative, complementary and overlapping search strategies to more comprehensively collect and evaluate potentially relevant documents. Moreover, six out of 10 families did not include the term H5N1 nor H1N1 in the claims, thus demonstrating the solidity of the approach adopted herein. Nevertheless, it is not suggested that this methodology is the only approach.

Furthermore, of those patent families scored as relevant for H5N1 or H1N1:

- Seventy-three percent were vaccines, 24% diagnostics and 3% therapeutics.

- Five were filed by members of the WHO collaborating centres/reference laboratories.

- A number of the patent applications had, as part of their families, issued patents/applications, many of which as continuations in part and divisionals, in African Regional Intellection Property Organization (ARIPO) filings, Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Costa Rica, Cuba, many European countries, Hong Kong, Israel, Japan, Mexico, New Zealand, Russian Federation, Republic of Korea, South Africa, Taiwan (Province of China) and the United States of America.

The results of this study, in conclusion, **highlight several critical points**:

1. In the pool of patent information assembled and analyzed in this report, no patent documents were identified that included claims having, as a sole and/or single element, either a complete native virion, a native viral strain, a native viral genome in its entirety or a complete assembled complement of native viral proteins from a specific virus.

2. The report discusses in detail certain patent families, represented by patent applications, where the scope of the claims is broad and could potentially be construed as covering known viral sequences, processes and compositions of matter. It is well established that issued patents frequently have narrower claims than the corresponding patent applications. Therefore the scope of the claims in the

patent applications, identified and analyzed in this search, may very well be restricted during the patent application prosecution and grant process.

3. While some patent applications from members of the WHO Global Influenza Surveillance Network are identified as falling within the scope of the search, the report does not analyse to what extent collaborations, licenses and technology transfer are taking place between these and other entities, including between and among developed and developing countries.

4. A number of patent applications were identified from companies based in industrialized countries that are now co-owned by companies of developing countries. This is arguably one form of technology transfer and should be seen in the light of emerging models that facilitate broad access to new technologies, including in health, by developing countries.

More generally, it should also be noted that a patent is an vehicle for disclosing inventions and for making technologies publicly known. As such, the intellectual property system seeks to strike a balance between the public domain and granting limited ownership. The public disclosure embedded in the intellectual property system, in turn, encourages new research leading to accelerated innovation.

As has been described in previous reports and publications, there are patent applications and patents on novel approaches to diagnosing, preventing or treating pandemic influenza. Some will, it is hoped, ultimately lead to the availability of new, safer and more effective vaccines, therapeutics and diagnostics to benefit humanity.

Disclaimer and limitations

The information, analyses and comments presented herein do not constitute legal advice or opinion on, and are not limited to, patentability, patent infringement, and/or the validity or term of any patent, patent application or claim. Whereas reasonable efforts were made to provide reliable information, the report is not claimed to be exhaustive. It is also possible that additional patents or applications could be interpreted as falling within the scope expressed in the request from WHO. Furthermore, new issued patents/applications, modification of patent applications, revocation or abandonment of patents, and evolving case law could result in changes in the analyses contained in this report. Therefore, this report should be seen as an input for illustrative purposes. As with any patent search report, the results are based on available data from public and private databases. Such databases may contain errors or incomplete data. WIPO makes no warranty as to the integrity of the public and fee-based databases used. This report is prepared as a technical input to support discussions on influenza vaccines, diagnostics and treatments and does not seek to advance, advocate or endorse any policy position, and does not present any official view attributable to WIPO, its Member States or its Secretariat.

Acknowledgements

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1. BACKGROUND AND INTRODUCTION

In view of the emergence and circulation of highly pathogenic H5N1 avian influenza strains, the recent appearance of H1N1 influenza as a pandemic, and possibly of other pandemic strains, numerous activities are being conducted to improve the ability of the global community to respond to influenza. These include the establishment of surveillance networks, the development of diagnostic reagents and kits, and the development of vaccines to prevent infection and therapeutics to treat infection.

1.1 Influenza vaccines, therapeutics and diagnostics

Vaccines: Vaccination, one of the most cost effective approaches to controlling infectious diseases, is, in the case of influenza, hampered by the fact that influenza viruses are in continual mutation, requiring a new vaccine to be developed every year. It takes more than four months to identify that a virus with pandemic potential is circulating in humans, and to get a vaccine produced using currently approved technologies, by which time the influenza pandemic may have devastated a population. Current methods of producing the vaccine (primarily in eggs) are both relatively slow, and produce too little vaccine for the global population, leaving large parts of the world exposed to risk.[1] Several approaches to increase the percentage of the population that can be immunized include the use of live attenuated influenza vaccines, which can be produced in a higher yield than classical inactivated vaccines, and also the use of adjuvants, which reduce the dose of inactivated vaccine antigen required. An additional challenge to producing the vaccine in eggs is that pathogenic H5N1 avian influenza viruses pose a unique problem: due to their peculiar virulence, they rapidly kill embryonated chicken eggs so conventional technology does not work. The application of proprietary, largely patented “reverse genetics”, methods can overcome this, or alternatively, non-egg based production methods need to be used.

To overcome these challenges that complement egg-based production methods, numerous non-egg based systems are under development. Production of influenza vaccine on mammalian tissue culture has been established for several years, and overcomes many of the problems associated with eggs. However the cost of producing such vaccines is higher than with eggs[2] and current capacity is limited. Newer recombinant methods where only the relevant antigen is produced, rather than the virus, are under development. The developers claim that once developed, these technologies could produce vaccines rapidly and with a high yield. Production of recombinant vaccines in insect cells, plants (such as tobacco), bacteria, and fungi are all under development.

DNA vaccines are another potential method for dealing with a global H5N1 pandemic. These vaccines are not related to the above technologies, which all rely on the traditional protein/peptide vaccination, possibly bolstered with adjuvant. In DNA (or genetic) vaccines, viral genes are injected into the patient. This is a promising technology because it does not require eggs, cell cultures, or prolonged cold storage facilities. However, several technical barriers remain.

Finally, a number of “universal” influenza vaccine technologies are being developed, based on common determinants in all influenza vaccines. This approach, while still in its infancy, may enable a single vaccine to protect against any and all strains of influenza. If successful, influenza pandemics could become a threat of the past.

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1 *http://apps.who.int/gb/pip/pdf_files/OEWG3/technical-studies-en.pdf*

2 http://www.oliverwyman.com/ow/pdf_files/VAC_infl_publ_rpt_10-07.pdf

Therapeutics: In terms of therapeutics, there are currently two classes of antiviral medicines that are used for pandemic influenza:

- neuraminidase inhibitors, including oseltamivir (known under the branded name Tamiflu®) and zanamivir (e.g. Relenza®)

- M2 inhibitors, including amantadine and rimantadine, which are authorized by certain countries' drug regulatory authorities

During the 2009 (H1N1) pandemic, the neuraminidase inhibitors, but not the M2 inhibitors, showed activity against the virus strain causing the pandemic.[3] These therapeutic drugs, while very useful, have limited use in pandemic control: They are expensive and will not be available for the entire population for the entire duration of a pandemic.

Diagnostics: Regarding diagnostic tests to identify pandemic virus strains, several are used to identify and confirm outbreaks of pandemic influenza and to guide clinical decisions on treatment. The network[4] of National Influenza Centre Laboratories and Collaborating Centres in WHO Global Influenza Surveillance Network represents the main mechanism by which countries identify outbreaks and monitor influenza activity in their countries and regions. Some laboratories in the Network provide critical reagents and set standards under their WHO terms of reference.[5]

In the clinical setting, some tests are conducted with so-called "rapid point of care diagnostic kits" for influenza. These tests have the advantage that they can be performed without a laboratory; however, they must be purchased commercially, their price varies, they generally have low sensitivity, and they provide less specific information than laboratory tests.

It is clear that significant improvements in the tools available to the global community are needed, and are under development. As identified later in this document, this is an area where there is significant innovation taking place, and many of the products that are potential improvements on current tools are subject of patents.

1.2 Previous influenza-related patent searches

To the best of the authors' knowledge, there has been **no previous qualitative patent search** specifically searching for inventions comprising a "component or a derivative of the H5N1 virus strain", for diagnosing, treating or preventing infections by H5N1 and H1N1 influenza virus strains in humans. The approach adopted here requires the reading of claims and to some extent of patents which is a very time-consuming and intensive task, not least because the basis for the analysis consists of over 1,000 patent applications or patents.

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[3] European Medicines Regulatory Agency: *http://tiny.cc/x64e9*

[4] - For a list of National Institutes, *see http://tiny.cc/4dyn3.*
- For a list of WHO Collaborating Centres for Influenza and Essential Regulatory Labs, see *http://tiny.cc/qk99q*
- For a list of WHO Reference Laboratories for Diagnosis of Influenza A/H5 Infection, see *http://tiny.cc/cn635*

[5] WHO (2010). Preliminary findings for the technical studies under resolution WHA63.1. *http://tiny.cc/j2x0b*

A number of reviews looked at aggregate patent data using various types of patent search strategies. For example, a series of WIPO and WHO reports,[6] one of which was commissioned by the WHO pursuant to WHA Resolution 60.28, were based on PCT patent application searches. The reports undertook a quantitative analysis of patents in the broad influenza and H5N1 subject area with the results discussed from different technological or Intellectual Property (IP) management strategy perspectives. The analyses showed that there had been a rapid increase in the early 2000s in patenting activity broadly referring to the H5N1 subtype of the influenza virus, in the context of vaccines especially, with some modest increase in patenting activity related to diagnosis and few related to therapeutics. The activity was shown to emanate from a wide, and widening, array of players, in both the public and private sectors, including established vaccine producers, new entrant firms, individual inventors, government agencies, public research and educational institutions, and researchers drawing on traditional medicine.

The subject matter of these issued patents and patent applications (hereinafter referred to as "patents/applications") covered in the above-mentioned reports included recombinant gene sequences, other extracts and derivatives from the virus genome, new genetic constructs making use of such material, diagnostics, and more general platform technologies for the production of vaccines and treatments that made use of genetic inputs from the virus. The WIPO report of 2006 noted that much of the relevant patenting activity was initiated very recently, meaning that it will be difficult, in the medium term, to make judgments about its impact on vaccine production and pandemic preparedness because:

- patent applications typically take several years at least to be examined and for a decision to be taken on whether or not to grant a patent; in that time, the application may be withdrawn or rejected, or the scope of its claims narrowed, and

- a PCT patent application only translates into patents with direct effect under national law if and when the applicant chooses to seek protection in a specific country, so the existence of a PCT application does not imply that protection will be actively sought in all PCT countries.

In all of these three reports, the patenting activity was interpreted as signaling an intensive, broad based and diverse practical response to a potential health crisis, a development that may in principle be welcome.

Another report,[7] commissioned by the Sasakawa Peace Foundation, had as its objective to study whether different IP management strategies, particularly patent pooling, could accelerate the development and access by developing countries of vaccines and diagnostics in the areas of avian influenza, malaria, and the Severe Acute Respiratory Syndrome (SARS). For this study, the authors reviewed entire patents and claims for specific technologies being developed at the time in response to pandemic H5N1 influenza which include:

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6 WIPO (2006). Working Paper: Patent issues related to influenza viruses and their genes - An overview. WIPO: Geneva. *http://tiny.cc/6xa2t* and WHO (2007). Patent Landscape for the H5 virus: Interim Report. *http://tiny.cc/xf6l4* and WHO (2007). Mapping of Intellectual Property Related to the Production of Pandemic Influenza Vaccines. WHO: Geneva. *http://tiny.cc/dnt37*

7 Krattiger A., Kowalski S., Eiss R. and Taubman A. (2006). Intellectual Property Management Strategies to Accelerate the Development and Access of Vaccines and Diagnostics: Case Studies on Pandemic Influenza, Malaria and SARS. *Innovation Strategy Today* 2(2):67-122. *http://tiny.cc/si006*

1. RNA molecular technology (including reverse genetics)
2. DNA recombinant technology (including attenuation mutants)
3. Cell culture production systems
4. Adjuvants
5. Excipients
6. Vaccine production, and
7. Antigen delivery *(*e.g. liposomal systems).

However, the scope of that report was not to search for all potentially applicable patents, but to identify in the authors' judgments as the most promising technologies for each of the seven components listed above. In other words, the authors mapped the field, identified key players based on their IP stakes, and then discussed overall options on how creative IP management could facilitate the deployment and use of pandemic vaccines. The study identified the specific issued patents or patent applications potentially relevant for each of the seven technological areas. At that time, "reverse genetics" was considered the most promising new technology with MedImmune having made great strides in the assembly (or in-licensing) of relevant IP related to reverse genetics. At the time, MedImmune had already announced that it would grant wide access to the technology, a statement that has now been expanded significantly (see Section 4 below). One of the conclusions of that study was that patent pooling approaches would not be viable strategies, except perhaps for SARS diagnostics, and that the overall investment into research and development (R&D) was the major constraint for the world to see the existence of an effective and rapidly producible pandemic influenza vaccine, together with increased investments into manufacturing capacity to rapidly produce high quantities of a pandemic influenza vaccine.

A different analysis, which also includes comprehensive and detailed discussion of the scientific basis, particularly the molecular aspect, of influenza viruses, was prepared by Cambia.[8] This patent landscape analysis differs from the others in that it focused the searches on specific DNA and proteins (based on amino acid sequence searches) and then analyzed and discussed in detail specific claims and claim language based on United States (US) granted patents/applications. In many countries, particularly Asian countries with avian flu occurrence, patent searches were impossible but, as with any such patent landscape, it is always hoped that the searches in online accessible databases cover most internationally operating actors.

Key findings of the Cambia study are:

- One-half of the patents are directed to equine influenza virus (assignee = Heska Corp.).

- None appear to claim the H5 subtype of segment 4, which encodes hemagglutinin (HA) or the N1 subtype of segment 6, which encodes neuraminidase (NA).

- Of the two patents that claim HA sequences, one claims sequence encoding the signal peptide region from HA1 and HA3 (US6245532), and the other claims an antigenic fragment of HA2 and HA3.

- Claims of three patent applications are directed to reassortment viruses, useful as vaccines against H5N1 (US20060008473) or H1N1 (US20050003349).

- Of the remaining patent applications that initially claimed influenza nucleic acids, only about one-half still claim nucleic acid sequences and most of these are directed

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[8] *http://www.patentlens.net/daisy/influenza/4132.html*

to sequences encoding internal proteins.

- For the granted patents with nucleotide claims, 75% were assigned to corporations and 25% were assigned to non-profit organizations. For the patent applications, 47% were assigned to corporations and 53% were assigned to non-profit organizations.

The comprehensive publication then goes on to discuss some of the specific claims to amino acid sequences and noted:

- Most of the patent claims are directed to short peptides.

- Most of the patent claims reciting full-length or near full-length proteins are drawn to equine influenza virus proteins.

- Patent claims can be open-ended with respect to subtypes of influenza proteins, such as claiming a reassortant virus in which the sequences of the six internal proteins are specified but the sequences of hemagglutinin (HA) and neuraminidase (NA) are unspecified.

- Peptides in the claims may be used for a variety of purposes, and especially for vaccines.

- Claims of the patent applications are similar to those from patent grants, except that the number of sequences in the claims is higher.

- For the granted patents with peptide claims, 45% were assigned to corporations and 55% were assigned to non-profit organizations. For the patent applications, 70% were assigned to corporations and 30% were assigned to non-profit organizations.

Finally, there are a number of other publications, two of which review different approaches to dealing with information and/or patents.[9, 10] Both of these reports, like the earlier WIPO report, found significant patent filing increase over the previous 5 to 8 years and discuss from different perspectives the potential implications of such patent filing trends.

1.3 Patents and the patent system

The **disclosure** of comprehensive technical information is a core function of the patent system and indeed one of the patentability requirements. It is not possible to seek patent protection without sufficiently clear and complete disclosure of an invention and the related technical information.

Whereas international treaties have created a framework for the international patent system, there is no world patent. This international framework has brought about certain synergies in law and practice and is the basis for considerable cooperation on patent administration. But a patent remains strictly **a territorial right** in both grant and

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[9] Andrews L.B. and Shackelton L.A. (2008). Influenza genetic sequence patents: where intellectual property clashes with public health needs. Future Virol. 3(3), 235–241. doi: 10.2217/17460794.3.3.235. *http://tiny.cc/peqt1*

[10] Hammond E. (2009). Some Intellectual Property Issues Related to H56N1 Influenza Viruses, Research and Vaccines. Third World Network: Penang. *http://www.twnside.org.sg/title2/IPR/ipr12.htm*

enforcement. Where no patent is in force, technology, even if patent protected in other countries, is free for use by anybody.

An invention, provided it relates to patentable subject matter, will be patentable only if the following **patentability criteria are cumulatively met**:

- An invention is regarded as ***new***, if it has not been known to the public before a date that is defined in the national law, for example the date of filing the patent application. The national law defines what the relevant public is, and which kind and form of documentation, if any, is required, etc. For instance, a virus delivered, in a country, from a health authority to a WHO Collaborating Centre on Influenza would be known to that health authority, a doctor, staff in a hospital, a research institution, the WHO Collaborating Centre, etc., and, for that reason, as such would no longer be considered new under patent law and therefore would not be patentable.

- The requirement of ***inventive step*** is also referred to as ***non-obvious*** by some laws. Patent law, in general, defines just the basic concept of what constitutes an inventive step and leaves the interpretation to the practice of national patent offices and the supervising courts. Practice has developed different methodologies based on a vast number of indicators that help a patent examiner in the determination of the *inventive step*. These indicators may not always be easily understood by the general public, but, in general, can be well handled by, and are clear to patent examiners. This approach of defining only the general concept in the law is of considerable value in dealing with technological development and new technologies. It reflects the inherent purpose of the patent system to deal with innovation. Since innovation is not known in advance, a legal determination would not give appropriate answers before knowing for what it would be applied. On the other hand, what was regarded as inventive at a given time might be standard later. For example, it might have been a huge scientific advance to isolate a virus in the 20th Century, but doing this today through regular techniques may no longer be considered inventive and therefore not patentable.

- The requirement *capable of* ***industrial application*** may be referred to as ***useful*** by some laws. This means that the invention can be made or used in any industry, including agriculture, or that it needs to have a specific, credible, and substantial utility. In general, the application of this requirement does not pose practical problems. However, in the field of biotechnology, namely in respect of inventions related to genes, it needs some considerations. While no common or broadly applied practice can be observed, it can be noted that some jurisdictions require that the function of a gene needs to be clearly identified and be related to the claimed invention. This practice, where applied, addresses concerns that patent applications claiming gene related inventions would block the use of the claimed gene sequence for uses that were not yet known by the applicant and, hence, would not justify the grant of a patent in respect of the function the applicant was not even aware of. In other words, if an inventor identified a naturally occurring substance and made it available for the first time, even if it would be considered patentable substance matter, inventive and a huge scientific advance, it would still not be patentable in case the function of that substance was unknown or incompletely understood. For example, when the substance could not be related to a disease or any other practical use like the production of a vaccine.

Generally, patents are granted on inventions which may be **products or processes**. Most jurisdictions typically identify subject matter that is not an invention, for example laws of nature, natural phenomena, or abstract ideas. Additional subjects may be regarded as not patentable according to the national legislations, for example biological processes, such as plant or animal breeding, diagnostic, therapeutic and surgical methods for the treatment of humans or animals, or where the commercial exploitation contravenes *ordre public* or morality.

Once granted, patents confer the right to its assignee to **exclude** others from making, using, offering for sale, selling or importing into the country (national jurisdiction) where the patent rights are granted. National laws, from a public interest perspective, normally provide certain exceptions and limitations to the rights conferred, such as private use or research exceptions. Often, anyone may freely use a patented invention privately or for the purposes of research and experiment.

Patent protection is **limited in time**. Patent laws provide in general for a patent protection term of 20 years from filing. Patent owners, on the other hand, may withdraw patents, for example, if the commercialization of the invention does not bring the expected return, or if it does not cover the costs of maintaining the patent. And patent owners may license or assign a patent to a third party. Patents may also be invalidated based on grounds established by the national law.

In exchange for the prospect of being granted a patent, the inventor discloses the invention in the patent application. In most countries, patent applications are published even if patents have not been granted. But in all countries patents are published upon grant. Thus, disclosing the invention is another public policy component of the patent system, whereby the technology is initially disclosed to teach and advance innovation for the benefit of the society, and subsequently, upon patent term expiration, released into the **public domain** for all to use.

2. OBJECTIVES, METHODS AND APPROACHES

2.1 Objectives

The objective, as per request of the Director-General of WHO to WIPO, was to seek information from WIPO on pandemic influenza preparedness-related patents, including patent applications, in connection with the H5N1 and H1N1 virus and pandemic.

The phrase “in connection with” is rather ambiguous when searching patents, hence, in technical consultation between WIPO and WHO this phrase was clarified as referring to:

- patents or patent applications claiming inventions comprising the virus, a component, or a derivative of the virus, for diagnostic, therapeutic or prophylactic purposes, and

- where the patent was applied for after the date at which it became clear that that strain of virus could be of pandemic potential (post 1995 for H5N1 and post-March 2009 for H1N1).

2.2 Overall patent search strategy

European and US patents/applications and international PCT patent applications were identified as follows:

- filed after January 1, 1996,[11] claiming inventions comprising a component or a derivative of the H5N1 virus strain, for diagnosing, treating or preventing infections by H5N1 influenza virus strains in humans; and

[11] H5N1 has crossed the species barrier to infect humans in Hong Kong in 1997.

- filed after April 1, 2009,[12] claiming inventions comprising a component or a derivative of the pandemic (H1N1) 2009 virus strain, for diagnosing, treating or preventing infections by pandemic H1N1 influenza virus strains in humans.

A subset of the above-mentioned patents or patent applications were identified where the assignee is a member of the WHO Global Influenza Surveillance Network,[13] distinguishing among the four categories of laboratories:

- WHO Collaborating Centre on Influenza
- National Influenza Centres
- H5N1 Reference Laboratories
- Essential Regulatory Laboratories.

The above-mentioned patents were categorized into the following categories:

- vaccines
- diagnostics, and
- therapeutics.

The patent search data/results presented in this study are current as of February 12, 2011.

2.3 Scope of patent coverage

Patent applications:

- USPTO
- EPO
- WO (PCT) applications covering 142 contracting States.

Granted patents:

- USPTO
- EPO
- Patent Cooperation Treaty filings

2.4 Patent document search methodology

A broad-based keyword search of “H5N1” or “H1N1” was conducted in the full patent specification fields (i.e. anywhere in the patent or patent application, be it a title, an abstract, the title of a cited reference, a specification or a claim), with a date limit of earliest priority date as:

- post 1995 for H5N1, and
- post-March 2009 for H1N1.

Primarily the MicroPatent® platform was used, complemented with some PatentScope® searches. The former allowed for easy elimination of duplicate results, the reduction of the dataset to one patent per patent family and the export of the data into spreadsheet.

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12 H1N1 was declared to be highly pathogenic in April 2009.

13 See supra note 4.

2.5 Patent families

A patent family is a collection of published patent documents relating to the same invention, or to several inventions sharing a common aspect, that are published at different times in the same country or published in different countries or regions. Each patent document in such a collection is normally based on the data for the application(s) on which the basis for its "priority right" has been claimed.[14] Without patent families, searches are both onerous and complicated because the multiple different jurisdictional applications are shown as independent results, making quick viewing and analysis of the patent landscape time-consuming, confusing and difficult. Therefore, using patent families eliminates the multiplicity of domestic and foreign filings when searching for patents, because a single representative member will be displayed in the results and all foreign filings of the same invention will be displayed in an organized, easy to read format.

However, while solving difficulties with multiplicity while searching, patent families are not infallible, and patent family analysis and data may, or may not, be congruent with all results presented in this study. Disparities could be due to a number of variables. For instance, country reporting of family, i.e. national jurisdictional status, might not be timely or complete. In addition, changes in prosecution status might affect document availability in databases, e.g. rejection of patent applications at various stages in prosecution, including continuations, continuations in part and divisional applications, or amendments of patent claims. Finally, there is currently no single convention for defining a patent family.[15] Thus different patent family generating services, e.g., INPADOC, Derwent® or MicroPatent®, assemble patent family data using different strategies. Depending on the patent family generating service used, the possibility exists the precise relationships, based on priority documents, can create somewhat complex family trees, with degrees of relationship among patent documents differentially represented. Again, for the present report, the algorithm of MicroPatent® was used to condense the list of patents and applications of patent families to one representative document per patent family.

2.6 "BLAST" sequence search

As a corroborative and complementary analytical strategy, a Basic Local Alignment Search Tool (BLAST) was performed sequentially, first using NCBI Genbank,[16] followed by searching through Cambia's PatentLens BLAST search engine.[17]

A number of representative sequences was selected to identify whether this search strategy significantly increased the number of patents/applications identified: NCBI viral accession numbers searched for sequence data included:

1. **ABD28180** 567 Human HA H5N1 China 2005 Influenza A virus (A/Anhui/1/2005(H5N1))

2. **ADR78646** 564 Human HA H5N1 Cambodia 2005/04/07 Influenza A virus (A/Cambodia/408008/2005(H5N1))

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[14] WIPO (2008*). WIPO Handbook on Industrial Property Information and Documentation***.** Part 8, Section 8.1, Glossary of Terms Concerning Industrial Property Information and Documentation, Geneva, WIPO, pages 8.1.18 to 8.1.19, and Appendix III (pages 8.1.34 to 8.1.36): *http://www.wipo.int/export/sites/www/standards/en/pdf/08-01-01.pdf*

[15] European Patent Office. *http://www.epo.org/searching/essentials/patent-families.html*

[16] *http://www.ncbi.nlm.nih.gov/nuccore/*

[17] *http://www.patentlens.net/sequence/blast/blast.html*

3. **ABI36406 568** Human HA H5N1 Indonesia 2006/05/22 Influenza A virus (A/Indonesia/CDC625L/2006(H5N1))

4. **ABI36439** 568 Human HA H5N1 Indonesia 2006/06/13 Influenza A virus (A/Indonesia/CDC669P/2006(H5N1))

5. **ABI36340.1** H5M1 Indonesia

Accession number searches on NCBI Genbank generated amino acid sequence data which were then BLAST analyzed on PatentLens for both granted US patents and US patent applications wherein the sequences were claimed, as per the search criteria for BLAST.

At the PatentLens search engine, results are displayed as patent documents, ordered according to degree of homology as to sequence entered, i.e., decreasing homology in the list of results. Analysis therefore proceeds from greatest homology downward, analyzing documents for relevance; this is ascertained by actual examination of the documents. Since homology is a gradient, there is a cut-off point in relevant results where related viruses, e.g., seasonal influenza (A, B, C) begin to appear. Therefore, these, and those below a certain degree of homology, were not considered in this analysis as they fall outside the H5N1 statistically significant range of homology.

The BLAST search was not performed for H1N1 because no patents have yet been issued for H1N1 that meet the criteria of this study. The BLAST search only looks for issued patents.

2.7 "Portfolio" search

Recognizing that the time available for this patent search report was very short, a very limited and narrow portfolio search was conducted of main assignees. That search could be extended to include additional assignees including frequent inventors. The rationale for this relates to the recognition that many patents/applications did not include H5N1 anywhere in the document and would further complement the BLAST search.

2.8 Patent scoring

All patents were read and analyzed by at least two of three reviewers. Each of them had previously been scientist with backgrounds in biology, genetics, molecular genetics and/or immunology and each with experience in IP managements and patents. One of the team members was also a law professor (IP specialty) with an advanced degree in biochemistry and genetics. In the cases where the scoring given by the first two reviewers did not concur, or where the scoring was not evident, the group of three people discussed and eventually agreed on the scoring.

Recognizing that the context of the report relates to the WHO Open-Ended Working Group (OEWG) of Member States on Pandemic Influenza Preparedness (PIP), which is currently discussing aspects of virus sharing, the analysis of the documents on pandemic influenza-related patents/applications in connection with the H5N1 virus and the pandemic H1N1 patents/applications led us to classify patents into three categories, with pandemic influenza H5N1 or H1N1[18] (Table 1):

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[18] As discussed in Section 1.1 of this report, there are a multitude of technologies to develop, manufacture and deliver pandemic influenza vaccines. These include: various vaccine production methodologies, including cell culture production systems, adjuvants, excipients, and possibly antigen delivery systems, such as liposomal systems. All of these technologies need

[Footnote continued on next page]

Table 1: Patent scoring and categories of patents/applications

	Group 1	**Group 2**	**Not applicable**
	Relevant and clearly within the scope of the request	Relevant and subject to interpretation	Not falling within the scope
Description	For example, sequences *per se,* or essential derivatives thereof. H5N1 or H1N1 sequences, either peptide or nucleic acid, is specifically claimed as the invention, for example, SeqABC, which is then disclosed in the specification	Sequences are one part (element) of claimed invention, however H5N1 or H1N1is an integral element of the invention, for example a H5N1 vaccine that articulates a section of the viral genome. For example, composition of matter wherein said sequences are an important element of the invention, but where said sequences are not claimed *per se*	H5N1 or H1N1 are neither claimed nor integral to the claimed invention, but may be included in an embodiment. In some cases, certain patent applications were not clear.[19] They included disclosure of H5N1 or H1N1 but it could not be ascertained whether a derivative of H5N1 or H1N1 sequence was claimed
Example of a patent or application	US20060024670A1, Influenza Virus Vaccine Composition and Methods of Use (claims sequences)	US20040142319A1, Kit for Detecting Non-Pathogenic or Pathogenic Influenza A Subtype H5 Virus (H5N1 sequence as part of a diagnostic kit)	US20090047728A1, Adenoviral Vectors for Influenza Virus Production (A general adenoviral platform which includes H5 as an embodiment)
Illustrative exemplary claim	*393. An isolated polynucleotide comprising a first nucleic acid fragment which encodes at least 20 contiguous amino acids of an influenza virus polypeptide, the amino acid sequence of which is selected from the group consisting of …*	*1. A kit for detecting non-pathogenic or pathogenic influenza A subtype H5 virus in a biological sample including …* *5. A kit for detecting non-pathogenic or pathogenic influenza A subtype H5 virus as claimed in claim 4, wherein the first DNA sequence encodes either one of the DNA sequences set forth in SEQ ID Nos.1, 2, or 3. …*	*24. The host cell of claim 23 wherein the HA is a H5 HA.*

[Footnote continued from previous page]

to be integrated to develop and deliver vaccines. However, the specific request from WHO was not aimed at (and thus the approach of the present patent search and patent interpretation was not designed to) covering non-virus related patents.

[19] Partially depending on national patent law and patent prosecution approaches.

- **Group 1 - Relevant and clearly within the scope of the request**

(Claiming sequences *per se,* or essential derivatives thereof)

Falling definitely within the scope: this includes patents claiming the virus, an isolated antigen from the virus, an isolated fragment of an antigen from the virus, and/or an isolated oligo- or poly-nucleotide sequence corresponding to the RNA sequence of the virus. In this category the invention is either derived from H5N1 or H1N1 sequences, or claim the antigens or nucleotide sequences in isolation.

- **Group 2 - Relevant but subject to interpretation**

(Viruses, components, or derivatives of the virus are only one part or element of the claimed invention; however, H5N1 or H1N1 is an integral element of the invention, for example a H5N1 vaccine that articulates a section of the viral genome)

Falling within the scope: this includes the applications or patents that claim fragments or derivatives of the virus, but where the invention is about a novel concept (novel method of making vaccines, novel adjuvant, vector etc.) and where the claims include the use of an H5N1 or H1N1 peptide(s), nucleic acid(s) or antigen in the invention, rather than the use as an isolated component. This is in contrast to Group 1 where the invention *per se* is derived from, and indeed articulates, H5N1 or H1N1 sequences. Group 2 therefore includes concepts such as nucleic acid primers, diagnostic kits and vaccine compositions that necessarily embody, but do not claim in isolation, viral peptide (s), protein(s), antigen(s) or nucleic acid components.

- **Not Falling Within the Scope**

In this category those applications and patents were included where it is not immediately clear that a derivative of H5N1or H1N1 sequence is claimed, but H5N1 or H1N1 is included in the disclosure. This categorization section also includes inventions wherein viral sequences are articulated as possible embodiments, but are as one embodiment not integral *per se* to the invention, e.g., adenoviral vectors (the “essential” invention) expressing H5N1 or H1N1 antigens. Of the 1024 applications and patents identified in the initial search, the vast majority are on therapeutic drugs to treat viral infections including antivirals, plant-derived remedies, and monoclonal antibodies. The antiviral drugs and plant derived therapies clearly do not fall within the scope of the search since they are not derived from the virus. Although making monoclonal antibodies requires using the virus, the compositions claimed in the applications or patent are in most cases not a derivative of the virus and hence should not be considered falling within the scope of the search.

3. RESULTS AND ANALYSIS

3.1 Introduction

The patent/application search using a simple search for H5N1 or H1N1 “anywhere” in the patents/applications generated an initial set of 2119 documents for H5N1 and 81 for H1N1. It is important to note that the number of documents does not represent the number of patents that claim any part or use of H5N1 or H1N1. Rather, the document numbers correspond to the total number of patents/applications that mention, or even cite in references, H5N1 or H1N1. As such, this aggregate number of documents is therefore quite inconsequential as it corresponds to an initially, intentionally broad keyword search designed to capture a large pool of documents that could subsequently be mined for potential relevancy.

The 2119 and 81 documents, respectively, were then condensed to one representative document per patent family (see Section 2.4 above). This generated a list of 1024 documents for H5N1 and 76 for H1N1.[20] Again, it should be noted that this consolidated list of patents/applications also does not represent the number of patents/applications that claim any part of H5N1 or H1N1. For example, application US20090175963A1 claims a composition of foods for preventing influenza virus diseases, comprising *Lycorissquamigera* extracts and a sitologically acceptable supplemental additive. In another application, DE202006001115U1, the subject matter is a rescue vehicle characterized in that the vehicle is negatively pressurized with air filters to prevent bacteria or viruses contaminating the environment during the transport of infectious patients. H5N1 is given as one example of the types of organisms that could thus be filtered.

Claims of one family representative of each of the identified patents/applications (1024 for H5N1 and 76 for H1N1) were then analyzed and scored for relevancy. This involved the reading of the claims and in many cases analysis of the entire patent/application, particularly the "enablement" specifications (see Section 2.7 above on the scoring and classification of the patents/applications). As with any such scoring/classification, there is an element of interpretation and judgment with the result that someone else could potentially argue that one or another patent/application could have been classified under a different group. Notwithstanding this, it is not believed that a few changes of classification would materially affect the results.

3.2 Group 1 patent families

(Relevant and clearly within the scope of the request)

Of the 1024 documents citing H5N1 anywhere in the document, 26[21] are classified as Group 1 (elements of the isolated virus, antigen or essential derivatives) and 35 as Group 2 (elements of the virus, antigen or derivative in a specific composition of matter or process). The majority, and remaining 964 patents/applications for H5N1 and 64 H1N1, including the 27 patents/applications that relate to inventions in the field of monoclonal antibodies (mAb), do not cover, in our view, the specific criteria for inclusion in either Group 1 or 2.

Table 2 lists the essential data of the H5N1 and H1N1 patents/applications that meet the scoring criteria for Group 1 patents/applications as per WHO's request. One patent identified through the BLAST search (see Section 3.5 below) is also listed in Table 2, including one patent identified through a limited portfolio search (see Section 3.6 below), bringing the total Group 1 patents to 27.

Note that only one family member is listed per data set. This primary family member is, in all cases, a patent application because the algorithm used by MicroPatent® to identify leading patents from families typically lists US applications and PCT (WO) applications as preferred representative documents of patent families (see also Section 2.5).

The patent applications listed in Table 2 clearly fall within the scope; they include patents/applications claiming isolated and sequenced elements of the virus, an isolated antigen from the virus, an isolated fragment of an antigen from the virus, or an isolated

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[20] The full table, including related family members, is available in Microsoft® Excel® spreadsheet, comprising full abstracts, full claims, priority filings, and designated States among other information. Please write to *global.challenges@wipo.int* if you wish to receive an electronic copy of the table.

[21] Twenty-five were identified with H5N1 in the text, one was identified using the BLAST search (see Section 3.5) and one with the portfolio search (see Section 3.6).

oligo- or poly-nucleotide sequence corresponding to the RNA sequence of the virus. In this category, the invention is either derived from H5N1 or H1N1 sequences, or claim the antigens or nucleotide sequences in isolation. It should be noted, once again, that all of the documents listed in Table 2 are patent applications and the claims may, and in many cases will, be amended during prosecution of the application and possibly be limited significantly prior to the patent issuance and grant. Nevertheless, certain claims could potentially be interpreted as having broad scope, as highlighted in the examples discussed below.

Example of a vaccine-related invention: US20050287172

This application[22] claims, among others:

1. A 6:2 reassortment influenza virus, wherein said virus comprises 6 gene encoding regions from one or more donor viruses other than A/Ann Arbor/6/60 and 2 gene encoding regions that encode an HA and/or a NA polypeptides from a pandemic virus strain.

2. The 6:2 reassortment influenza virus of claim 1, wherein said donor virus has one or more of the following properties: temperature-sensitivity, cold-adaption, or attenuated.

3. The 6:2 reassortment influenza virus of claim 1, wherein said donor virus is PR8.

4. The 6:2 reassortnent influenza virus of claim 1, wherein said donor virus is A/Leningrad/17.

5. Etc.

Importantly, these broad claims could be interpreted to be claiming certain reassortant influenza virus strains to be used against pandemics, including elements from reference strains and live attenuated strains. However, the granted US patent (US7527800) derived from this application is much narrower and claims:

1. A reassortant influenza virus, wherein said virus comprises 6 internal genome segments from one or more donor viruses other than A/Ann Arbor/6/60, a first genome segment encoding a neuramidinase polypeptide comprising the amino acid sequence of SEQ ID NO:16, and a second genome segment encoding a hemagglutinin polypeptide comprising the amino acid sequence of SEQ ID NO:15, wherein said second genome segment comprises the nucleotide sequence of SEQ ID NO:5.

2. Etc.

The sequences 5, 15 and 16 in this case refer to A/Hong Kong/491/97 (HA)+A/Hong Kong/486/97 (NA), A/Hong Kong/491/97 H5, and A/Hong Kong/486/97 N1 respectively. The claims have thus been significantly restricted in this granted form.

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[22] Other family members include, some have of which been issued: AU2005248375A1, AU2005248375B2, AU2005248377A1, CA2568015A1, CA2568020A1, EP1766059A2, EP1766059A4, EP1771552A2, EP1771552A4, JP2008500041T, JP2008500042T, US20060008473A1, US20090136530A1, US20090175909A1, US7504109B2, US7527800B2, US7744901B2, WO2005116258A2, WO2005116258A3, WO2005116260A2, WO2005116260A3.

Table 2: List of Patent Families in Group 1

Publication No.	Assignee or Applicant or Inventor[a]	Country[b]	Network[c]	Invention[d]
H5N1				
US20050287172A1	MedImmune, LLC	US	No	VD
US20060024670A1	Catherine J. Luke	US	No	V
US20070259337A1	Intelligent Medical Devices, Inc.	US	No	D
US20070286873A1	John V. Williams	US	No	VD
US20080057081A1	MedImmune Vaccines, Inc.	US	No	V
US20080193471A1	BoehringerIngelheimVetmedica, Inc.	US	No	V
US20080193472A1	Variation Biotechnologies Inc.	Canada	No	V
US20080254065A1	Chiron Corporation	US	No	V
US20080261198A1	EeCheeRen	Singapore	No	D
US20090060949A1	David D. Ho	US	No	VT
US20090061417A1	Agency for Science, Technology and Research	Singapore	No	D
US20090074804A1	National Health Research Institute	Taiwan, Province of China'	No	V
US20090106864A1	Dow Agrosciences LLC	US	No	V
US20090305243A1	Biomerieux SA	France	No	D
US20090317795A1	Harumi Minekawa	Japan	No	D
US20100074916A1	US Government, Dept. HHS	US	No	V
US20100136098A1	National Institute of Infectious Diseases, National Univ. Corp. Hokkaido University, Saitama Medical University & NOF Corp.	Japan	CCI, NIC, RL	V
US20100166787A1	David B. Weiner	US	No	V
US20100189745A1	Baxter International Inc. & Baxter Healthcare S.A.	US	No	V
US20100285982A1	US Government, Dept. HHS	US	No	V
US20100291128A1	Gaetano T. Montelione	US	No	V
US7566458	MedImmune, LLC	US	No	V
WO2008124331A1	Cytogenix, Inc.	US	No	V
WO2009092038A1	US Government, Dept. HHS	US	No	V
WO2010111597A2	The Johns Hopkins University	US	No	V
WO2010151673	MedImmune	US	No	V
WO2011008171A1	Agency for Science, Technology and Research	Singapore	No	D
H1N1				
US20110033490A1	Massachusetts Institute of Technology	US	No	V
US20110052618A1	MedImmune, LLC	US	No	V
WO2010124373A1	Her Majesty the Queen in Right of Canada as Represented by the Minister of Health	Canada	No	V
WO2011008171A1	Agency for Science, Technology and Research	Singapore	No	D

[a] Assignee	As listed on patent document. To simplify the table, in cases where no assignee institution was listed, the first inventor's name was included. In cases where assignee institutions and inventors were listed, only the institution was included. Data on assignees and inventors is available in the Annex.
[b] Country	The country listed here is the country where the primary applicant or first inventor is located. It does not necessarily represent the headquarters of the parent institution, nor the priority country of the patent application, nor the country where the invention was made.
[c] Network	CCI: WHO Collaborating Centre on Influenza; NIC: National Influenza Centre; RL: H5N1 Reference Laboratories; ERL: Essential Regulatory Laboratories
[d] Type of Invention	V: vaccine; D: diagnostic; T: Therapeutic.

Example of a diagnostic-related invention: WO2011008171A1

This application, claims, among others:

1. An isolated oligonucleotide comprising at least one nucleotide sequence selected from the group consisting of: SEQ ID NO:1 to SEQ ID NO:19, fragment(s), derivative(s), and complementary sequence(s) thereof.

2. The oligonucleotide according to claim 1, wherein the oligonucleotide sequence is between 13 and 35 linked nucleotides in length and comprises at least 70% sequence identity to any one of SEQ ID NO:1 to SEQ ID NO:19.

3. Etc.

32. A method of detecting and/or quantitating the presence of influenza in a biological sample, the method comprising the steps of: (a) providing at least one biological sample; (b) contacting at least one oligonucleotide according to any one of claims 1 to 4, with at least one nucleic acid in the biological sample, and/or with at least one nucleic acid extracted, purified and/or amplified from the biological sample; and (c) detecting and/or quantitating any binding resulting from the contacting in step (b) whereby the virus is present when binding is detected.

33. Etc.

This particular application claims the use of specific sequences for a particular diagnostic. However, independent claims do articulate, *per se*, isolated nucleic acids. The sequences claimed in this application are found in a very large range of either H1N1 or H5N1 viruses, and are not specific to a unique viral isolate. We consider, however, that this falls within the scope of the definition of “claiming a viral component or derivative”. Several of the diagnostic applications fall within this scope, where sequences found across a broad range of isolates are claimed either in isolation, or as tools to identify viruses.

Example of isolated nucleotide sequences as vaccines : WO2009092038

This application claims, amongst other things:

1. An Influenza vaccine comprising one or more DNA constructs encoding at least two divergent HAs, wherein each of said one or more DNA constructs encode one or more of said at least two divergent HAs, wherein an immune response is induced to a plurality of strains of influenza virus upon administration of the vaccine to a subject, wherein at least one strain of the plurality of strains is not the same strain as each strain that contains a gene that encodes each of said at least two divergent HAs.

The claims go on to specify the use of specific strains including for example H5 HAs from A/Anhui/1/2005, A/Indonesia/05/2005, and A/chicken/Nigeria/64 1/2006 (claims 2-26 are not shown):

27. The method of Claim 12 wherein the DNA construct encodes H5 HAs from A/Indonesia/05/2005, A/Anhui/1/2005 and A/Vietnam/ 1203/2004.

28. Etc.

This and several other applications describe the use of DNA to vaccinate people, and claims the use of DNA sequences which are essential derivatives of the viral RNA sequences.

3.3 Group 2 patent families
(Relevant but subject to interpretation)

The H5N1 and H1N1 patents/applications that meet the second tier scoring criteria are given in Table 3. As with Table 2, only one family member per patent family is listed; this primary family member is, in all cases, a patent application. However, some family members have been issued in certain jurisdictions and these can be identified in the Annex.

Falling within the scope in Group 2 are the applications where patent claims include fragments or derivatives of the virus, but where the invention is about a novel concept (novel method of making vaccines, novel adjuvant, vector etc.) and where the claims include the use of an H5N1 or H1N1 antigen in the invention, rather than as an isolated component. This is in contrast to Group 1 patents/applications where the invention is derived from H5N1 or H1N1 sequences. This section therefore includes concepts such as adenoviral vectors expressing H5N1 or H1N1 antigens, compositions comprising a novel adjuvant and an H5N1 or H1N1 antigen (where the invention is on the adjuvant, but the claims include H5N1 or H1N1), etc. Also included in this category are those applications which are on novel antigen production methods (such as antigen expression in plants, fungi, insect cells etc.) and where the claims include the use of the production method for H5N1 or H1N1 antigens.

Example of a vaccine composition-related invention WO2010148386

This application claims:

1. An influenza virus-like particle (VLP) comprising an Ml protein, an HA protein, and an NA protein, wherein said HA protein and/or said NA protein is derived from a swine-origin influenza A virus.

2. The VLP of claim 1, wherein said swine-origin influenza A virus is an H1N1strain.

3. Etc.

The claims go on to include claims wherein said Ml protein is derived from avian influenza strain A/Indonesia/5/05, and also where the H1N1strain is influenza A/California/04/09. In this context, the application clearly falls within the scope of the search in that specific H5N1 and H1N1 sequences are claimed, however these are claimed in this specific vaccine technology which is a VLP, and as disclosed in the application, the VLP is made in insect cells.

Example of a vaccine-related invention: US20100189731A1

This invention encompasses influenza vaccines, in particular avian influenza vaccines. The vaccine may be a subunit vaccine based on the hemagglutinin of influenza. The hemagglutinin may be expressed in plants including duckweed. The invention also encompasses recombinant vectors encoding and expressing influenza antigens, epitopes or immunogens which can be used to protect animals against influenza. It encompasses also a vaccination regimen compatible with a strategy of differentiation of infected from vaccinated animals (so-called “DIVA” strategy), including a prime-boost scheme using vector and subunit vaccines.

This application claims, amongst other:

1. A composition comprising an avian influenza antigen and a pharmaceutical or veterinarily acceptable carrier, excipient, or vehicle.

2. The composition of claim 1, wherein the avian influenza antigen comprises an immunogenic fragment comprising at least 15 amino acids of an avian influenza polypeptide.

Table 3: List of Patent Families in Group 2

Publication No.	Assignee or Applicant or Inventor [a]	Country[b]	Network[c]	Invention[d]
H5N1				
EP1923070A1	Intervet International B.V.	Netherlands	No	V
US20040142319A1	Albert Cheung-Hoi Yu	China	No	D
US20060257860A1	Gen Probe Inc.	US	No	D
US20070003576A1	Andrea Bambotto	US	No	V
US20070031453A1	St. Jude Children's Research Hospital	US	CCI, RL	VD
US20080032921A1	Pharmexa Inc.	US	No	V
US20080118531A1	Wyeth & St. Jude Children's Research Hospital	US	CCI, RL	V
US20080299151A1	Statens Serum Institut	Denmark	NIC	V
US20090111089A1	US Government, Dept. HHS, Centers for Disease Control and Prevention	US	CCI, NIC, RL	D
US20090123909A1	The Board of Trustees of the Leland Stanford Junior University	US	No	D
US20090136532A1	Steven Robert Webb	US	No	V
US20090169505A1	RuxandraDraghia-Akli	US	No	V
US20090169576A1	Roberto Crea	US	No	V
US20090304730A1	Yeda Research and Development Co. Ltd. at the Weizman Inst. of Science	Israel	No	V
US20090324644A1	Oliberto Sanchez Ramos	Cuba	No	V
US20100098721A1	St. Jude Children's Research Hospital	US	CCI, RL	V
US20100137412A1	Institut Pasteur of Shanghai	China	No	D
US20100166769A1	Academia Sinica	China	No	V
US20100189731A1	XuanGuo	US	No	V
US20100239610A1	Medicago Inc.	Canada	No	V
US20100297174A1	Adolfo Garcia-Sastre	US	No	V
WO2007065967A1	Remedal OY	Finland	No	V
WO2007129984A1	Temasek Life Sciences Laboratory Ltd.	US	No	V
WO2008040098A1	Medvet Science PTY LTD	Australia	No	V
WO2008059018A2	Intervet International B.V.	Netherlands	No	V
WO2009068992A1	Novartis AG	Switzerland	No	V
WO2009074861A2	Powderject Research Ltd.	GB	No	V
WO2009150532A1	Novartis AG	Switzerland	No	V
WO2010036970A2	Fraunehofer USA, INC.	US	No	V
WO2010092476A1	Novartis AG	Switzerland	No	V
WO2010103022A2	Sanofi Pasteur	France	No	V
WO2010125201A1	Redbiotec AG	Switzerland	No	VD
WO2010134094A1	Panacea Biotech Ltd.	India	No	V
WO2010148386	Novavax, Inc.	US	No	V
WO2011003100A2	Massachusetts Institute of Technology	US	No	VTD
H1N1				
US20110045022A1	Theodore Tsai	US	No	V
WO2010125202A1	Cytus Biotechnology AG	CH	No	V
WO2010125461A1	Novartis AG	US	No	V
WO2010127252A2	Vanderbilt University	US	No	VD
WO2010129558A1	IBIS Biosciences, Inc.	US	No	D
WO2010148386A1	Novavax, Inc.	US	No	V
WO2011011390A1	Novavax, Inc.	US	No	V

See Table 2 above for notes.

3. The composition of claim 1, wherein the avian influenza antigen is expressed in duckweed.

4. Etc.

Although the application articulates the production of H5 haemagglutinin antigen derived from A/chicken/Indonesia/7/2003 in duck weed (*Lemna minor*) cells, the claims, as currently written are broader than this; it is possible that subsequent prosecution of the patent application will lead to narrowing of the claims, with a focus on the plant expression system (claims 5 to 20 are not given here):

21. A stably transformed duckweed plant or culture transformed with a gene for expressing an avian influenza antigen or fragment or variant thereof.

22. Etc.

Example of a vaccine-related invention: WO2010103022

This application claims an H5 derived antigen, but in a very restricted and limited use: i.e., two steps, where two different H5 antigens are used. In other words, this invention claims the use of a composition comprising at least one antigen derived from a H5 influenza virus strain, for the preparation of an influenza immunization composition for administration according to a regimen comprising at least a first and a second administration step timely separated, wherein the H5 influenza virus strain of the first administration step is different from the H5 influenza virus strain of the second administration step and wherein the immunization composition used in at least one of the first or the second administration step comprises an oil-in-water emulsion as an adjuvant, wherein said oil-in-water emulsion comprises at least squalene, an aqueous solvent, a polyoxy ethylene alkyl ether hydrophilic nonionic surfactant, a hydrophobic nonionic surfactant, and wherein said oil-in-water emulsion is obtainable by a phase inversion temperature process and wherein 90% of the population by volume of the oil drops has a size less than 200 nm, and optionally less than 150 nm.

Example of a vaccine-related invention: US20090304730

This application describes a vaccine where at least two influenza virus epitopes are expressed as a chimeric polypeptide wherein at least one epitope is influenza A virus matrix protein epitope and the second epitope is a haemagglutinin peptide epitope. The application claims, among others (note that claims 1 to 37 have been cancelled):

38. A vaccine for immunization of a subject comprising a plurality of chimeric proteins comprising at least two influenza virus peptide epitopes wherein the first peptide epitope is an influenza A virus matrix (M) peptide epitope and a second peptide epitope is a haemagglutinin (HA) peptide epitope, wherein the vaccine elicits cross strain protection.

39. Etc.

Example of a vaccine-related invention: US20080118531

This application claims, among others:

1. A vaccine composition which is effective in preventing or ameliorating avian influenza, and which additionally prevents the growth, shedding and transmission of the challenge influenza virus to other species which comprises a reverse genetics virus consisting of an HA portion derived from a highly pathogenic strain of H5 avian influenza, a N portion derived from a second low pathogenic strain which has an N subtype different from that of the virus from which the HA portion is derived, and the

remaining viral genome selected from a low pathogenic virus which may be the same or different than the virus from which the N portion is derived, adjuvanted with a biologically acceptable adjuvant material.

2. The vaccine composition of claim 1, wherein the HA portion derived from a highly pathogenic strain of H5 avian influenza is derived from an Asian strain of H5N1.

3. The vaccine composition of claim 2, wherein the Asian strain of H5N1 is A/chicken/Vietnam/C58/05H5N1.

4. Etc.

Again, specific sequences from specific H5N1 strains are claimed, but within the context of a very narrow composition of matter.

3.4 Patents families not falling within the scope

Of the 1024 documents of H5N1, 964 patents/applications identified in the search do not fall within the scope of the study. For H1N1, of the 76 documents, 64 patents/applications identified in the search do not fall within the scope of the study. The majority of these are on therapeutic drugs to treat viral infections including antivirals, plant-derived remedies, and monoclonal antibodies; there are also numerous ancillary patent documents which are unrelated to influenza, containing the keyword “H5N1” in another context, e.g., relating to meteorological technologies. The antiviral drugs and plant derived therapies clearly do not fall within the scope of the search since they are not derived from the virus nor claim viral sequences *per se*. Although making monoclonal antibodies requires using the virus, the compositions claimed in the patent/application are essentially not a derivative of the virus and hence do not fall within the scope in our view of the search. For the avoidance of doubt, in those cases where the claim encompasses essential and significant elements of the virus, as in patent application US20100189731A1, the patents/applications were classified as Group 2.

Example of an invention to grow viruses: US20110033859A1

This application describes an improved method for growing influenza viruses in cell culture. It is applicable to all influenza viruses, and is not limited to H5N1 or H1N1, and does not claim sequences specific to these viruses. While it is of relevance to the general influenza vaccine field, it is not within the scope of the requested search.

The application claims, among others:

1. A method of enhancing gene expression of an influenza gene in cell culture comprising, (a) contacting a cell culture with an RNA agent, wherein the cells of said cell culture have been engineered to express a recombinant influenza target gene; (b) measuring the level of gene expression of said recombinant influenza target gene; and (c) comparing the level of expression determined in step (c) to the level of expression in mock-treated cells, wherein an increased level of expression over mock-treated cells is evidence that enhanced gene expression of an influenza gene has occurred.

2. The method of claim 1 wherein recombinant influenza target gene is at least 80% homologous to a consensus sequence selected from group consisting of the MP gene (SEQ ID NO: 1453), the NP gene (SEQ ID NO: 1454), the PA gene (SEQ ID NO: 1455), the PB1 gene (SEQ ID NO: 1456), and the PB2 gene (SEQ ID NO: 1457).

3. The method of claim 2 wherein recombinant influenza target gene is selected from group consisting of the MP gene (SEQ ID NO: 1453), the NP gene (SEQ ID NO: 1454), the PA gene (SEQ ID NO: 1455), the PB1 gene (SEQ ID NO: 1456), and the

PB2 gene (SEQ ID NO: 1457).

4. The method of claim 3 wherein the RNA agent targets the first 500 nucleotides of said recombinant influenza target gene.

5. Etc.

Example of an adjuvant: WO2011007961A2

This application was identified since it refers to influenza H5N1 in the disclosure, but the invention is actually about an adjuvant with application to vaccines against many infectious diseases, including H5N1. It is therefore out of the scope, even though the patentee claims the use of his invention with H5N1.

This application claims, among others:

1. A composition for enhancing an immune response comprising as an active ingredient (a) an immunostimulatory oligonucleotide and (b) an epitope encapsulated in a liposome containing an anionic surfactant and a neutral phospholipid.

2. The composition according to claim 1, wherein the anionic surfactant is selected from the group consisting of phosphatidylglycerol, cardiolipin, phosphatidylserine, diacylphosphatidylserine, dicetylphosphate, phosphatidic acid, diacylphosphatidic acid, oleic acid, N-dodecanoylphosphatidylethanoloamine, NSPE (N-succinylphosphatidylethanolamine), NGPE (N-glutarylphosphatidylethanolamine), LPG (lysylphosphatidylglycerol) and CHEMS (cholesterylhemisuccinate).

3. The composition according to claim 2, wherein the anionic surfactant is CHEMS (cholesterylhemisuccinate).

4. Etc.

Example of an adjuvant and vaccine: WO2011003920A1

This application, while using influenza H5N1 in the examples is actually about adjuvants for addition to any influenza vaccines, and hence is outside the scope of the search.

This application claims, among others:

1. Influenza vaccine comprising a combination of: (a1) a detoxified or non-toxic mutant of subunit A of an AB type exotoxin; (a2) at lease one aluminium salt; and (b) at least one influenza-specific antigen.

2. The influenza vaccine according to claim 1, wherein said component (a1) is derived from heat-labile enterotoxin (HLT), cholera toxin (CT), Shiga toxin (Stx, including Stx1 and Stx2), verotoxin, diphtheria toxin (DT), pertussis toxin (PT), butolinum toxin, Pseudomonas aeruginosa exotoxin A (ETA), or Ricin.

3. The influenza vaccine according to any one of the preceding claims, wherein said detoxified or non-toxic mutant of subunit A has reduced ADP-ribosylating activity.

4. The influenza vaccine according to any one of the preceding claims, wherein said detoxified or non-toxic mutant of subunit A is subunit A of heat-labile enterotoxin (HLT) of Escherichia coli.

5. Etc.

Example of specific sequences within a specific method: US20100310591A1

This application discloses a method of identifying potential epitopes, and specifically potential epitopes from H5N1, that could be included in a vaccine. Since it claims only the method of identifying those sequences, not the actual sequences, this is not directly relevant to the search requested.

This application claims, among others:

1. A method for identifying a specific influenza antigenic epitope which stimulates a predetermined T lymphocyte or clonal cells derived therefrom using combinatorial chemistry procedures for peptide synthesis, comprising: a) providing a T lymphocyte or clonal cells derived therefrom; b) further providing a library of candidate compounds of influenza antigenic epitopes, with each candidate compound in the library being independently joined covalently at its N-terminus to a mammalian Ii-key peptide LRMKLPKPPKPVSKMR (SEQ ID NO: 1) or modifications thereof which retain antigen presentation enhancing activity, the candidate compound and the Ii-key peptide being covalently linked by an intervening chemical structure to form a hybrid polypeptide, the intervening chemical structure being a joined group of atoms which when arranged in a linear fashion forms a flexible chain which extends up to the length of 20 amino acids likewise arranged in a linear fashion; and c) identifying hybrids from step b) which stimulate the T lymphocyte of step a) when presented in the context of an MHC class II molecule of an antigen presenting cell, the candidate compound of the specific hybrid identified corresponding to the specific antigenic epitope which stimulates the T lymphocyte.

2. The method of claim 1, wherein said influenza antigenic epitopes are derived from the H5N1 influenza virus.

3. The method of claim 1, wherein said influenza antigenic epitopes are derived from the H1N1 influenza virus.

4. Etc.

Examples of a Therapeutic: US20090186101A1

This application is on a natural plant extract and claims, among others:

1. The use of a Sambucusnigra L. extract in the preparation of a pharmaceutical formulation for the treatment of an influenza viral infection in a subject in need thereof.

2. The use as claimed in claim 1, wherein the influenza viral infection is caused by influenza type A virus H5N1.

Although H5N1 is mentioned in the claim, this natural product is clearly out of the scope of the requested search.

3.5 Verification of H5N1 results with BLAST search

As a corroborative and iteratively redundant search strategy, a BLAST search (see Section 2.6 above) using the published amino acid sequences of five prevalent and well-

characterized H5N1[23] strains was also performed.

The broad keyword and BLAST results were complementary and overall consistent. All but two of the resulting patents from the BLAST search were already on the comprehensive list of the 1024 patents/applications family list. The exceptions were as follows:

US6720409[24]

This patent has been issued to Takara Shuzo Co. relates to a mAb invention[25] and therefore does not fall into either Group 1 or Group 2 patents. The BLAST search picked up the patent because it claimed a sequence related to H5N1. The reason our initial search had not identified patent US6720409 is that "H5N1" does not appear as a term anywhere in the document. Only the BLAST search caught the patent because it searches for the amino acid sequence. The patent, therefore, "appears" to claim H5N1, or closely homologous, sequences, but does not articulate H5N1. This might illustrate that the claimed sequences of various influenza viruses might have sufficient homology overlap.

US7566458[26]

This patent was identified via the BLAST search strategy, but was not, nor were any putative family members[27], captured in the keyword "H5N1" search. Assuming that the sequence related to group 1This illustrates the added value of combining iterative, complementary and overlapping search strategies to more comprehensively collect and evaluate potentially relevant documents. This patent has thus been included in Table 2.

These two exceptions demonstrate that the BLAST search essentially validated our H5N1 keyword search in that the results were highly congruent with the patent/application search strategy and results.

3.6 Verification by "portfolio" search

A highly selective and limited portfolio search of main assignees (e.g. MedImmune) yielded one additional patent in Group 1, namely WO2010151673, filed by MedImmune. As with the BLAST search, this exception demonstrates the validity and value of the iterative, complementary and overlapping search approaches.

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[23] The BLAST search was not performed for H1N1. The BLAST search was not performed for H1N1 because no patents have yet been issued for H1N1 that meet the criteria of this study. The BLAST search only looks for issued patents.

[24] For a list of family members, see *http://v3.espacenet.com/inpadoc?submitted=true&CC=US&NR=6720409&KC=&FT=E*

[25] Patents/applications claiming monoclonal antibodies (mAbs), whether derived from H5N1 or not, are not inventions which claim viruses, virus fragments, or derivatives. Therefore, these patents/applications do not fulfill the criteria for inclusion as a relevant patent under the terms stipulated by WHO which underpins this present study.

[26] For a list of family members, see *http://v3.espacenet.com/inpadoc?submitted=true&CC=US&NR=7566458&KC=&FT=E*

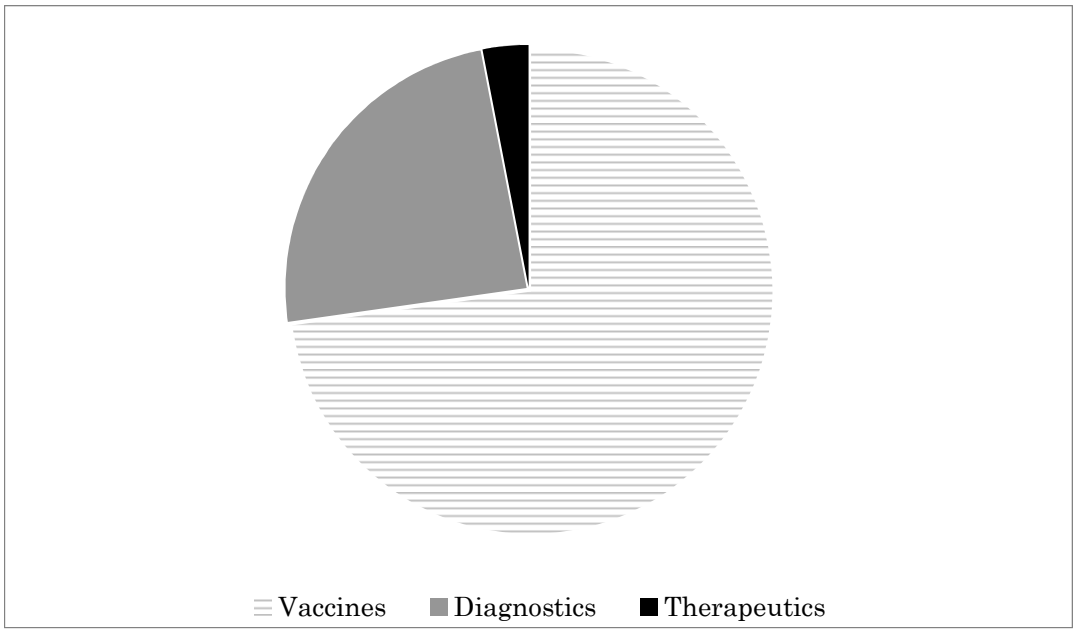
[27] *Ibid.*

3.7 Patents families by type of invention

Figure 1 shows the proportion of vaccines, diagnostics and therapeutics of H5N1[28] from both Group 1 and Group 2 patents. There were a total of 48 vaccine-related patents, 16 in diagnostics and 2 in therapeutics.

Note that the total number of patent applications from Group 1 and Group 2 is 59, but some invention disclosures include vaccines and diagnostics, and in one case a vaccine, diagnostic and therapeutic; hence the total in the pie chart is higher than the sum of Group 1 and Group 2 patents.

Figure 1: Proportion of vaccine, diagnostic and therapeutic patents/applications for H5N1 classified as Group 1 and 2



3.8 Patents filings by members of the WHO Global Influenza Surveillance Network

Of the patent applications in Tables 2 and 3, five were filed by four members of the WHO Collaborating Centre on Influenza, the National Influenza Centre, the H5N1 Reference Laboratories or the Essential Regulatory Laboratories. While these institutions were identified, it is outside the scope of this report to analyse or discuss to what extent collaborations, licenses and technology transfer are taking place between public and private entities, including between and among developed and developing countries.

3.9 Patents *versus* patent applications

The nature of the approach to identify patent families used (*viz*. MicroPatent®) typically lists US applications and PCT (WO) applications as preferred representative documents of patent families. A number of the patent applications had, as part of their families, issued patents/applications, many of which as continuations in part and divisionals, in African Regional Intellection Property Organization (ARIPO) filings, Argentina, Australia, Brazil,

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[28] H1N1 was not included in this analysis because of the limited number of results and some overlap (*viz.* some patents of H5N1 also apply to H1N1).

Canada, Chile, China, Colombia, Costa Rica, Cuba, many European countries, Hong Kong, Israel, Japan, Mexico, New Zealand, Russian Federation, Republic of Korea, South Africa, Taiwan (Province of China) and the United States of America.

It should be noted that a national application has effect for the country in which it is filed. A regional or international application requires an indication of the applicant saying for which state the application shall have effect (the so-called designation). This report does not provide information on the designation of States in patent applications because such information would not provide further insights. An international application filed under the PCT automatically designates all PCT Contracting States.[29] Hence, the PCT application has the effect, in terms of priority dates, of a regular national application in each of the PCT Contracting States at the date of filing of the PCT application.[30] If a patent family has a member that is an international application, a patent application may exist in any or all relevant PCT Contracting States.

A PCT application does not mean that a patent application will be pursued in all the PCT Contracting States. Whether an actual patent should be granted is decided under the jurisdiction of the national law and by the national competent authority and depends on a specific procedural step, known as the entry into the national phase. The applicant would have to decide on, and separately initiate, the processing of the national patent proceedings and grant in each country. In practice, most international applications are pursued on the national level only in a relatively small number of PCT Contracting States. In all other PCT Contracting States, the application loses effect when the national phase is not entered timely so that the claimed invention enters into the public domain in these States, unless that invention has not been covered by any other national patents.

No further analysis has been made on the distinction of claims between patent applications and granted patents. This was a conscious choice because the study tried to gather maximum information on virus related patent documents within the limited time available for preparing this report. In this context, it should be noted that granted patents, in many cases, differ significantly from patent applications in that the claims are restricted in scope during the patent examination and grant procedure. However, patent law does not allow for broadening the scope of the claims going beyond the application as filed. In other words, a correctly granted patent will not cover broader claims than what had been described already in the disclosure of the invention submitted by the applicant at the time of filing the application.

4. DISCUSSION AND CONCLUSIONS

The analysis identified many patent families claiming innovative technologies that could, at some future date, have the potential to provide more effective responses to an influenza pandemic than is the case with current vaccine manufacturing technologies which nevertheless are beneficial.

The specific request from WHO was that WIPO develop fact-based information on Pandemic Influenza Preparedness-related patents, including patent applications, relevant to the H5N1 and H1N1 viruses. Recognizing the complexity surrounding the science, technology and intellectual property thereof (such as which patents are valid in which countries and which patents are applicable to specific products), this comprehensive report, it is hoped, has shed light on the types of patents/ applications that are emerging as

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[29] 142 PCT Contracting States as of March 25, 2011, for a List of PCT Contracting States, see *http://www.wipo.int/pct/guide/en/gdvol1/annexes/annexa/ax_a.pdf*

[30] PCT Article 11 (3).

a result of investments in pandemic influenza research by both the public and private sectors.

This report is based on publicly available information and constitutes an analysis of patents/applications. Whereas it is believed that the approach is solid and rigorous, and an appropriate reply to the specific request from WHO, it is not claimed that the methodology is the only approach. The combination of iterative, complementary and overlapping search approaches (including the BLAST and portfolio searches) shows the value of such strategies even though the portfolio search was limited. This limited portfolio search, nevertheless, is not believed to materially affect the results or conclusions of this study.

Recognizing that a patent application typically differs significantly from the granted patent, the number of patent families identified in this study as “relevant and clearly within the scope of the request” and “relevant but subject to interpretation” is likely to be smaller. This is because the analysis was based on the reading of patent applications as representatives of patent families. This is an appropriate strategy since initial applications are the most comprehensive representatives of patent families which, over time, often contain divisional applications, continuations in part, and various national patent applications. Furthermore, patent applications will describe and claim an invention as broadly as possible to gain maximum coverage. From the viewpoint of a patent applicant, this is a commonly-practiced and legitimate strategy. From a public interest perspective, the scope of protection conferred by a patent, when granted, must be limited to the true innovation in so far as it complies with patentability requirements. For this reason, claims are restricted during the patent examination procedure. The publication of a patent application does not indicate that a patent will be granted nor does it indicate the scope of the granted patent. To obtain information about the grant, the validity of the patent as well as the eventual scope of patent protection, it is necessary to check the publication of the granted patent and its legal status, for example whether an application has been rejected, a patent granted, corrected or whether the patent has lapsed.

Several other critical points emerging from this study are highlighted:

1. In the pool of patent information assembled and analyzed in this report, no patent documents were identified that included claims having, as a sole and/or single element, either a complete native virion, a native viral strain, a native viral genome in its entirety or a complete assembled complement of native viral proteins from a specific virus.

2. The report discusses in detail certain patent applications where the scope of the claims is broad and could potentially be construed as covering known viral sequences, processes and compositions of matter. In these cases, the public health community could be concerned that applicants may be seen as attempting to patent naturally occurring viruses, or derivatives of those viruses, in known methods or compositions. It is important to point out that the majority of the identified documents are patent applications as opposed to granted patents, and it is the responsibility of the national patent office to grant claims, or to narrow the claims, so as to limit patent coverage to novel, non-obvious and useful products. It is well established that issued patents frequently have narrower claims than the corresponding patent applications.

3. Any specific vaccine or product from a “freedom-to-operate” perspective was not analyzed. This would have been outside the scope and purview of the report and would, in any case, not have been possible at this stage since such a review would require that the specific technology, vaccine composition and manufacturing process are precisely defined, as well as the territory in which production and sales are envisaged.

4. While some patent applications from members of the WHO Global Influenza Surveillance Network are identified as falling within the scope of the search, the report does not analyse to what extent collaborations, licenses and technology transfer are taking place between these and other entities, including between and among developed and developing countries.

More generally, the report's findings should be considered in a broader innovation framework, most notably:

1. New intellectual property management models are emerging that facilitate broad access to new technologies, including in the area of health, by developing countries. These include, among others:

   - open innovation and networked innovation models that encourage both public and private sector research and development of health solutions,

   - the growing investments in and ability of developing countries to undertake health innovation, including broader networks that expand linkages among like-minded organizations,[31]

   - public-private product development partnerships (commonly called PDPs) that essentially emerged in the 1990s and are now a major driving force of R&D specifically aimed at of health solutions needed by the poor,

   - industry's growing willingness to work proactively to increase developing country licensing, including lower royalty rates, offering concessionary terms on technology,[32] tiered pricing, or donation of products, and technology transfer,[33] and

   - non-assertion covenants.[34]

2. Developing countries are increasingly using intellectual property as a tool to contribute to their economic growth and development. The benefits of such strategies are well illustrated by the many innovation and technology centers being built in developing countries, most notably in Brazil, China and India, among others. The investment in innovation is contributing to the development of increasingly globalized system of health innovation.[35] In addition, during the search and analysis

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31 Morel C.M. *et al*. (2005). Health Innovation Networks to Help Developing Countries Address Neglected Diseases. *Science* 309:401-404.

32 For example, see MedImmune created a pathway for manufacturers to gain access to and become familiar with reverse genetics prior to an actual pandemic crisis. This includes zero royalties if licensees donate their vaccine free of charge to any government or entity, the waiving of IP costs for pandemic vaccines for developing/least developed nations, and also zero royalties in developing countries where governments domestically manufacture and distribute free-of-charge pandemic influenza vaccine products.

33 For example, the Lilly Multiple Drug Resistant (MDR)-Tuberculosis Partnership (*www.lillymdr-tb.com).*

34 Krattiger A. (2007). The Use of Nonassertion Covenants: A Tool to Facilitate Humanitarian Licensing, Manage Liability, and Foster Global Access. In *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices* (eds. A. Krattiger, R.T. Mahoney, L. Nelsen, *et al*.). MIHR: Oxford, U.K., and PIPRA: Davis, U.S.A. Chapter 7.6. pp. 739-744. *www.ipHandbook.org*

35 Mahoney R.T. and Morel C.M. (2006). A Global Health Innovation System (GHIS). *Innovation Strategy Today* 2(1):1-12. *www.biodevelopments.org/innovation/index.htm*

exercise several patent applications were identified from biotechnology groups based in industrialized countries that are now owned by developing country companies.

3. The need for private sector investment also underpins the rationale of the intellectual property policies of many, if not most, public sector research institutions around the world. These policies are often designed to enable the licensing of technology to the private sector for product development leading to regulatory approval and eventual use, thus serving the public interest in general. Increasingly, as public sector institutions have been taking the management of intellectual property more seriously, they have also found ways to put intellectual property to work specifically with humanitarian goals in mind.

4. Finally, a patent is a vehicle for disclosing inventions and for making technologies publicly known. As such, the intellectual property system seeks to strike a balance between the public domain and granting limited ownership. The public disclosure embedded in the intellectual property system, in turn, encourages new research leading to accelerated innovation in any given field of endeavor.

As has been described in previous reports and publications, there are patent applications and patents on novel approaches to diagnosing, preventing, or treating pandemic influenza. Some will, it is hoped, succeed ultimately and lead to the availability of new, safer and more effective vaccines, therapeutics and diagnostics to benefit humanity.

[Annex follows]

ANNEX

PATENT AND PATENT APPLICATION DATA FOR H5N1 AND H1N1

For Group 1 and 2 patents/applications (Tables I and II), the column on the left is the representative family member which was analyzed and studied in detail. The column on the far right lists the related family members. For patents not falling within the scope (Table III), the table provides one representative of each of the individual patent families.

All patents can readily be viewed in full by visiting USPTO, EPO or PATENTSCOPE®.

The full table, including related family members, is available in a Microsoft® Excel® spreadsheet, comprising full abstracts, full claims, priority filings and designated States among other information. Please write to *global.challenges@wipo.int* if you wish to receive an electronic copy of the table.

Table I: Group 1

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
H5N1					
US20050287172A1	MedImmune	Yang, Chin Fen	5/20/2005	US	AU2005248375A1 | AU2005248375B2 | AU2005248377A1 | CA2568015A1 | CA2568020A1 | EP1766059A2 | EP1766059A4 | EP1771552A2 | EP1771552A4 | JP2008500041T | JP2008500042T | US20060008473A1 | US20090136530A1 | US20090175909A1 | US7504109B2 | US7527800B2 | US7744901B2 | WO2005116258A2 | WO2005116258A3 | WO2005116260A2 | WO2005116260A3
US20060024670A1	None	Luke, Catherine	5/18/2005	US	AU2005248361A1 | AU2005248361B2 | CA2566355A1 | EP1766094A2 | EP1766094A4 | JP2008505660T | US20070286869A1 | US20080057080A1 | US20100197771A1 | US7537768B2 | US7785603B2 | WO2005116270A2 | WO2005116270A3
US20070259337A1	Intelligent Medical Devices, Inc.	Hully, James, Robert	11/29/2006	USS	AU2006320541A1 | CA2632380A1 | EP1960555A2 | JP2009517087T | US20070174661A1 | US7447940B2 | WO2007061440A2 | WO2007061440A3 | WO2007064758A2 | WO2007064758A3
US20070286873A1	None	Williams, John, V.	5/23/2007	US | US	None
US20080057081A1	MedImmune Vaccines, Inc.	Yang, Chin-Fen	8/9/2007	US	AU2007286161A1 | CA2659267A1 | EP2056872A2 | JP2010500034T | KR10-2009-0053794A | US20080069821A1 | WO2008021959A2 |
US20080193471A1	BoehringerIngelheimVetmedica, Inc.	Vaughn, Eric	10/24/2007	US	AR063427A1 | AU2007308869A1 | CA2664914A1 | CL31022007A1 | CN101553248A | CO6210831A2 | EP2086576A2 | EP2086576A4 | JP2010508030T | KR10-2009-0078362A | MX2009004243A | WO2008052173A2 | WO2008052173A3 | WO2008052173A8 | ZA200902023A
US20080193472A1	VARIATION BIOTECHNOLOGIES INC.	Ogrel, Andrei	11/30/2007	US | US	CA2670965A1 | CN101622009A | EP2097103A1 | EP2097103A4 | JP2010510994T | US20110020381A1 | US7807173B2 | WO2008064488A1
US20080254065A1	CHIRON CORPORATION	Podda, Audino	12/5/2007	US | US | US | US	CA2559371A1 | EP1722815A1 | JP2007528411T | WO2005107797A1
US20080261198A1	None	Ren, EeChee	9/24/2007	US | US | SG	AU2005252615A1 | CA2567793A1 | EP1761645A1 | EP1761645A4 | JP2008502362T | US20090226888A1 | WO2005121367A1 | WO2005121367A8 | WO2006132601A1
US20090060949A1	None	Ho, David D.	1/23/2008	US | US	US20100041740A1 | WO2008091657A1
US20090061417A1	AGENCY FOR SCINECE TECHNOLOGY AND RESERCH	Inoue, Masafumi	10/2/2008	GB | US | SG	CA2630252A1 | CN101360825A | EP1948797A2 | EP1948797A4 | GB0523347D0 | GB2432419A | JP2009515551T | WO2007058629A2 | WO2007058629A3
US20090074804A1	National Health Research Institute (an institution of Taiwan, R.O.C.)	Lee, Min-Shi	9/5/2008	US | US	None
US20090106864A1	DOW AGROSCIENCES LLC	Henry, Matthew	11/3/2008	US | US | US	AR061484A1 | AU2007261196A1 | CA2654178A1 | CN101472607A | EP2029167A2 | EP2029167A4 | JP2009540801A | KR10-2009-0027216A | WO2007149715A2 | WO2007149715A3 | ZA200808845A

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
US20090305243A1	BIOMERIEUX	Lefeuvre, Aurélie	5/23/2008	FR | FR | US | FR	AT485402T | AU2006319001A1 | CN101313079A | DE602006017727D1 | EP1954839A1 | EP1954839B1 | FR2902429A1 | FR2902430A1 | JP2009517013T | WO2007060366A1
US20090317795A1	None	Minekawa, Harumi	8/23/2007	JP | JP | US | JP	CN101052720A | CN101613700A | EP1826269A1 | EP1826269A4 | WO2006049061A1
US20100074916A1	US Government/ DHHS	Nabel, Gary J.	4/1/2009	US | US | US | US | US | US | US	CN101627050A | EP2069393A2 | KR10-2009-0101883A | WO2008112017A2 | WO2008112017A3
US20100136098A1	National Institute of Infectious Diseases | National University Corporation Hokkaido University | Saitama Medical University | NOF Corporation	UCHIDA, Tetsuya	3/9/2009	JP | US	WO2010061924A1
US20100166787A1	None	Weiner, David B	10/27/2009	US | US | US | US | US | US	AU2007278831A1 | CA2659262A1 | CN101679475A | EP2049559A2 | JP2009544333T | KR10-2009-0046899A | MX2009001099A | WO2008014521A2 | WO2008014521A3
US20100189745A1	BAXTER INTERNATIONAL INC. | BAXTER HEALTHCARE S.A.	Kistner, Otfried	12/16/2009	US | US	WO2010077986A2 | WO2010077986A3
US20100285982A1	US Government/ DHHS	Golding, Hana	7/12/2010	US | US | US	WO2008157419A2 | WO2008157419A3
US20100291128A1	None	Montelione, Gaetano T.	10/27/2008	US | US | US | US	WO2007061969A2 | WO2007061969A3
US7566458	MedImmune, LLC	Yang; Chin-Fen	06/16/2004	US	CA252964A1 | CA2600730A1 | EP1633312A2 | EP1856271A1 | US2006252132A1 | US7459162B2 | US2005042229A1 | US7566458B2 | US2009175898A1 | US2009175908A1 | US2011002960A1 | US2011070263A1 | WO2005018539A2 | WO2005018539A8 | WO2006098901A2 | WO2006098901A3
WO2008124331A1	CYTOGENIX, INC. | KENDIRGI, Frederic | CHEN, Yin	KENDIRGI, Frederic	3/27/2008	US | US	None
WO2009092038A1	US Government/ DHHS | RAO, Srinivas | NABEL, Gary, J. | YANG, Zih-yong | WEI, Chih-jen | KONG, Wing-pui	RAO, Srinivas	1/16/2009	US | US | US	WO2009092038A8
WO2010111597A2	THE JOHNS HOPKINS UNIVERSITY |	SADEGH-NASSERI, Scheherazade	3/26/2010	US | US	None
WO2011008171A1	AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH | INOUE, Masafumi	INOUE, Masafumi	7/13/2010	SG | SG	None
WO2010148386	Novavax, Inc.	Gale Smith	6/21/2010	US	None
WO2010151673	MedImmune	Hong JIN	24/06/2010	US	Not known

WO2010148386	Novavax, Inc.	Gale Smith	6/21/2010	US	None

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Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
US20110033490A1	Massachusetts Institute of Technology	Jayaraman, Akila	7/2/2010	US | US	WO2011003100A2
US20110052618A1	MEDIMMUNE, LLC | GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT	YANG, Chin-Fen	4/28/2010	US	None
WO2010124373A1	HER MAJESTY THE QUEEN IN RIGHT OF CANADA AS REPRESENTED BY THE MINISTER OF HEALTH | HE, Runtao | LI, Xuguang | VAN DOMSELAAR, Gary	HE, Runtao	4/29/2010	US | CA	None
WO2011008171A1	AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH | INOUE, Masafumi	INOUE, Masafumi	7/13/2010	SG | SG	None

Table II: Group 2

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
H5N1					
EP1923070A1	Intervet International BV	The designation of the inventor has not yet been filed	11/15/2006	EP	None
US20040142319A1	None	Yu, Albert, Cheung Hoi	4/7/2003	CN | CN | US	AT435305T | AU1493602A | AU2002214936B2 | BR0114468A | CA2424867A1 | CN1258604C | CN1476485A | DE60139136D1 | EP1330553A1 | EP1330553A4 | EP1330553B1 | HK1057768A1 | JP2004509648T | MXPA03002995A | NZ525190A | US20100112548A1 | US7611837B2 | WO0229118A1 | ZA200302671A
US20060257860A1	GEN PROBE INCORPORATED	Marlowe, Elizabeth	5/4/2006	US | US	AU2006244460A1 | AU2006244460B2 | AU2010202899A1 | CA2605015A1 | EP1877418A2 | EP1877418A4 | JP2008539733T | US20100285450A1 | WO2006121773A2 | WO2006121773A3
US20070003576A1	None	Gambotto, Andrea	12/9/2005	US | US	BRPI0518728A2 | EP1819357A2 | EP1819357A4 | JP2008522621T | US20100008952A1 | WO2006063101A2 | WO2006063101A3
US20070031453A1	None	Hoffmann, Erich	7/27/2006	US | US	AU2006278696A1 | AU2006278696A8 | CA2617483A1 | CN101283099A | EP1924281A2 | JP2009502197A | KR1020080042864A | RU2008107875A | US7871626B2 | WO2007019094A2 | WO2007019094A3 | ZA200800505A
US20080032921A1	Pharmexa Inc.	Alexander, Jeffery, L.	5/18/2007	US | US | US	AU2007314550A1 | CA2657849A1 | EP2023952A2 | EP2023952A4 | WO2008054540A2 | WO2008054540A3 | WO2008054540A2
US20080118531A1	Wyeth | St. Jude Children's Research Hospital	Hoffmann, Erich	4/18/2007	US | US	AP200804625D0 | CN101448520A | WO2007124479A2 | WO2007124479A3
US20080299151A1	Statens Serum Institut	Fomsgaard, Anders	5/30/2008	DK | US | US	EP2160198A2 | MX2009013008A | US20100160421A1 | WO2008145129A2 | WO2008145129A3
US20090111089A1	US Government/ DHHS, Centres for Disease Control and Prevention	Lindstrom, Stephen	8/13/2008	US | US | US	CA2646132A1 | EP1991700A2 | WO2007095155A2 | WO2007095155A3
US20090123909A1	The Board of Trustees of the Leland Stanford Junior University	Pourmand, Nader	11/27/2007	US | US	None
US20090136532A1	None	Webb, Steven Robert	10/10/2008	US | US | US	AR060565A1 | AU2007213423A1 | AU2007319715A1 | AU2007319715A8 | CA2650091A1 | CN101415430A | CN101578111A | EP1981510A1 | EP2010210A2 | EP2010210A4 | JP2009526038T | JP2009535306T | KR10-2008-0109094A | US20080274985A1 | WO2007091165A1 | WO2008060669A2 | WO2008060669A3
US20090169505A1	None	Draghia-Akli, Ruxandra	11/12/2008	US | US	AU2008331673A1 | CA2705461A1 | CN101877965A | EP2217064A2 | KR10-2010-0096164A | WO2009073330A2 | WO2009073330A3
US20090169576A1	None	Crea, Roberto	8/27/2008	US | US | US	CA2627105A1 | EP1948227A2 | EP1948227A4 | WO2007051036A2 | WO2007051036A2

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
US20090304730A1	Yeda Research and Development Co. Ltd at the WeizmanInstitute of Science	Arnon, Ruth	11/4/2008	US | US | US | IL	AU2006322907A1 | CA2632483A1 | EP1968632A1 | IL191977D0 | WO2007066334A1 | WO2007066334A9
US20090324644A1	None	Ramos, Oliberto Sanchez	6/9/2009	CU | US | CU	AR059647A1 | AU2007219571A1 | CA2638832A1 | CN101421302A | CU23576A1 | EP1997831A1 | JP2009528305T | KR10-2008-0113217A | MX2008011143A | RU2008138535A | WO2007098718A1 | WO2007098718A1
US20100098721A1	St. Jude Children's Reseach Hospital	McCullers, Jonathan A.	11/24/2009	US | US | US | US	WO2008048984A2 | WO2008048984A3
US20100137412A1	INSTITUT PASTEUR OF SHANGHAI	ZHOU, Paul	6/29/2009	US | IB | US	CA2673994A1 | CN101888854A | EP2111233A2 | JP2010514439A | MX2009007106A | WO2008087563A2 | WO2008087563A3
US20100166769A1	Academia Sinica	Hsiao, Pei-Wen	2/12/2010	US | US	US20080063664A1
US20100189731A1	None	GUO, Xuan	11/30/2009	US | US	WO2010063033A2 | WO2010063033A3
US20100239610A1	MEDICAGO INC.	D'Aoust, Marc-André	6/11/2010	US | US | US | CA | US | US | CA | US	AU2008278222A1 | AU2009202819A1 | AU2009267759A1 | CA2615372A1 | CA2693956A1 | CA2707235A1 | CN101883856A | CR11209A | EA201000195A1 | EP2173886A1 | EP2173886A4 | EP2238253A1 | JP2010533001T | KR10-2010-0032920A | KR10-2010-0120157A | MX2010000525A | US20100310604A1 | WO2009009876A1 | WO2009076778A1 | WO2009076778A8 | WO2010003225A1 | WO2010003225A8
US20100297174A1	None	Garcia-Sastre, Adolfo	3/30/2010	US | US | US	WO2010117786A1
WO2007065967A1	REMEDAL OY | HEINO, Pekka	HEINO, Pekka	12/4/2006	FI | FI	FI20051255D0
WO2007129984A1	TEMASEK LIFE SCIENCES LABORATORY LIMITED | KWANG, Jimmy | LU, Li Qun	KWANG, Jimmy	5/5/2006	SG	CN101460628A | EP2021483A1
WO2008040098A1	MEDVET SCIENCE PTY LTD | LI, Peng | KOK, Tuckweng | MILLER, Darren	LI, Peng	10/4/2007	AU | AU	None
WO2008059018A2	INTERVET INTERNATIONAL B.V. | LIN, Fengsheng | TARPEY, Ian	LIN, Fengsheng	11/15/2007	EP | EP	WO2008059018A3
WO2009068992A1	NOVARTIS AG | PODDA, Audino | RAPPUOLI, Rino	PODDA, Audino	11/25/2008	US | GB | IB	AU2008331238A1 | CA2706619A1 | EP2211901A1 | GB0810305D0 | KR10-2010-0108527A
WO2009074861A2	POWDERJECT RESEARCH LIMITED | LYNCH, Deborah, Taylor	LYNCH, Deborah, Taylor	12/9/2008	US | IB	WO2009074861A3
WO2009150532A1	NOVARTIS AG | BANZHOFF, Angelika | CLEMENS, Ralf	BANZHOFF, Angelika	6/12/2009	US | GB | IB	AU2009259006A1 | CA2727322A1 | GB0905570D0
WO2010036970A2	FRAUNHOFER USA, INC. | YUSIBOV, Vidadi | METT, Vadim | MUSIYCHUK, Konstantin	YUSIBOV, Vidadi	9/25/2009	US | US	WO2010036970A3

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
WO2010092476A1	NOVARTIS AG | GROTH, Nicola | FRAGAPANE, Elena	GROTH, Nicola	2/10/2010	US | IB	None
WO2010103022A2	SANOFI PASTEUR | CAILLET, Catherine | PIRAS-DOUCE, Fabienne | KUSTERS, Inca Carola	CAILLET, Catherine	3/10/2010	EP | US | EP	None
WO2010125201A1	REDBIOTEC AG | JOHN, Corinne | SCHAUB, Christian | WELLNITZ, Sabine	JOHN, Corinne	4/30/2010	EP | EP	None
WO2010134094A1	PANACEA BIOTEC LTD | JAIN, Rajesh | VINAYAK, Virender Kumar | SHUKLA, Nidhi | AGGARWAL, Neeraj | MEHTA, Rajan	JAIN, Rajesh	5/17/2010	IN | IN	WO2010134094A9
WO2011003100A2	MASSACHUSETTS INSTITUTE OF TECHNOLOGY | JAYARAMAN, Akila | VISWANATHAN, Karthik | RAMAN, Rahul | SHRIVER, Zachary, H. | SASISEKHARAN, Ram	JAYARAMAN, Akila	7/2/2010	US | US	None

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US20110045022A1	None	Tsai, Theodore	1/29/2010	US	None
WO2010125202A1	CYTOS BIOTECHNOLOGY AG | BACHMANN, Martin | JEGERLEHNER, Andrea | SAUDAN, Philippe	BACHMANN, Martin	4/30/2010	EP | EP	None
WO2010125461A1	NOVARTIS AG | STÖHR, Klaus | DORMITZER, Philip | DEL GIUDICE, Giuseppe | BRÖKER, Michael	STÖHR, Klaus	4/27/2010	US | US | US | US | IB	None
WO2010127252A2	VANDERBILT UNIVERSITY | CROWE, Jr., James, E. | KRAUSE, Jens, C. | BASLER, Christopher, F.	CROWE, Jr., James, E.	4/30/2010	US | US	None
WO2010129558A1	IBIS BIOSCIENCES, INC. | SAMPATH, Rangarajan | ECKER, David, J. | BLYN, Lawrence, B. | LI, Feng | HALL, Thomas, A. | MASSIRE, Christian | HOUSLEY, Roberta | LOVARI, Robert, J.	SAMPATH, Rangarajan	5/4/2010	US | US	None

Patent/ Publication No.	Assignee/ Applicant	Inventor (1st only)	Appl. Date	Priority Country	Family Members
WO2010137873A2	BIONEER CORPORATION | LEE, Yun Kyung | CHO, Eun-Jin | HWANG, Byoung-Oh | BYUN, Sang-Jin | KIM, Seong-Youl | PARK, Hae-Joon | PARK, Han Oh	LEE, Yun Kyung	5/26/2010	KR | KR	None
WO2010148386A1	NOVAVAX, INC. | SMITH, Gale | PUSHKO, Peter	SMITH, Gale	6/21/2010	US | US | US	None
WO2011011390A1	NOVAVAX, INC. | SMITH, Gale | PINCUS, Steven	SMITH, Gale	7/20/2010	US | US	None

Table III: Not falling within the scope

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EP2154144A1
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