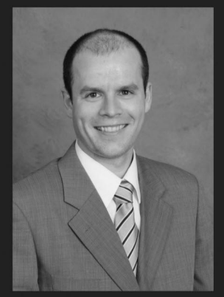
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EDUCATIONAL REPORT SERIES : PATENT LANDSCAPE OF INFLUENZA A PROPHYLACTIC VACCINES AND RELATED TECHNOLOGIES FALL 2013

ITTI
International Technology Transfer Institute

THE FRANKLIN PIERCE *Center for* INTELLECTUAL PROPERTY

University *of* New Hampshire
School *of* Law

PATENT LANDSCAPE OF INFLUENZA A PROPHYLACTIC VACCINES AND RELATED TECHNOLOGIES



FALL 2013

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Fall 2012 Educational Report:

Patent Landscape of Influenza A Virus Prophylactic Vaccines and Related Technologies

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Introduction

Executive Summary

This report focuses on patent landscape analysis of technologies related to prophylactic vaccines targeting pandemic strains of influenza. These technologies include methods of formulating vaccine, methods of producing of viruses or viral subunits, the composition of complete vaccines, and other technologies that have the potential to aid in a global response to this pathogen. The purpose of this patent landscape study was to search, identify, and categorize patent documents that are relevant to the development of vaccines that can efficiently promote the development of protective immunity against pandemic influenza virus strains.

The search strategy used keywords which the team felt would be general enough to capture (or "recall") the majority of patent documents which were directed toward vaccines against influenza A virus. After extensive searching of patent literature databases, approximately 33,500 publications were identified and collapsed to about 3,800 INPADOC families. Relevant documents, almost half of the total, were then identified and sorted into the major categories of vaccine compositions (about 570 families), technologies which support the development of vaccines (about 750 families), and general platform technologies that could be useful but are not specific to the problems presented by pandemic influenza strains (about 560 families). The first two categories, vaccines and supporting technologies, were further divided into particular subcategories to allow an interested reader to rapidly select documents relevant to the particular technology in which he or she is focused. This sorting process increased the precision of the result set.

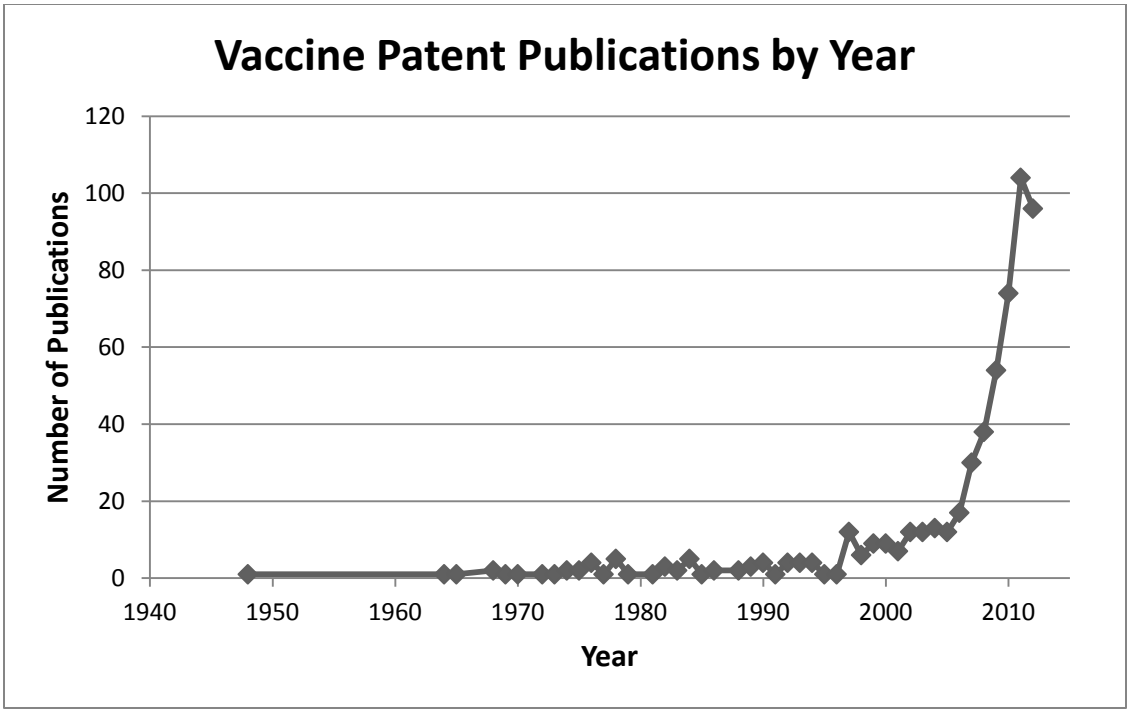
The two major categories (vaccines and supporting technologies) were subjected to a range of analytics in order to extract as much information as possible from the dataset. First, patent landscape maps were generated to assess the accuracy of the sorting procedure and to reveal the relationships between the various technologies that are involved in creating an effective vaccine. Then, filings trends are analyzed for the datasets. The country of origin for the technologies was determined, and the range of distribution to other jurisdictions was assessed. Filings were also analyzed by year, by assignee, and by inventor. Finally, the various patent classification systems were mapped to find which particular classes tend to hold influenza vaccine-related technologies. Besides the keywords developed during the searches and the landscape map generation, the classifications represent an alternate way for further researchers to identify emerging influenza technologies.



ThemeScape map of terms from influenza vaccine patent documents. This category contained approximately 570 INPADOC patent families. See Figure 10.

The analysis included creation of a map of keywords, as shown above, describing the relationship of the various technologies involved in the development of prophylactic influenza A vaccines. The map has regions corresponding to live attenuated virus vaccines, subunit vaccines composed of split viruses or isolated viral polypeptides, and plasmids used in DNA vaccines. Important technologies listed on the map include the use of reverse genetics to create reassortant viruses, the growth of viruses in modified cell lines as opposed to the traditional methods using eggs, the production of recombinant viral antigens in various host cells, and the use of genetically-modified plants to produce virus-like particles.

Another major finding was that the number of patent documents related to influenza being published has been steadily increasing in the last decade, as shown in the figure below. Until the mid-1990s, there were only a few influenza patent documents being published each year. The number of publications increased noticeably when TRIPS took effect, resulting in publication of patent applications. However, since 2006 the number of vaccine publications has exploded. In each of 2011 and 2012, about 100 references disclosing influenza vaccine technologies were published. Thus, interest in developing new and more efficacious influenza vaccines has been

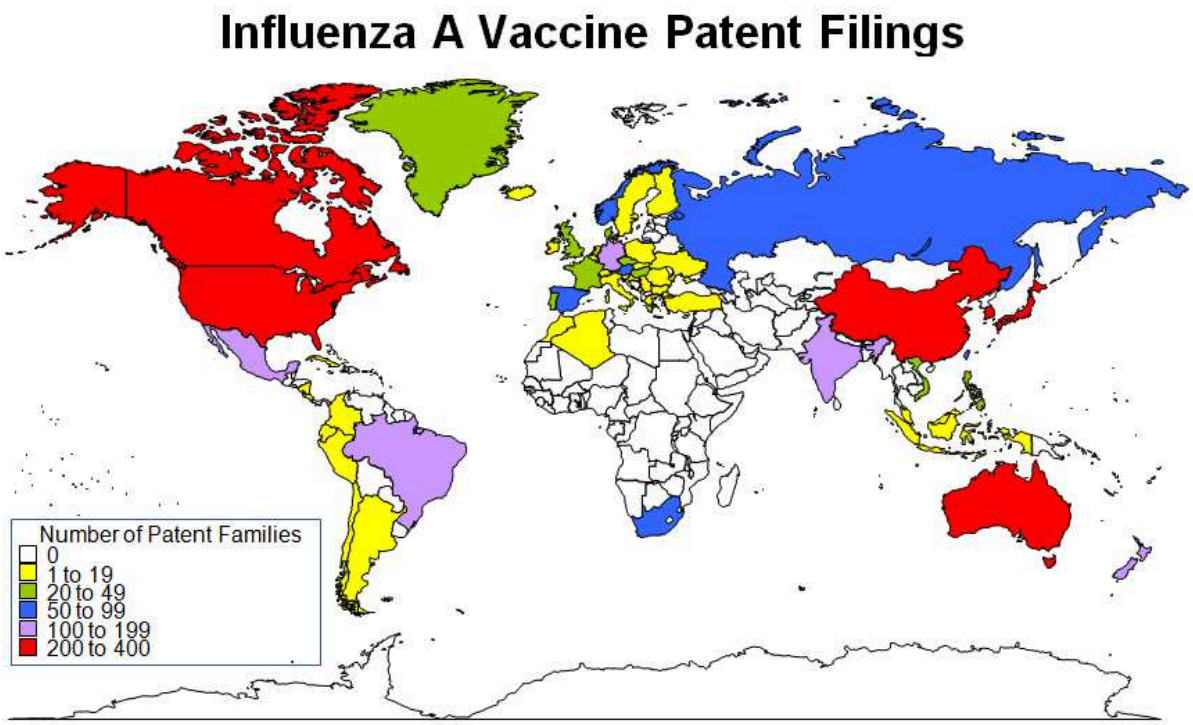


Publication trends for influenza vaccine documents. Publications increased in the 1990s when patent applications began to be published, and then the numbers soared after outbreaks of H5N1 and H1N1. Similar results were observed with documents related to supporting technologies. See Figure 16.

growing in recent years. This interest is probably being driven by recent influenza outbreaks, such as the H5N1 (bird flu) epidemic that began in the late 1990s and the 2009 H1N1 (swine flu) pandemic.

The origins of the vaccine-related inventions were also analyzed. The team determined the country in which the priority application was filed, which was taken as an indication of the country where the invention was made or where the inventors intended to practice the invention. By far, most of the relevant families originated with patent applications filed in the United States. Other prominent priority countries were the China and United Kingdom, followed by Japan, Russia, and South Korea. France was a significant priority country only for supporting technologies, not for vaccines. Top assignees for these families were mostly large pharmaceutical companies, with the majority of patent families coming from Novartis, followed by GlaxoSmithKline, Pfizer, U.S. Merck (Merck, Sharpe, & Dohme), Sanofi, and AstraZeneca. Governmental and nonprofit institutes in China, Japan, Russia, South Korea and the United States also are contributing heavily to influenza vaccine research.

Lastly, the jurisdictions were inventors have sought protection for their vaccine technologies were determined, and the number of patent families filing in a given country is plotted on the



Jurisdictions for filing applications and issuing patents related to influenza vaccines. Filings in multi-jurisdictional agencies, such as ARIPO, the Gulf Cooperation Council, WIPO and the European Patent Office, are not shown. The number of patent families is out of 570 total families. See Figure 15 for a more detailed description.

world map shown below. The United States, Canada, Australia, Japan, South Korea and China have the highest level of filings, followed by Germany, Brazil, India, Mexico and New Zealand. However, although there are a significant number of filings in Brazil, the remainder of Central and South America has only sparse filings. Of concern, with the exception of South Africa, few other African nations have a significant number of filings.

In summary, the goal of this report is to provide a knowledge resource for making informed policy decisions and for creating strategic plans concerning the assembly of efficacious vaccines against a rapidly-spreading, highly virulent influenza strain. The team has defined the current state of the art of technologies involved in the manufacture of influenza vaccines, and the important assignees, inventors, and countries have been identified. This document should reveal both the strengths and weaknesses of the current level of preparedness for responding to an emerging pandemic influenza strain. The effects of H5N1 and H1N1 epidemics have been felt across the globe in the last decade, and future epidemics are very probable in the near future, so preparations are necessary to meet this global health threat.

Acknowledgements

We would like to thank those who provided invaluable assistance in the completion of this project.

We are thankful to the University of New Hampshire School of Law Dean John Broderick, and Associate Dean Jordan Budd, as well as to the faculty of the Franklin Pierce Center for Intellectual Property, for supporting this project.

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We are thankful to Mr. Mark Bauer and Thomson-Reuters for graciously facilitating access to Thomson-Innovation, for providing invaluable guidance, and training on other aspects of patent database mining and research. We also thank LexisNexis and GenomeQuest for providing access to their platforms.

Disclaimer

This educational report is neither inclusive nor comprehensive. Rather, it is an informational resource intended to facilitate a better understanding of the international patent literature landscape regarding vaccines against influenza A viruses.

This report is not a list of all potentially relevant patents. Importantly, it is not a Freedom to Operate (FTO) opinion, but instead constitutes an educational analysis of potentially relevant material. While the search platforms utilized in this project were extensive, none were comprehensive, and some countries and jurisdictions were underrepresented in the databases, either in the time frame covered, the availability of translated documents, and the completeness of the records. Further, it is likely that the International Technology Transfer Institute (ITTI) team did not obtain the entire spectrum of relevant patents utilizing the various search strategies and methods articulated herein. Therefore, the ITTI team does not guarantee that all relevant patents were discovered during the creation of this report.

As the ITTI team members are not experts in the field of influenza A virus related vaccines, it is likely that the categorization of the patents found and coded are incomplete. Further, many patent documents contain material relevant to multiple categories; the documents were placed in the category that the team, in its judgment, felt best represented the overall focus of the document. The ITTI team cannot guarantee that the patents discovered were evaluated at the level of expert scientific sophistication.

The limited time frame, competing academic demands, and the general press of business dictated the number of patents evaluated. As such, additional patents may have been available that were not considered due to time constraints.

Many names are capitalized and may or may not be trademarked and/or otherwise protected intellectual property. The team apologizes for any errors or mistaken omissions.

Abbreviations and Definitions

Below is a list of abbreviations and definitions for terms and keywords used throughout the ITTI Fall 2012 report and the reported results.

Adjuvants – defined herein as a substance sometimes included in a vaccine formulation to enhance or modify the immune-stimulating properties of a vaccine.[1]

Antibody – defined herein as an infection-fighting protein molecule in blood or secretory fluids that tags, neutralizes, and helps destroy pathogenic microorganisms (e.g., bacteria, viruses) or toxins. Antibodies, known generally as immunoglobulins, are made and secreted by B-lymphocytes in response to stimulation by antigens. Each specific antibody binds only to the specific antigen that stimulated its production.[2]

Antibody-mediated immunity – defined herein as the immunity that results from the activity of antibodies in blood and lymphoid tissue (also called humoral immunity).[3]

Antigens - (immunogens; substances capable of provoking an immune response) – defined herein as foreign substances in the body that are capable of causing disease. The presence of antigens in the body triggers an immune response, usually the production of antibodies. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however only the portion of the protein of polysaccharide molecule known as the antigenic determinant combines with antibody or a specific receptor on a lymphocyte.[4]

Anti-idiotype - herein defined as a manufactured antibody (Ab2) that can recognize the idiotype of another antibody (Ab1). Theoretically, the anti-idiotype antibody mimics the structure of the antigen recognized by Ab1. When Ab2 is injected into the host, the host develops immunological memory comprising antibodies (Ab3) which have similar specificities as Ab1.[5]

Attenuated - weakened or treated in such a way as to decrease the ability of a microorganism (such as parasite or virus) to cause infection or disease.[6]

Attenuated vaccine - a vaccine in which live bacteria or viruses are weakened through chemical or physical processes in order to produce an immune response without causing the severe effects

[1] American Heritage Dictionary definition: http://education.yahoo.com/reference/dictionary/entry/adjuvant.
[2] http://medical-dictionary.thefreedictionary.com/antibody.
[3] http://medical-dictionary.thefreedictionary.com/humoral+immunity.
[4] http://medical-dictionary.thefreedictionary.com/antigen.
[5] http://en.wikipedia.org/wiki/Anti-idiotypic_vaccine.
[6] http://medical-dictionary.thefreedictionary.com/attenuated+virus.

of the disease. Attenuated vaccines currently licensed in the United States include measles, mumps, rubella, polio, typhoid, yellow fever, and chickenpox/shingles. This is also known as a live vaccine.

Attenuation -- defined herein as established by introduction of a heritable genetic alteration or gene mutation, or by radiation exposure (preferred), chemical exposure or environmental exposure.

B cells – defined herein as small white blood cells that help the body defend itself against infection. These cells are produced in bone marrow and develop into plasma cells that produce antibodies. These cells are also known as B-lymphocytes.[7]

BLAST – defined herein as the acronym for Basic Local Alignment Search Tool. This program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance of matches.

Booster – defined herein as a second or later vaccine dose given after the primary dose(s) to increase the immune response to the original vaccine antigen(s). The vaccine given as the booster dose may or may not be the same as the primary vaccine.[8]

Delivery Systems – defined herein as a method or system by which a vaccine is delivered to the host body.[9]

DNA (deoxyribonucleic acid) - defined herein as the double-stranded, helical molecular chain found within the nucleus of each cell. DNA carries the genetic information that encodes proteins and enables cells to reproduce and perform their functions.[10]

DNA vaccine (nucleic acid vaccine) - defined herein as direct injection of a gene(s) coding for a specific antigenic protein(s), resulting in direct production of such antigen(s) within the vaccine recipient in order to trigger an appropriate immune response.[11]

DWPI – defined herein as Derwent World Patent Index, which is the world's most comprehensive database of patent documents. DWPI includes over 20 million patent document families, which covers over 42.5 million patent documents. The DWPI database includes coverage from over 44 worldwide patent authorities.[12]

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[7] http://en.wikipedia.org/wiki/B_cell.
[8] http://en.wikipedia.org/wiki/Booster_dose.
[9] Crystal Chan, et. al., *Advancing Adjuvants and Vaccine Delivery Systems for Better Vaccination Strategies*, BioPharm Int'l Supplements, Jan. 2, 2010.
[10] http://education.yahoo.com/reference/dictionary/entry/DNA.
[11] http://www.who.int/biologicals/areas/vaccines/dna/en/index.html. *See also* http://www.dnavaccine.com/.
[12] http://thomsonreuters.com/products_services/legal/legal_products/a-z/derwent_world_patents_index/.

Efficacy - defined herein in vaccine research, the ability of a vaccine to produce a desired clinical effect, such as protection against a specific infection or disease, at the optimal dosage and schedule in a given population. A vaccine may be tested for efficacy in Phase 3 clinical trials if it appears to be safe in Phase 1 trials and has shown efficacy at certain dosages in Phase 2 trials.[13]

Endemic - defined herein as the continual, sometimes low-level presence of disease in a community.[14]

Epitope - defined herein as a specific site on an antigen that stimulates specific immune responses, such as the production of antibodies or activation of immune cells**.**[15]

Expression system - defined herein as in genetic engineering, the cells into which a gene has been inserted into a host cell in order to manufacture desired proteins.[16]

Functional antibody - defined herein as an antibody that binds to an antigen and has an effect that can be demonstrated in laboratory tests**.**[17]

Gene – defined herein as a unit of genetic material (DNA); a segment of DNA encoding a protein molecule; a segment of DNA that contains the information for a specific function.[18]

Hemagglutinin (HA) – a major membrane protein of influenza viruses and thus a frequent target for immunization strategies to generate protective antibodies. HA recognizes sialic acid residues on the surface of host cells and it functions to attach viral particles to target cells, leading to infection of those target cells.[19] This term is also spelled **haemagglutinin**.

Host - defined herein as a plant or animal harboring another organism or a pharmaceutical composition.[20]

Immune system - defined herein as the complex system (network of specialized cells and organs) in the host body responsible for fighting and responding to disease (immune response). Its primary function is to identify foreign substances (antigens of bacteria, viruses, fungi, or parasites) in the body and develop a defense against them. It involves production of proteins

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[13] http://en.wikipedia.org/wiki/Vaccine_efficacy.
[14] http://en.wikipedia.org/wiki/Endemic_%28epidemiology%29.
[15] http://medical-dictionary.thefreedictionary.com/epitope.
[16] http://www.news-medical.net/health/Gene-Expression-System.aspx.
[17] http://en.wikipedia.org/wiki/Antibody.
[18] http://en.wikipedia.org/wiki/Gene.
[19] http://en.wikipedia.org/wiki/Hemagglutinin_%28influenza%29.
[20] http://en.wikipedia.org/wiki/Host_%28biology%29.

called antibodies to eliminate these foreign organisms that have invaded the host, and the generation of cytotoxic activity to eliminate infected cells.[21]

Immunity - defined herein as a natural or acquired resistance provided by the immune system to a specific disease. Immunity may be partial or complete, specific or nonspecific, long lasting or temporary. Immunity is indicated by the presence of antibodies and antigen-reactive cells in the blood and can usually be determined with a laboratory test.[22]

Immunization - defined herein as the process by which a person or animal becomes protected against a disease; the process of inducing immunity by administering an antigen (vaccine) to allow the immune system to prevent infection or illness when it subsequently encounters the infectious agent. This term is often used interchangeably with vaccination or inoculation.[23]

Influenza- herein defined as a virus originating from the family of RNA viruses Orthomyxoviridae. The family Orthomyxoviridae contains three genera, Influenzavirus A, Influenzavirus B, and Influenzavirus C.[24]

INPADOC (International Patent Document Center) – defined herein as a patent database maintained by the European Patent Office (EPO).[25]

ITTI – defined herein as International Technology Transfer Institute, an intellectual property clinic at the University of New Hampshire School of Law.[26]

Neuraminidase (NA) - a major membrane protein of influenza viruses and thus a frequent target for immunization strategies to generate protective antibodies. NA is an enzyme which cleaves sialic acid residues from proteins on influenza virus membranes, thereby preventing aggregation of viral particles.[27]

NCBI – defined herein as the acronym for National Center for Biotechnology Information. NCBI provides access to biomedical and genomic resources, such as BLAST.[28]

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[21] http://en.wikipedia.org/wiki/Immune_system.
[22] http://medical-dictionary.thefreedictionary.com/immunity.
[23] http://www.who.int/topics/immunization/en/.
[24] http://www.niaid.nih.gov/topics/Flu/understandingFlu/Pages/definitionsOverview.aspx.
[25] http://www.epo.org/searching/essentials/patent-families/inpadoc.html.
[26] http://law.unh.edu/franklin-pierce-ip-center/international-technology-transfer-institute.
[27] MJ Sylte and DL Suarez. 2009. *Influenza neuraminidase as a vaccine antigen*, Curr. Top. Microbiol. Immunol. 333:227-4.
[28] http://www.ncbi.nlm.nih.gov/.

Pandemic Influenza - herein defined as a highly pathogenic virus from the family Orthomyxoviridae. The viruses that fall under this category have the capacity to spread rapidly from person to person and have to potential to create a global pandemic.[29]

Passive immunization – defined herein as the introduction of antibodies or antiserum into a host to treat an infection, wherein such treatment does not result in immunological memory and long-lasting immunity in the host.[30]

Patent document count – defined herein as an expanded patent family which includes all issued patents and patent applications that fall within that family.

Patent family – defined herein as a group of patent documents having a commonality such as priority document (INPADOC) or claimed invention (DWPI). The patent documents can be from any jurisdiction.

PCT – defined herein as the Patent Cooperation Treaty, which is an international treaty whose goal is to provide a unified procedure for filing patent applications in the contracting states. A contracting state is a country which has signed onto the treaty. A patent application filed under the PCT is commonly referred to as an international application, or PCT application.[31]

Pharmaceutical Compositions – defined herein as the combination of distinct parts or elements to form a whole relating to pharmacy, drugs, or medicine. This can include anything from vitamins, antibodies, antigens, medicaments, and adjuvants.

Seasonal Influenza - herein defined as a virus from the family Orthomyxoviridae that regularly infects humans between early fall and late winter seasons.[32]

Vaccine - defined herein as a preparation that stimulates an immune response that can prevent an infection or create resistance to an infection based upon an antibody response to an antigen**.**[33]

Veterinary Vaccines- herein defined as vaccines for pandemic influenza for the specific use in non-human animals. Target animals include fowl (chicken, ducks, geese, etc.), pigs, horses, and dogs.[34]

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[29] http://www.cdc.gov/flu/pandemic-resources/.
[30] http://en.wikipedia.org/wiki/Passive_immunity.
[31] http://www.wipo.int/pct/en/texts/articles/atoc.htm.
[32] http://www.flu.gov/about_the_flu/seasonal/index.html#.
[33] http://en.wikipedia.org/wiki/Vaccine.
[34] http://www.ott.nih.gov/Technologies/abstractDetails.aspx?RefNo=1731.

Background of the Technology

Influenza Infections: The Disease

Influenza, more commonly known throughout the world as the flu,[35] is a highly infectious disease caused by the RNA virus family Orthomyxoviridae. The family Orthomyxoviridae consists of three genera of viruses, influenza A, influenza B, and influenza C. Influenza is believed to have originated in birds as this family of viruses has resided in birds for millions of years and generally does them no harm.[36] An influenza-like disease was described as early as 412 BC by Hippocrates, and the term influenza first appeared in 1357. The first known influenza pandemic began in 1580.[37]

Influenza viruses frequently mutate and can readily jump the species barrier from wild birds to domesticated fowl, such as chickens, ducks or geese, and finally to pigs.[38] Pigs can be infected by both avian influenza and forms of influenza that can infect humans.[39] In a setting such as a farm where chickens, humans, and pigs live in close proximity, pigs can be infected with avian and human flu simultaneously and the two types of virus may exchange genes in a process called genetic drift.[40] Such a "reassorted" flu virus can sometimes spread from pigs to people.[41] It is these reassorted viruses that are believed to be the strains that can cause an influenza pandemic.

Nature of an outbreak of a pandemic strain

As previously mentioned, influenza pandemics occur when a new strain of the influenza virus is transmitted from another animal species to human.[42] These novel strains are unaffected by any immunity people may have to older strains of human influenza and can therefore spread extremely rapidly and infect very large numbers of people. Within the past 150 years roughly five influenza pandemics have occurred, the 1918 influenza (H1N1) being the earliest and deadliest of the pandemics.[43] Subsequent pandemics were Asian influenza (H2N2) in 1957 and Hong Kong influenza (H3N2) in 1968. The 2009 swine influenza (H1N1) pandemic was the most recent.[44] Because the avian influenza (H5N1, or bird flu), first identified in 1997, was not transmitted directly from humans to humans, this outbreak is only termed an epidemic.[45]

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[35] The term "flu" is often also used to describe infections by viruses other than influenza, so the more exact term "influenza" is used in this report.
[36] http://www.ncbi.nlm.nih.gov/pubmed/7821758.
[37] http://www.naturalnews.com/026178_flu_influenza_bird.html.
[38] http://www.ncbi.nlm.nih.gov/pubmed/7821758.
[39] *Id.*
[40] *Id.*
[41] *Id.*
[42] *Id.*
[43] http://www.influenzavirusnet.com/history-of-influenza.html.
[44] http://www.flu.gov/pandemic/history/index.html#.
[45] http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0004522/.

An example of a pandemic strain of influenza would be the strain more commonly known as the 1918 Spanish flu. Given this strain of influenza virus was a novel virus to humans and those infected had no previous immunity to this type of virus, the pathology of this disease was particularly severe and an estimated 10%-20% of those infected eventually died.[46] About a third of the world's population was infected and approximately 3%-6% died.[47] Given the technological advances since the 1920's, such as increased travel and trade, the globalized society we now live in is far more conducive to the rise of another influenza pandemic, as seen with the 1957, 1968 and 2009 outbreaks.[48]

The Influenza Virus and its Lifecycle

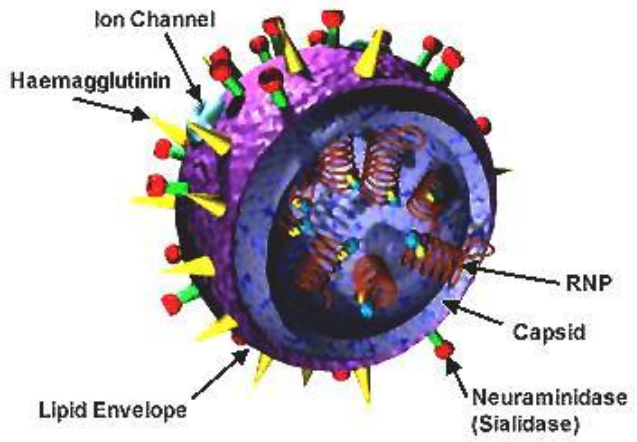


Figure 1. A rendition of the structure of the influenza virus. Image taken from the California Department of Health services. "RNP" denotes ribonucleoprotein, the genetic material of the virus.

Influenza viruses A, B and C are very similar in overall structure. The influenza virus is made of a viral envelope containing two main types of glycoproteins, wrapped around a central core.[49] The central core contains the viral RNA genome and other viral proteins that package and protect the RNA. The influenza genome is not a single piece; instead, the genome contains seven or eight pieces of segmented negative-sense RNA, each piece of RNA containing either one or two genes, which code for a protein.[50] For example, the influenza A genome contains eight genes on eight pieces of RNA, encoding for 11 proteins: hemagglutinin (HA); neuraminidase (NA); nucleoprotein (NP); matrix protein (M1); ion channel protein (M2); nonstructural protein (NS1); nuclear export protein (NEP, also called NS2); a polymerase complex composed of PA, PB1, and PB2; and the apoptosis-inducing protein PB1-F2.[51]

Hemagglutinin (HA) and neuraminidase (NA) are two large glycoproteins found on the outside of the viral particles. HA is a lectin that mediates the binding of the virus to a target cells and

[46] http://www.ncbi.nlm.nih.gov/pubmed/7821758.
[47] *Id.*
[48] *Id.*
[49] http://www.med.ufl.edu/biochem/bch6415/flu%20lecture%20bfv3.pdf.
[50] University of Florida School of Medicine: http://www.med.ufl.edu/biochem/bch6415/flu%20lecture%20bfv3.pdf.
[51] *Id.* see also http://www.virology.ws/2009/05/01/influenza-virus-rna-genome/.

entry of the viral genome into the target cell.[52] NA is involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles.[53] The HA proteins are commonly used as antigens to which antibodies can be raised.[54] The influenza A viruses are classified into subtypes based on antibody responses to HA and NA. These different types of HA and NA form the basis of the *H* and *N* distinctions, for example, *H5N1*. There are 17 hemagglutinin and 9 neuraminidase subtypes known, but only H1, H2 and H3, and N1 and N2 are commonly found in humans.[55,56]

Replication

Viruses can replicate only in living cells. Influenza infection and replication is a multi-step process. First, the virus has to bind to and enter the cell, then deliver its genome to a site where it can produce new copies of viral proteins and RNA, assemble these components into new viral particles, and, last, exit the host cell.[57]

Influenza viruses bind through hemagglutinin onto sialic acid sugars on the surfaces of epithelial cells, typically in the nose, throat, and lungs.[58] The hemagglutinin is then cleaved by a protease, the cell imports the virus by endocytosis.[59]

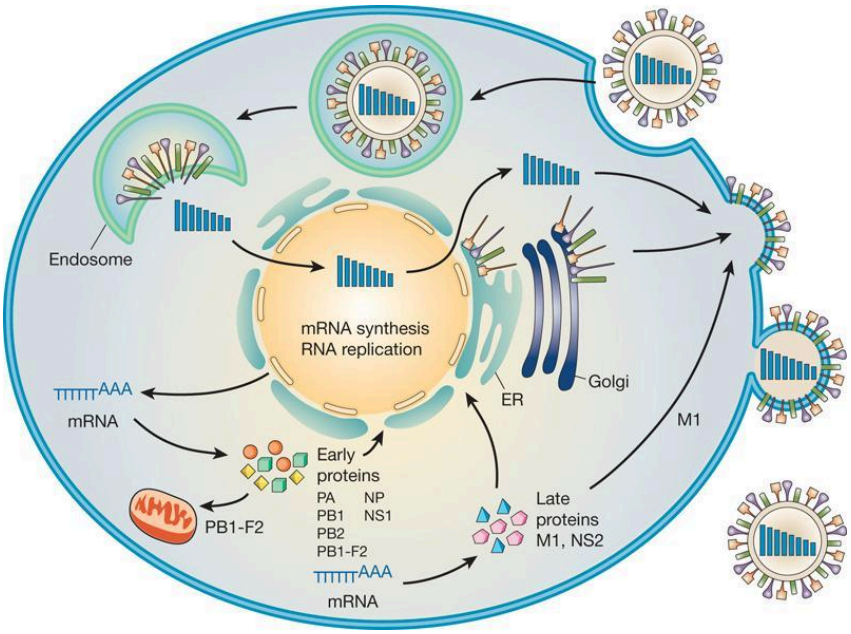


Figure 2. Adapted from Neumann et al., *Nature* **459**, 931-939 (18 June 2009).

[52] *Id.*
[53] http://www.rcsb.org/pdb/101/motm.do?momID=113.
[54] http://www.rcsb.org/pdb/101/motm.do?momID=76.
[55] *Id.*
[56] http://www.nhs.uk/news/2012/03march/Pages/cdc-finds-h17-bat-influenza.aspx.
[57] http://www.stanford.edu/group/virus/1999/rahul23/replication.html.
[58] http://www.stanford.edu/group/virus/1999/rahul23/replication.html.
[59] http://www.ncbi.nlm.nih.gov/pubmed/20237084.

Once inside the cell, the acidic conditions of the endosome cause two events to occur: first, part of the hemagglutinin fuses the viral envelope with the vacuole's membrane, then the M2 ion channel allows protons to move through the viral envelope and acidify the core of the virus, which causes the core to dissemble and release the viral RNA and core proteins.[60] The viral RNA (vRNA) molecules, accessory proteins and RNA-dependent RNA polymerase are then released into the cytoplasm.[61]

These proteins and vRNA form a complex that is transported into the cell nucleus, where the RNA polymerase begins transcribing complementary positive-sense vRNA.[62] The vRNA can be exported into the cytoplasm and be translated or the vRNA can remains in the nucleus.[63] The newly synthesized viral proteins can be either secreted through the Golgi apparatus onto the cell surface or transported back into the nucleus to bind vRNA and form new viral genome particles.

Negative-sense vRNAs that form the genomes of future viruses and other viral proteins are assembled into a virion.[64] Next, molecules of hemagglutinin and neuraminidase cluster into a bulge in the cell membrane. The vRNA and viral core proteins leave the nucleus and enter this membrane protrusion.[65] The mature virus buds off from the cell in a sphere of host phospholipid membrane, acquiring hemagglutinin and neuraminidase with this membrane coat. As before, the viruses adhere to the cell through hemagglutinin; the mature viruses detach once their neuraminidase has cleaved sialic acid residues from the host cell. After the release of new influenza viruses, the host cell dies.[66]

Influenza symptoms

In humans, common symptoms of influenza infection are fever, sore throat, muscle pains, severe headache, coughing, and fatigue.[67] Most people who get influenza will recover in a few days to less than two weeks, but some people will develop complications (such as pneumonia) as a result of the infection, some of which can be life-threatening.[68]

Pneumonia, bronchitis, and sinus and ear infections are three examples of complications from influenza infections.[69] Further, influenza can make chronic health problems worse. For example, people with asthma may experience asthma attacks while they are infected with influenza, and people with chronic congestive heart failure may have worsening of this condition that is triggered by influenza.[70]

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[60] http://www.stanford.edu/group/virus/1999/rahul23/replication.html.
[61] *Id.*
[62] http://www.ncbi.nlm.nih.gov/pubmed/12921991.
[63] *Id.*
[64] http://www.stanford.edu/group/virus/1999/rahul23/replication.html.
[65] *Id.*
[66] http://www.stanford.edu/group/virus/1999/rahul23/replication.html.
[67] http://www.cdc.gov/flu/about/disease/symptoms.htm .
[68] *Id.*
[69] *Id.*
[70] *Id.*

Transmission

Influenza virus shedding (the time during which a person might be infectious) begins a day before typical symptoms appear; the virus is then released for between 5 to 7 days, although some people may shed virus for longer periods.[71] People who contract influenza are the most infective between the second and third days after the initial infection takes place.[72] The amount of virus shed appears to correlate with fever, a higher amount of virus being shed when temperatures are higher.[73]

Influenza is transmitted in three main ways: by direct transmission (when an infected person sneezes mucus directly into the eyes, nose or mouth of another person); the airborne route (when someone inhales the aerosols produced by an infected person coughing, sneezing or spitting) and through hand-to-eye, hand-to-nose, or hand-to-mouth transmission, either from contaminated surfaces or from direct personal contact such as a hand-shake.[74] In the airborne route, the droplets that are small enough for people to inhale are between 0.5 to 5 μm in diameter, and inhaling just one droplet may be enough to cause an influenza infection.[75] Although a single sneeze can release up to 40,000 droplets, most of these droplets are quite large and will quickly settle out of the air.[76]

As the influenza virus can persist outside of the body, it can also be transmitted by surfaces such as banknotes, doorknobs, light switches and other household items contaminated with the virus.[77] The length of time the virus will persist on a surface varies, with the virus surviving for one to two days on hard, non-porous surfaces such as plastic or metal, for about fifteen minutes from dry paper tissues, and only five minutes on skin.[78] However, if the virus is present in mucus, this can protect it for longer periods (up to 17 days on banknotes). Avian influenza viruses can survive indefinitely when frozen.[79]

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[71] http://www.niaid.nih.gov/topics/Flu/understandingFlu/Pages/howFluSpreads.aspx.
[72] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626479/.
[73] http://www.cdc.gov/h1n1flu/recommendations.htm.
[74] http://www.niaid.nih.gov/topics/Flu/understandingFlu/Pages/howFluSpreads.aspx.
[75] http://www.ncbi.nlm.nih.gov/pubmed/18848358.
[76] http://www.ajicjournal.org/article/S0196-6553(98)70046-X/abstract.
[77] http://www.ncbi.nlm.nih.gov/pubmed/18848358.
[78] *Id*.
[79] http://www.cfsph.iastate.edu/Factsheets/pdfs/influenza.pdf.

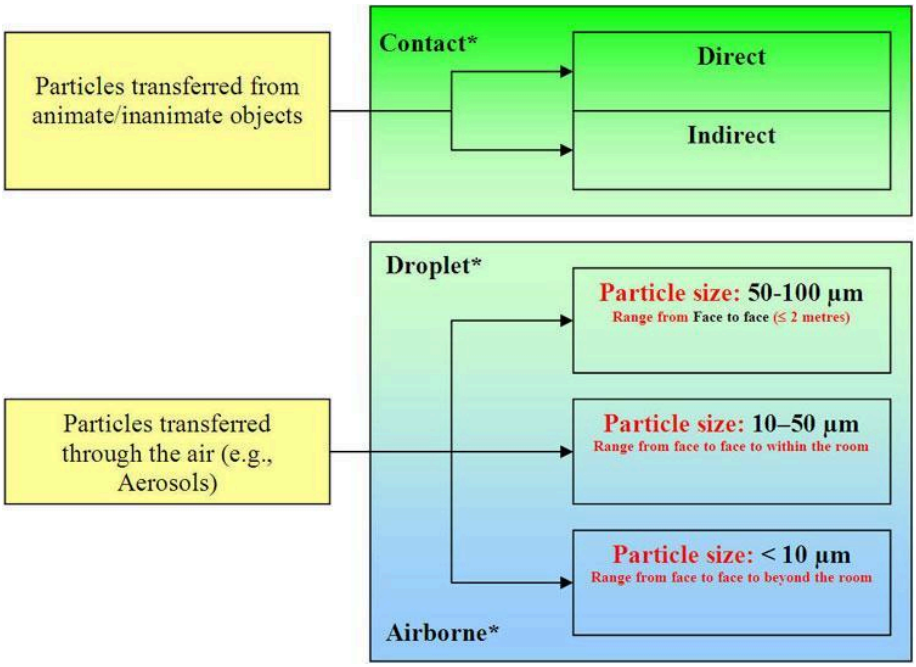


Figure 3. Courtesy of the Public Health Agency of Canada.

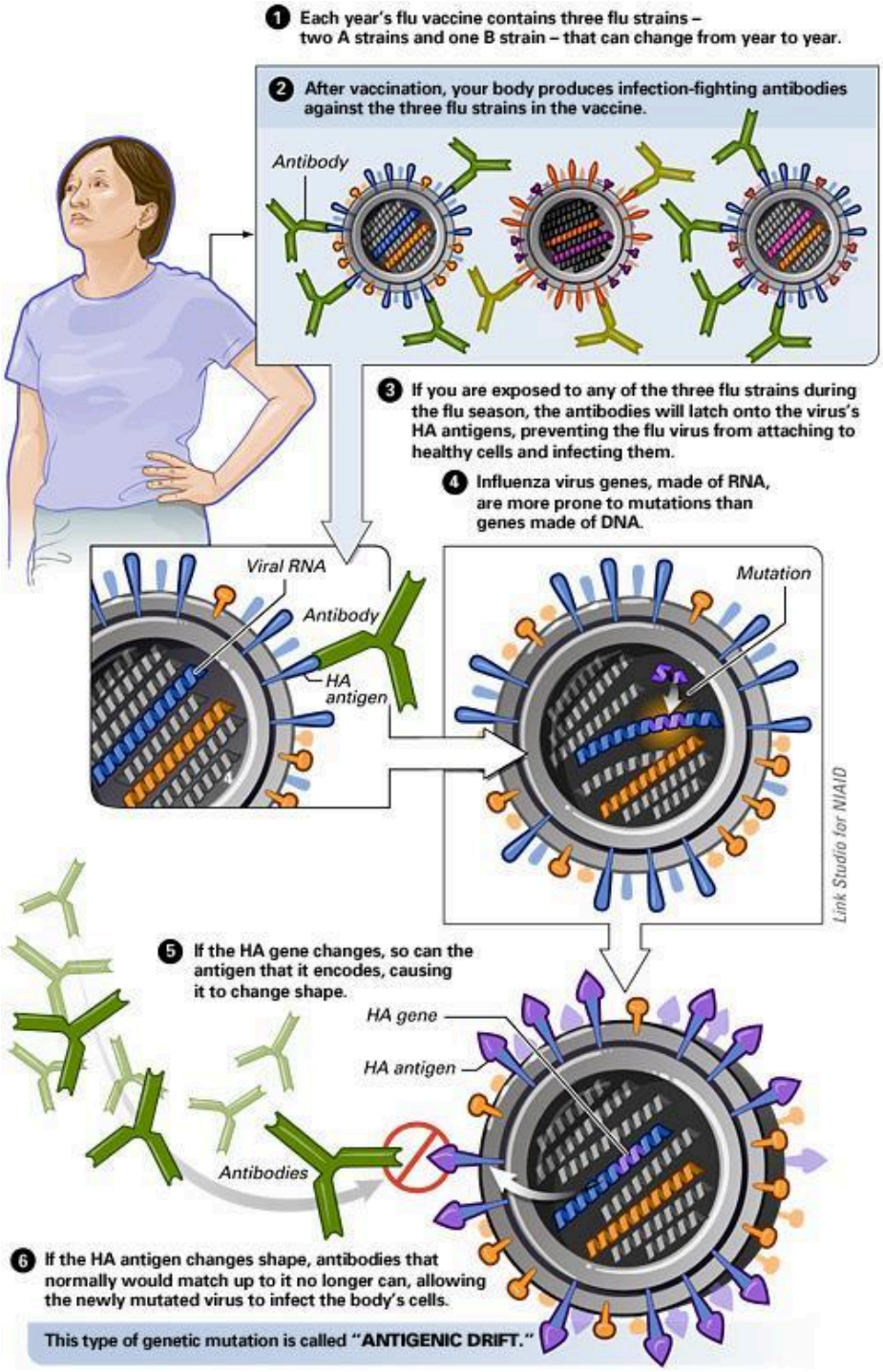
Antigenic Drift and Antigenic Shift

The composition of the influenza virus can change over time. This is accomplished through two means: antigenic drift and antigenic shift. Antigenic Drift occurs when small changes in the virus (i.e. point mutations in the viral genome) happen continually over time.[80] These gradual changes can produce new virus strains that may not be recognized by the body's immune system. A person infected with a particular influenza strain develops antibody against that particular virus. When a new virus strain appears and infects the person, her antibodies which recognize the older strains no longer recognize the "new" virus, and re-infection may occur. This explains why people can get influenza repeatedly. In most years, one or two of the three virus strains in the influenza vaccine are updated to keep up with the changes in the circulating influenza viruses. Thus, people who want to be protected from influenza need to get a "flu shot" every year.[81]

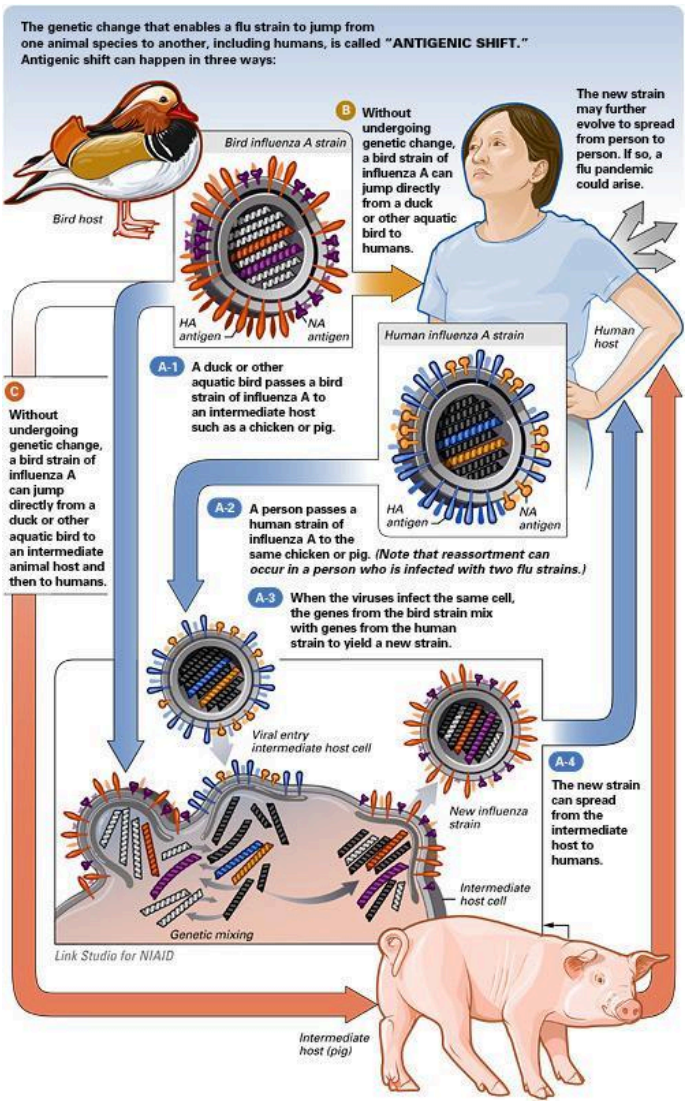
The other type of change, antigenic shift, is an abrupt, major change in the influenza A viral genome, resulting in new hemagglutinin and/or new neuraminidase proteins.[82] Antigenic shift is a recombination event between two viral strains such that a new strain emerges from an animal population. This new strain is so different from subtypes humans have previously seen that most people do not have immunity to the new virus.[83] Such a shift was seen during the spring of

[80] http://www.cdc.gov/flu/about/viruses/change.htm.
[81] *Id.*
[82] http://www.cdc.gov/flu/about/viruses/change.htm.
[83] *Id.*

2009, when a new H1N1 virus with a new combination of genes emerged to infect people and quickly spread, causing a pandemic. While influenza viruses are changing by antigenic drift all the time, antigenic shift happens only occasionally. Type A viruses undergo both kinds of changes; influenza type B viruses change only by the more gradual process of antigenic drift.[84]



[84] *Id.*



Figures 4A and 4B. Illustrations depicting antigenic drift and antigenic shift. Courtesy of the U.S. National Institutes of Health.

Types of Vaccines

Whole virus vaccines - This type of vaccine can be comprised of killed whole viruses or attenuated viruses.[85] Attenuated viruses are live viruses that have been cultivated under conditions that disable their virulent properties, or which use closely related but less dangerous organisms to produce a broad immune response.[86] Attenuated virus vaccines typically provoke more durable immunological responses and are the preferred type for healthy adults.[87] Attenuated vaccines have some advantages and disadvantages. For example they have the capacity of transient growth so they give prolonged protection, and no booster dose is required. However, the attenuated virus may revert to the virulent form and cause disease.[88] Attenuated

[85] http://www.niaid.nih.gov/topics/vaccines/understanding/pages/typesvaccines.aspx.
[86] *Id.*
[87] *Id.*
[88] *Id.*

influenza viruses were traditionally produced in fertilized chicken eggs, but today commercial production is more commonly accomplished using mammalian cell cultures (Fig. 5).[89]

Protein subunit – This type of vaccine is formed by introducing a fragment of microorganism to the immune system to create an immune response.[90] Examples include the subunit vaccine against Hepatitis B virus that is composed of only the surface proteins of the virus.[91]

DNA vaccines – These vaccines use modified. This modified DNA is injected into the cells of the body, where the "inner machinery" of the host cells "reads" the DNA and uses it to synthesize the pathogen's proteins.[92] Because these proteins are recognized as foreign, when they are processed by the host cells and displayed on their surface, the immune system is alerted, which then triggers a range of immune responses.[93]

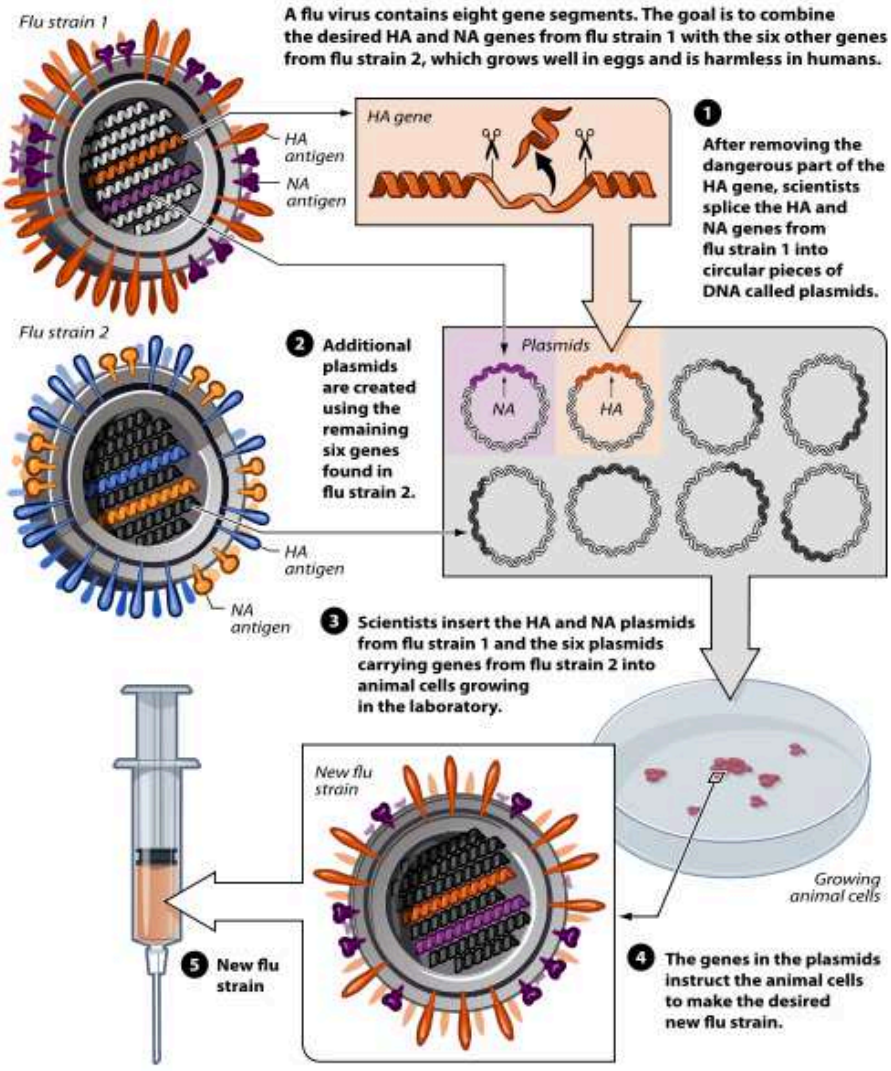


Figure 5. Production of recombinant viruses in cell lines.

[89] http://who.int/vaccine_research/diseases/influenza/Flu_vacc_manuf_tech_report.pdf.
[90] http://www.niaid.nih.gov/topics/vaccines/understanding/pages/typesvaccines.aspx.
[91] *Id.*
[92] http://www.niaid.nih.gov/topics/vaccines/understanding/pages/typesvaccines.aspx.
[93] *Id.*

Scope of the Project

The ITTI team began this project after consultation with Dr. Anatole Krattiger, Director of the Global Challenges Division at the World Intellectual Property Organization (WIPO). After the discussion, the subject of the project was set to the produce a patent landscape report surveying the technologies necessary to produce a vaccine targeted against an outbreak of pandemic influenza. For such a broad subject the ITTI team needed to limit the scope of the project. The ITTI team set the scope of the project to include the following: all types of complete vaccines, veterinary vaccines, novel viruses, methods of vaccine production and formulation, methods of producing viruses or viral subunits, and general platforms related to influenza vaccines.

The ITTI team decided that complete vaccines are relevant to the subject and thus fall within the scope of the project. Although the ITTI team did not know all of the types of vaccines patents a landscape analysis would discover, the ITTI team subdivided the vaccine category into whole/attenuated virus vaccines, subtype vaccines, and DNA vaccines.

In reviewing the patents related to vaccines, the ITTI team recognized the need to address the issue of when the claims of a patent were directed to vaccines mainly used in animals. Given that a pandemic often involves transmission of virus from animals to humans, and that there is a need to vaccinate livestock against influenza, vaccines directed solely to the use in animals were included as relevant documents and given a separate category.

Another important decision was whether or not to include vaccines and related technologies only covering seasonal influenza. The issue arose as some seasonal vaccine technologies could be potentially adapted to be used to treat pandemic strains of influenza. The ITTI team decided to include technologies that were used for both seasonal and pandemic influenza and for some seasonal influenza technologies but not vaccines or antigens restricted solely to seasonal influenza.

One of the most important decisions made was how to deal with adjuvants. The main problem with adjuvants is that an adjuvant patent often claims use in vaccines for pandemic influenza in a large Markush group, along with hundreds of other diseases. On the other hand, an adjuvant could be limited to just pandemic influenza. Faced with these two issues, adjuvants were divided into two groups, general adjuvants, defined as an adjuvant that listed pandemic influenza in a large Markush group, would be excluded from the report[94] and related adjuvants, defined as adjuvants used just for pandemic influenza would be considered relevant.[95]

[94] For example US20090047306A1.
[95] For example US20110165193A1.

Patent Search Methodology

> *Guess, compute the consequences to see what that guess would imply, and compare directly with observation to see if it works. If it disagrees with the experiment, it's wrong. It's that simple. It doesn't matter how beautiful your guess is, how smart you are, or what your name is. Looking at the universe, the great power of science, there's no such thing as authority of nature. If it doesn't agree with the experiment, then it's wrong.*
>
> - *Richard Feynman*

Iterative Process

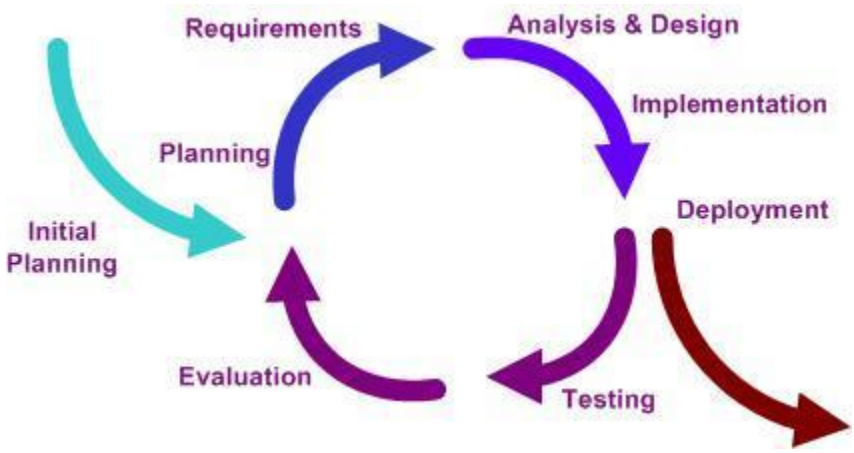


Figure 6. Iterative development model. Taken from Wikipedia.

The iterative process is defined as the act of repeating a process with the aim of approaching a desired goal, target, or result. Each repetition of the process is called an iteration, and the results of one iteration are used as the starting point for the next iteration. In the field of patent searching, the iterative process is a searching methodology wherein at the end of a search cycle, the search is evaluated, and its shortcoming assessed. The shortcomings are then addressed in the next cycle of searches in order to capture the documents. The next search can be either wider in scope or could be a narrower search depending on the results gained from the previous search.

In this study, keyword searching identified relevant documents, from which were extracted further keywords as well as classification codes. The classification codes were used to locate additional documents. Keywords were adjusted and used for another round of searching.

Precision and Recall[96]

The number of patent documents worldwide, including patents (issued, re-issued, and re-examined) and applications, is over 60 million[97]. Selecting relevant documents from such a huge dataset can be difficult, and this type of document retrieval is governed by the mathematical theory of Precision and Recall. Precision is the percentage of retrieved documents that are relevant and is calculated as the number of retrieved relevant documents divided by the total number of retrieved documents. Recall is the fraction of relevant documents retrieved and is calculated as the number of retrieved relevant documents divided by the total number of existing relevant documents. These concepts are illustrated in Figure 7[98] below.

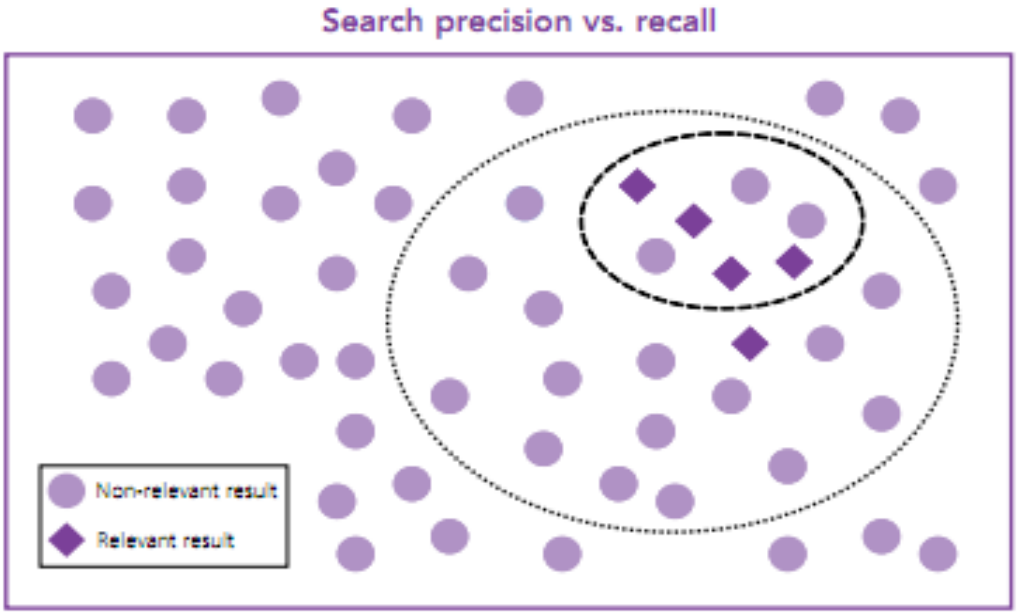


Figure 7. Increasing precision of a search means some relevant results are excluded.

Thus, any set of retrieved of documents will always include a certain fraction of irrelevant documents, also termed false positives. As a search attempts to capture an ever higher fraction of relevant documents, the sensitivity of the search will decrease because the proportion of false positives will increase. In the extreme, every relevant document can only be captured if every irrelevant document is also captured, as depicted in Figure 8[99].

[96] *See also* J. Davis and M. Goadrich, The relationship between precision-recall and ROC curves, Proceedings of the 23rd International Conference on Machine Learning, Pittsburgh, PA, 2006.
[97] Based on data from 2007. http://www.taeus.com/article.php?id=66.
[98] http://www.wipo.int/freepublications/en/patents/434/wipo_pub_l434_03.pdf
[99] Precision Recall Graph, Mirrored ROC Curve, www-csli.stanford.edu.

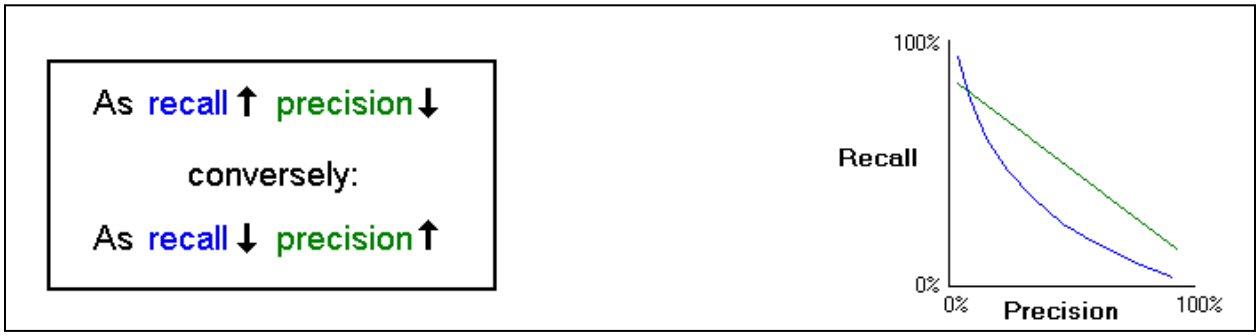


Figure 8. Inverse relationship between recall and precision.

Stated another way, a high **recall** means you haven't missed anything but you may have a lot of useless results to sift through (which would imply low **precision**). High **precision** means that everything returned was a relevant result, but you might not have found all the relevant items (which would imply low **recall**).[100]

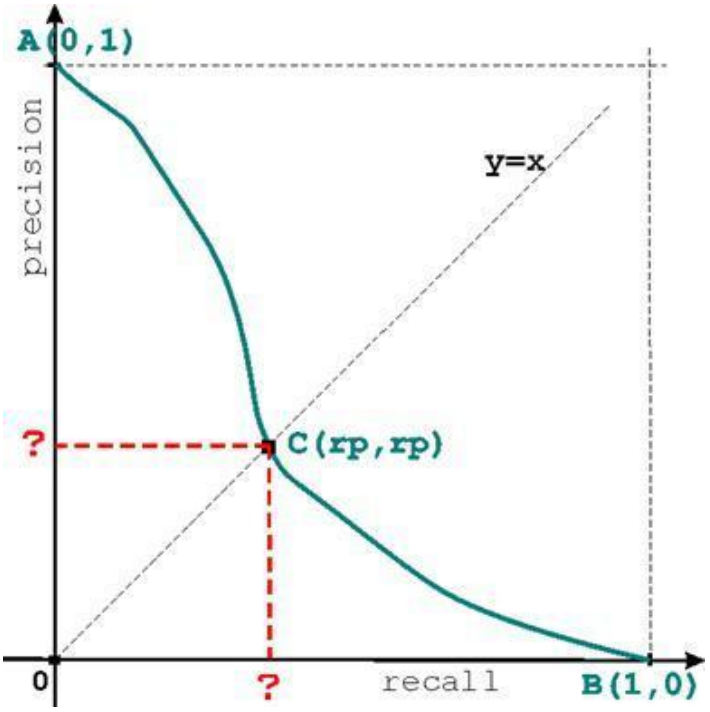


Figure 9. An optimal balance can be achieved which is neither 100% precise nor contains 100% recall.

An optimal balance, point C in Figure 9[101], must therefore be achieved between precision (degree of relevance of all retrieved documents) and recall (fraction of relevant documents retrieved). In terms of patent searching, and in particular searching for relevant vaccine patents within the

[100] Wikipedia, the free encyclopedia, http://en.wikipedia.org/wiki/Precision_and_recall.
[101] http://www.ccs.neu.edu/home/jaa/CSG339.06F/Homeworks/hw.01.html.

influenza vaccine landscape, one deciding on that balance point must have experience in patent searching in general, knowledge concerning the technology involved, and an understanding of the goal of the search. The purpose of the methodology described in the previous report and refined in this update is to provide a framework for such a decision-making process.

A search method example that resulted in high levels of recall and low levels of precision is semantic searching. In this search method, recall was high but precision was low. The reason semantic searching may have been less than effective is that the boundaries that create accuracy in a search, the keywords, were computer generated. Although it is difficult to judge the precision levels of semantic searching based on our limited attempts, this results seem to indicate that the keywords generated by a computer do not result in high levels of precision.

Other databases were more successful for obtaining high levels of precision. For example, when the search string was controlled and the database being searched was efficient, the results that were obtained were an optimal balance between precision and recall. For example, Derwent is a pre-screened database, where language and classifications are carefully standardized. Therefore, precision is increased due to accuracy and efficiency of searching.

Platform Services

U.S. Patent and Trademark Office[102]

ITTI utilized the USPTO database for classification searching, a patent search platform created by the United States Patent and Trademark Office, which provides function to search for patents within any of the USPTO's classifications. The USPTO database also allows for non-classification searching.

Thomson Innovation[103]

ITTI utilized Thomson Innovation, a patent search platform that integrates the best of the suite of Thomson tools, Aureka, Delphion and MicroPatent. Thomson Innovation is a single, integrated tool that combines intellectual property, scientific literature, business data and news with analytic, collaboration, and altering tools in a robust platform.

TotalPatent[104]

ITTI also utilized TotalPatent, a LexisNexis platform, to search patents and patent applications world-wide. TotalPatent provides several additional countries that are not included in other platforms. Also, TotalPatent offers useful tools such as semantic searches, the ability to search for subsidiary companies and corporate structure, and analytics.

[102] http://www.uspto.gov/.
[103] http://info.thomsoninnovation.com/.
[104] http://www.lexisnexis.com/en-us/products/total-patent.page.

Sequence Searching

ITTI also performed sequence searching to corroborate the results from conventional search methods. ITTI performed the sequence searches after searching non-patent literature in NCBI's PubMed.[105] The non-patent literature documents were generally scientific articles containing nucleotide and protein sequences related to the relevant technology. The sequences referenced in the articles were inserted into GenomeQuest[106] and ITTI used the BLAST algorithm[107] to perform a search that produced patents with the same or similar nucleotide or protein sequences.

The sequence searches were performed concurrently with the conventional search methods. The sequence search results were used to corroborate results and also to ensure that ITTI was not overlooking any patents within the relevant technology field.

Sequence searching using PubMed and GenomeQuest produces an abundance of non-patent literature and provides a way to narrowly search for patents related to the relevant technology. Overall sequence searching allowed ITTI to corroborate its results and revealed that ITTI had not missed any major portions of the relevant technology. However, sequence searching produces results narrowly confined to those nucleotide or protein sequences and thus becomes a tedious search method if used predominantly. ITTI's sequence searching method is thus best used as an initial search for non-patent literature and also as a way to corroborate search results.

Deduplication Process and Collapsing into Families

The search results from ITTI's secondary patent searches were combined to form a single list of patent documents. The combined search results were placed into Microsoft Excel as publication numbers and deduplicated. The number of duplicates was taken as an indication of the level of recall. For example, a high percentage of duplicates would mean that most of the relevant results had been identified. However, publications numbers with different file extensions, such as PCT extensions A1, A2, and A3, would be recognized as different even though the numbers corresponded to the same application.

A further method of deduplication employed Thompson Innovation. A publication number search was performed and all related INPADOC family members were returned in the result set. The data was saved as a work file. The same procedure was performed with a different team member's search results. One work file could be subtracted from the other, and the size of the subtracted file would indicate the level of overlap and thus the level of recall being achieved.

[105] http://www.ncbi.nlm.nih.gov/pubmed/.
[106] http://www.genomequest.com/.
[107] http://blast.ncbi.nlm.nih.gov/Blast.cgi.

The work files could also be merged, and Innovation would automatically remove duplicates in the merged work file.

Once a compiled list of all search results was deduplicated, the results were then collapsed by INPADOC family to reduce the initial search results into representative patent family documents. ITTI gave preference to US documents because these documents were easier for the team to analyze and they tended to contain the most complete bibliographic information available. The collapsed list was a much more manageable number of documents which the team could efficiently code into categories. The team recognizes that the representative family member could be a divisional application and thus would not claim the full limit of the invention. Although this could result in an error, either towards inclusion or exclusion, time constraints prohibited coding of every publication individually.

Results

Relevant/Irrelevant Determination

A master of list of influenza-related documents was assembled following three complete rounds of searching by each of the four team members.[108] On the second round of searching, about 25% of over 15,000 documents were repeated among the different members' results. However, the third round of searching generated only 78 new INPADOC families, compared to over 3,700 previously identified families, which was only a 2% increase in the results. Thus, the team was confident that at least 98% of the influenza-related documents had been captured.

The results were compiled and a publication number search was performed using Innovation to expand the families. Approximately 33,500 total documents were identified, and these results were collapsed into almost 3,800 INPADOC patent families.[109] Representative family members were then subjected to a coding process. Publications that were irrelevant to influenza or were outside the scope of this project were excluded. Documents were also excluded if they were duplicates (such as an application and a patent that was issued from that application which was not assigned properly to the same INPADOC family[110]), or if there was too little information in the record to support a coding decision, such as some documents that had only a title[111].

Documents were considered relevant if they specifically claimed influenza or members of the orthomyxovirus family. Coding was done on the claims of the representative family members, or, if no claims were available, coding was done using other family members. INPADOC family members were given preference, but DWPI family members were used alternatively. Family members were selected in the following order, as available: a U.S. application (assumed to have the broadest claims), U.S. patent, a PCT application, and finally a document having claims in English, such as a document from Great Britain or Australia. If no family members had claims in English, foreign language claims were translated into English using Google Translate.[112] If there were no family members having claims in their records, the family was coded using a DWPI summary of the claims, or if absolutely necessary, on the abstract alone. In the final case, the coding was done very conservatively and the document was excluded unless it obviously related to a prophylactic influenza A vaccine.

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[108] The keywords used in patent searching are located in Appendix L.
[109] Results are given in approximations because new family members were continually being identified and publications were added to existing families. Thus, the actual numbers changed each week with total documents increasing and the number of families decreasing.
[110] For example, IE6500388A is the application for issued patent IE28884L, but the documents were not assigned to the same INPADOC family.
[111] For example, IT1379280B.
[112] http://translate.google.com/.

In this manner, over 97% of the results were either assigned to one of the coding categories given below or were excluded as outside the scope of this report. Many documents were relevant to multiple categories, but each representative family was placed in only one category, that category being the best fit for the overall focus of the document. For example, a document claiming both a complete vaccine and the components to be assembled into that vaccine was placed into one of the vaccine categories. Alternatively, if the document focused on the process of making the vaccine, the document was coded to one of the method categories. In general, there were four major categories for coding documents: vaccines, supporting technologies, general platforms, and excluded documents. The first two categories were divided into subcategories. The definitions and criteria for each category are given below. The Master Coding Document can be found in Appendix A.

Coding Categorization of Patent Documents

General platforms.
A document had to specifically claim influenza in order to be considered relevant. However, about 15% of the results claimed influenza only generally, such as in a large Markush group[113] or only in one dependent claim[114]. The technology described in such documents could be useful in constructing an influenza vaccine, but could just as easily serve as a platform for vaccines against a wide range of pathogens. These documents were considered to have a low level of relevance. While these documents are captured and reported in Appendix B, they are not included in any of the analysis below.

Vaccines.
Vaccines were divided into three subcategories: whole virus vaccines, subunit vaccines, and DNA vaccines. Whole virus vaccines included live, attenuated (live but avirulent), or killed whole virus particles. This group would also contain split (digested) but unfractionated preparations of viruses, so that the vaccine contained all possible influenza antigens. Many of these whole viruses were recombinant virions which contained one or more antigens from a pandemic virus expressed by an otherwise nonpathogenic virus.

Subunit vaccines contain individual influenza antigens or a mixture of a limited number of antigens, but less than a complete virus. The antigens could either be purified from whole viruses or produced as recombinant versions of the native protein. The subunits could be also be expressed by non-influenza viruses that act as a carrier for the influenza antigen or as a secondary source of antigens to create a multivalent vaccine, such as a recombinant vaccinia

[113] For example US6207171B1.
[114] For example US20110111017A1.

virus carrying an influenza H5 antigen.[115] The influenza antigens could also be expressed by bacteria such as salmonella[116] or by yeast.[117]

DNA vaccines are nucleic acid constructs which, when injected into an animal, cause expression of an influenza antigen by host cells that take up the nucleic acid constructs. DNA vaccines are typically very good at stimulated cell-mediated immunity, such as cytotoxic T lymphocytes which would in turn destroy influenza-infected host cells. These nucleic acid constructs could be either linear pieces of DNA or RNA, which are short-lived in the host, or DNA plasmids, which can persist for a period of time.

To be considered a vaccine-related publication, the representative document must have claimed compositions of matter having all aspects of a true vaccine: antigen(s), adjuvant (if necessary), carriers/diluents, and a means or route of delivery. If the claims do not meet these aspects, or were solely method claims, the family was placed in one of the supporting technology categories. Merely terming a composition was not sufficient; the claims must have had enough detail to describe an actual vaccine. Some allowance was made for foreign language documents in that a broader range of terminology was accepted as a description of a vaccine. Vaccine documents are reported in Appendix C.

Supporting Technologies.

Some documents claimed influenza in independent claims yet did not sufficiently claim a vaccine composition for use in humans. These documents were coded as one of the supporting technologies which are important for the construction or manufacture of vaccines. Included in the supporting technologies subcategories are novel viruses useful in vaccines and novel subunit constructs useful in vaccines. These documents describe the antigenic components of a vaccine, but lack detail of carriers, adjuvants, and route of administration. Thus these two subcategories were focused on compositions of matter.

Two other subcategories of the supporting technologies were focused more on methods utilized in vaccine manufacture. The first such subcategory contains documents describing methods of making vaccines, which includes procedures for purifying antigens[118] and for formulating vaccines, such as the addition of a specific adjuvant[119] or preparations for intranasal delivery.[120] The other subcategory was established for documents which disclosed methods of producing virus or viral subunits. These method including nucleic acid constructs which could be used to

[115] For example US20110020391A1.
[116] For example HK1145448A0.
[117] For example CN1923288A.
[118] For example US20100330119A1.
[119] For example US20100330190A1.
[120] For example US4512972A.

produce recombinant viruses,[121] cell lines which could be used to produce viruses,[122] or nucleic acid constructs encoding recombinant versions of influenza antigens.[123] While the former subcategory was mostly for method patent documents, the latter subcategory contained a mixture of method and composition of matter claims.

A final subcategory under the heading of supporting technologies was for veterinary vaccines. While the documents in this subcategory described complete vaccines, those vaccines were not for use in humans, although it is possible some may have been able to be adapted for human use. These vaccines were for birds (mostly chickens), pigs, horses, dogs, and other domesticated animals. Such vaccines may be useful not only veterinary purposes but also to prevent transmission of novel influenza strains to humans.

The heading of supporting technologies thus contains a broad spectrum of patent documents covering a variety of different technologies. However, all of these documents are relevant to the production of influenza vaccines and the prophylactic treatment of human populations. The entire list of these documents is presented in Appendix D.

Note on the order of placement

As mentioned above, representative documents may have fit in multiple categories, but the documents were placed in the category which was the most relevant to the overall focus of the document. The order of placement was:

1. Whole virus vaccines
2. Subunit vaccines
3. DNA vaccines
4. Methods of making vaccines
5. Methods of producing virus or viral subunits
6. Veterinary vaccines

Documents were placed in the highest category in which the claims from that document fit. However, if no claims were available in the record of that document or any of its family members, the document were conservatively coded, mostly in the lower categories. If the available record mentioned multiple pathogens, the document without claims was often placed in the platform category.

Excluded irrelevant documents

Approximately half of the documents were excluded as irrelevant or as having insufficient information to allow coding. The full list of these documents can be found on the Master Coding Sheet in Appendix A, but it is useful to detail the reasons for exclusions here, to clarify the scope of the project.

[121] For example US7723094B2.
[122] For example US20100233674A1.
[123] For example US7960609B2.

1. Therapeutic interventions, such as small molecule medicines which inhibit viral replication or function. Therapeutics also include interfering RNA (RNAi) molecules.
2. Means of detecting the presence of influenza virus.
3. Diagnostic methods.
4. Passive immunization.
5. Antibodies directed against influenza. These could be used in any of the above categories. A few patent document mentioned using anti-influenza antibodies to stimulate anti-idiotype responses, but none of those documents disclosed an anti-idiotype monoclonal antibody that could be used to immunize humans.
6. Adjuvants, when influenza is not specifically claimed.
7. Devices, such as surgical masks to prevent infection.
8. Delivery systems for vaccines.
9. Immunization schedules, when a particular vaccine formulation is not disclosed.
10. Herbal medicines, which were common among Chinese documents.
11. Documents actually related to *Haemophilus influenzae*, a bacteria often present in lung infections. Searches for the influenza virus often returned this pathogen as well.
12. Documents actually related to parainfluenza, a distantly-related virus in the *paramyxovirus* family. Searches for the influenza virus often returned this pathogen as well.
13. Documents in which influenza is used only as a tool, such as a fusion partner for other antigens or as immunostimulatory peptides employed as adjuvants. Sometimes recombinant influenza viruses were constructed to contain antigens for other pathogens. While these documents did relate to anti-influenza immune responses, they are not relevant to the generation of prophylactic immunity against pandemic influenza.
14. Documents related to seasonal influenza only, such as influenza B.
15. Quality control methods for standardizing vaccines. The team decided such documents were too peripheral to vaccine production.
16. Sterilizing methods or devices. This includes removal of viruses from blood products prior to transfusion, for example.
17. Computer programs used to predict antigenic epitopes, unless such epitopes were specifically identified and claimed.
18. Dietary supplements which supposedly boosted immunity or otherwise prevented infections.
19. Documents in which influenza was not claimed. Particularly in some general platform technologies, influenza may be mentioned in the abstract but not in the claims.
20. Documents which were not related to influenza.

The last reason needs to be expanded upon, as a small percentage of the results had no relation to influenza but the presence of such documents in a result set is always a concern. In some cases,

influenza peptides were used in assays which were summarized in the Derwent abstract, but the document was not focused on influenza. Other documents did not relate to the vaccine field in any way. These documents may have been returned because some jurisdictions re-use patent numbers with different file extensions, and TotalPatent mistakenly considers the two documents to be family members. For example, CN1147316C is a patent disclosing a subunit vaccine and is a family member with US5948410A, but CN1147316A is a patent for bricks used in walls and floors. Other countries, such as Japan, also have confusingly similar patent numbers to describe unrelated technologies.

Distribution of coding categories

The relative distribution of the results into the various categories is given in Table I. One-third of the results were considered relevant as either a vaccine document or a document describing one of the supporting technologies. Analytics was performed on these patent documents. The remainder of the results are reported in the appendix but were not included in the analysis.

Table I. Distribution of results (3,800 families) into coding categories.

Vaccines	15.0%
Whole virus vaccines	(6.5%)
Subunit vaccines	(6.7%)
DNA vaccines	(1.9%)
Supporting Technologies	19.8%
Novel viruses useful in vaccines	(2.3%)
Novel subunits useful in vaccines	(2.7%)
Method of making vaccines	(6.7%)
Method of producing virus or viral subunits	(4.5%)
Veterinary vaccines	(3.7%)
Platform technologies	14.7%
Excluded due to lack of information or as duplicates	2.3%
Excluded as irrelevant	48.2%

Pandemic Influenza Documents

Searching was done for influenza-related patent documents which were then categorized based on their relationship to vaccines for influenza A. Not all documents were specific as to whether the technology could be used with pandemic influenza strains, seasonal influenza strains, or both. The team decided to err on the side of inclusion, so that a document was considered relevant if it mentioned influenza generally, pandemic influenza strains, or both pandemic and seasonal strains. Only if the document was specifically limited to seasonal influenza was it excluded. Approximately 20% of families in the vaccine category and 10% of families in the supporting technology category referenced either pandemic or epidemic influenza in the DWPI title or

abstract. Documents representing each family are presenting in Table II. Full information on those documents can be found in Appendices C and D.

Table II. Documents representing a patent family referencing pandemic influenza.

Publication Number	**Title - DWPI**	**Assignee/Applicant**
Vaccine Category		
AU2012216357A1	New recombinant adenovirus vector comprises a polynucleotide encoding at least one antigen of an avian influenza strain, useful for producing vaccines for eliciting an immune response against avian or pandemic influenza	PURDUE RESEARCH FOUNDATION | GOVERNMENT OF THE US SECRETARY OF THE DEPT OF HEALTH AND HUMAN SERVICES CT S FOR DISEASE CONTROL AND
CN101053658A	Preparing composite multi-epitope bivalent nucleic acid vaccine for preventing H3,H9 subtype influenza virus, by obtaining a composite multi-epitope target Epi gene, and inserting into pIRES1neo expression vector	JIN Ning-yi,Changchun, Jilin 130062,CN
CN101450209B	New transdermal influenza immunization multivalent vaccine comprising transdermal agent, transdermal immune adjuvant, and influenza multivalent vaccine antigen, useful for immunizing Balb/c mouse, ferret, monkey, and humans	Academy of Military Medical Sciences of The CPLA Institute of Microbiology and Epidemiology,CN
CN101524538A	New influenza-pandemic influenza bivalent combined vaccine comprises influenza immunogen, pandemic influenza immunogen, and vaccine adjuvant, for treating or preventing influenza, pandemic influenza, or bird flu viral epidemic influenza	Chengdu Kanghua Biological Products Co. Ltd.,Chengdu, Sichuan 610100,CN
CN101745109A	Influenza virus vaccine preparation involves inoculating Influenza A and B influenza viruses into allantoid cavity of ten days old thousand healthy chick embryos to amplify influenza viruses	Yunnan Valvax Biotechnology Co. Ltd.,Kunming, Yunnan 650106,CN
CN101808659A	Inactivated influenza vaccine comprises beta propiolactone inactivated whole influenza virus and a mono- or disaccharide derivative having specific fatty acid ester groups, as an adjuvant	NOBILON INTERNAT B V,NL

CN101816785B	Preparing H9N2 subtype avian influenza inactivated vaccine comprises screening, identifying, and domesticating virus in a cell line, and initial amplification culturing the virus in the cell	Yangzhou Youbang Biopharmaceutical Co. Ltd.,CN
CN101879312B	New M2e-carrier protein coupler, chemically coupled by ectodomain M2e of influenza A H1N1 virus M2 protein, useful for preventing influenza	Beijing Jingyi Technology Development Co. Ltd.,CN
CN101926994B	Immunoadjuvant used in influenza vaccine, comprises turtle shell extract and carrier, and has low side effect and is prepared in simple, cost-effective and eco-friendly manner	Institute of Medical Biology Chinese Academy of Medical Sciences,CN | Chinese Academy of Sciences Kunming Institute of Botany,CN
CN101926995A	Immunoadjuvant used in influenza vaccine, comprises Asparagus extract and carrier, and is safe and prepared in simple, cost-effective and eco-friendly manner	Chinese Academy of Sciences Kunming Institute of Botany,CN | Institute of Medical Biology Chinese Academy of Medical Sciences
CN102068692A	Influenza virus split vaccine comprises influenza virus hemagglutinin (H1N1), H3N2 and B types, CpG oligodeoxynucleotides adjuvant and aluminum adjuvant	Beijing Minhai Biotechnology Co. Ltd.,CN
CN102397559A	New HA218-72-carrier protein conjugate useful for preventing or treating influenza	Beijing Jingyi Technology Development Co. Ltd.,CN
CN1810961B	Recombinant influenza virus useful as vaccine, involves inserting PB2, PB1, PA, M, NS and NP coding genes from cold-adapted strain of type-A or type-B influenza virus into eukaryotic cell expression plasmid	INST MICROBIOLOGY & EPIDEMIOLOGY
EP1599581A2	New attenuated influenza virus, useful as vaccine, has altered protease cleavage site in hemagglutinin, is not pathogenic but still immunogenic	Transmit Gesellschaft für Technologietransfer mbH,35394 Giessen,DE,03201700 | Philipps Universität Marburg,35032 Marburg,DE,04124880
FR2866031B1	Viral chimer, useful to e.g. treat viral diseases, comprises capsid and/or lipidic envelop, defective genome, genome to serve a helper virus and genome comprising nucleotide sequences encoding polypeptides used in viral antigenicity	MILLET DAVID FRANCOIS JOSEPH

HK1144374A0	Preparing an influenza vaccine from influenza virus grown in a culture of a mammalian cell line by testing the vaccine or culture for an infectious agent that can grow in the cell line but that does not grow in embryonated hen eggs	
HK1144904A0	Eliciting or inducing a protective immune response in a subject against a pandemic subtype of influenza virus, comprises administering to the subject a composition comprising an immunogen of an endemic influenza subtype	
HK1146807A0	New monovalent influenza vaccine, useful particularly for preventing infection by pandemic strains, contains low dose of egg-derived antigen	
HK1155639A0	Kit for raising immune response in patient for protecting against influenza virus infection comprises aqueous inactivated influenza vaccine	
IN200703448P2	Immunogenic composition for preparing vaccines against e.g. influenza virus comprises influenza antigen from at least two influenza virus strains and at least one strain associated with pandemic outbreak and oil-in-water emulsion adjuvant	
IN200703777P4	New nucleic acid construct, comprises chimeric promoter sequence, coding sequence, non-translated leader sequence, and enhancer sequence, for inducing an immune response against influenza virus hemagglutinin (HA) antigen	
IN200704067P2	Use of an influenza virus or antigenic preparation, and an oil-in-water emulsion adjuvant, for inducing at least one of an improved CD4 T-cell immune response, and an improved B-memory cell response against the virus	

IN200704150P2	New recombinant adenovirus vector comprises a polynucleotide encoding at least one antigen of an avian influenza strain, useful for producing vaccines for eliciting an immune response against avian or pandemic influenza	
IN200801841P2	New immunogenic composition comprising an influenza virus antigen, an oil-in-water emulsion adjuvant and a cytokine-inducing agent, useful in raising an immune response against influenza virus infection in a patient	
IN200801873P2	New immunogenic composition comprises split influenza virus antigen and oil-in-water emulsion, where the emulsion includes free surfactant in its aqueous phase, useful as vaccine for protecting against influenza virus infection	
IN200805247P2	New monovalent influenza vaccine composition comprises low amount of influenza virus antigen from an influenza virus strain that is associated with a pandemic, useful for protecting a human from influenza infection	
IN200903238P2	New immunogenic influenza composition, comprises an influenza virus antigen or antigenic preparation in combination with an oil-in-water emulsion adjuvant, useful for treating or preventing diseases caused by influenza infection	
IN201001237P2	Eliciting or inducing a protective immune response in a subject against a pandemic subtype of influenza virus, comprises administering to the subject a composition comprising an immunogen of an endemic influenza subtype	
IN201001619P4	Inactivated influenza vaccine comprises beta propiolactone inactivated whole influenza virus and a mono- or disaccharide derivative having specific fatty acid ester groups, as an adjuvant	

IN201004612P2	Kit for raising immune response in patient for protecting against influenza virus infection comprises aqueous inactivated influenza vaccine	
IN201100348P4	Immunogenic composition, useful for treating influenza, comprises types A and B influenza hemagglutinin proteins	
JP04031478B2	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	PROTEIN SCI,JP
JP2009102416A	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	PROTEIN SCIENCES
JP2011519828A	New flagellin amino acid sequences for treating e.g. influenza virus infection comprises specific deletion and replacement constructs having sequence identity to specific flagellin sequences, where sequences activate toll-like receptor-5	
KR1999022028A	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	
KR2010045436A	New isolated attenuated influenza virus strain comprises internal genome segments of A/PR/8/34(H1N1) and surface antigens hemagglutinin and neuraminidase of A/Aichi/2/68(H3N2), useful as vaccines against influenza virus infections	BIOTRION INC.
MX290169B	Use of an influenza virus or antigenic preparation, and an oil-in-water emulsion adjuvant, for inducing at least one of an improved CD4 T-cell immune response, and an improved B-memory cell response against the virus	

MX293233B	Stabilizing influenza vaccine composition comprises diluting liquid bulk composition, subjecting regular droplets to freezing to form frozen regular spherical micropellets or particles, and drying	
PH12009500128A	New monovalent influenza vaccine composition comprises low amount of influenza virus antigen from an influenza virus strain that is associated with a pandemic, useful for protecting a human from influenza infection	
RU2077581C1	New vaccine strain A (47) Texas-91(2)6 (H1N1) can be used in medicinal virology, for production of live influenza vaccine for children	NIIEX MEDITSINY RAMN
RU2077582C1	New vaccine strain A (17) Shangdong (93) 3/5 (H3N2) can be used in medicinal virology, for production of live influenza vaccine for adults	NIIEX MEDITSINY RAMN
RU2099086C1	Prevention of influenza epidemics in children by intranasal administration of live attenuated cold adapted vaccine	NIIEX MEDITSINY RAMN
RU2110277C1	New strain A(17) of influenza virus Johannesburg (94) 1 (H3 N2) GISK N 391 used for production of live intranasal influenza vaccine for adults	NI SKIJ I EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2110278C1	New strain A(17) of influenza virus Johannesburg (94) 1 (H3 N2) GISK N 392 used for production of live intranasal influenza vaccine for children	NOJ MEDITSINY RAMN | NI SKIJ I EHKSPERIMENTAL
RU2127757C1	Strain a/47/nanchang/95/13 (h3n2) for production of live antiinfluenza intranasal vaccine for children	NOJ MEDITSINY RAMN | NI SKIJ I EHKSPERIMENTAL
RU2128223C1	Strain a/17/nanchang/95/4 (h3n2) for production of living an antiinfluenza intranasal vaccine for adults	NOJ MEDITSINY RAMN | NI SKIJ I EHKSPERIMENTAL
RU2144955C1	Strain of influenza virus a/17/pert/95/29(H1N1) for production of live anti-influenza intranasal vaccine for adult humans	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2159809C1	Influenza virus strain a/47/sydney/97/14 (h3n2) for production of live influenza intranasal vaccine for babies	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN

RU2159810C1	Influenza virus strain a/47/peking/95/35 for the production of live influenza intranasal vaccine for babies	NII EHKSPERIMENTAL NOJ MEDITSI
RU2159811C1	Influenza virus strain a/17/peking/95/25 (h1n1) for production of live influenzal intranasal vaccine for adults	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2183672C1	A novel strain of influenza virus A/17/New Caledonia/99/145 (H1N1) for production of live anti-influenza, intranasal vaccine for adults	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2185437C1	Strain of influenza virus a/47/new caledonia/99/156 (H1N1), useful for production of live influenza intranasal vaccine for children	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2248394C1	New influenza virus strain A/47/panama/99/234 (H3N2) for producing a live anti-influenza intranasal vaccine for children	
RU2248395C1	New strain A/17/Panama/99/242 (H3N2) for producing a live anti-influenza intranasal vaccine for adults	
RU2266329C1	Strain for production of living influenza intranasal vaccine for adults and infants	
RU2315101C2	Vaccine strain of influenza virus a/17/california/04/6 (h3n2) and attenuation donor a/leningrad/134/17/k7/57 (h2n2) for its preparing	
RU2319744C2	Strain of influenza virus, gisk 147, used for preparing influenza intranasal vaccine for adults and children	GU NII EHKSPERIMENTAL NOJ MEDI
RU2416640C1	Vaccine strain of a/17/brisbane/07/1 (h3n2) influenza virus for preparing live influenza intranasal vaccine for adults and children	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM
RU2416641C1	Vaccine strain of a/17/brisbane/07/28 (h1n1) influenza virus for preparing live influenza intranasal vaccine for adults and children	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM

RU2422518C1	Vaccine strain of a/17/solomon islands/06/9 (h1n1) influenza virus for preparing live influenza intranasal vaccine for adults and children	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM
RU2422519C1	Vaccine strain of b/60/florida/04/181 influenza virus for preparing live influenza intranasal vaccine for adults and children	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM
SU1571067A1	Influenza virus strain used in prepn. of living influenza vaccine for children and adults	VNII GRIPPA | LE NII VAKTSIN SYVOROTOK | GNII STANDARTIZAT KONTROL
SU1655985A1	Live intranasal vaccine against influenza gp. A virus for children involves using specified recombinant strain of virus to increase efficiency	NIIEX MEDITSINY AMN SSSR | MO NII VIRUSNYKH PREPARATOV | VNII GRIPPA | GNII STANDARTIZAT KONTROL
TW200628611A	New nucleic acid construct, comprises chimeric promoter sequence, coding sequence, non-translated leader sequence, and enhancer sequence, for inducing an immune response against influenza virus hemagglutinin (HA) antigen	
TW200700078A	Immunogenic composition for preparing vaccines against e.g. influenza virus comprises influenza antigen from at least two influenza virus strains and at least one strain associated with pandemic outbreak and oil-in-water emulsion adjuvant	
TW200700079A	Immunogenic composition for preparing vaccines against e.g. influenza virus comprises influenza antigen from at least two influenza virus strains and at least one strain associated with pandemic outbreak and oil-in-water emulsion adjuvant	
TW200722101A	Immunogenic composition for preparing vaccines against e.g. influenza virus comprises influenza antigen from at least two influenza virus strains and at least one strain associated with pandemic outbreak and oil-in-water emulsion adjuvant	

US20060121447A1	New subfragment of an RNA sequence coding for a neuroaminidase protein NAy, useful in preparing a vaccine against avian influenza virus infection with specific epidemic strain HxNy	
US20080254065A1	Vaccine for protecting a human patient against infection by a human influenza virus strain, comprises an antigen from an avian influenza virus strain that can cause highly pathogenic avian influenza	CHIRON CORPORATION,Emeryville,CA,US
US20100008952A1	Novel replication-defective adenoviral vector comprising nucleic acid encoding influenza A polypeptide, useful for inducing immune response in subject, and as vaccine to reduce risk of infection by influenza	
US20100099745A1	Inhibiting viral infection in a subject by administering recombinant adenovirus vector comprising a nucleic acid encoding a caspase recruitment domain from melanoma differentiation-associated gene 5 or retinoic acid inducible gene I	
US20100129399A1	New linear expression construct that is free of any amplification and/or selection sequences, useful for preparing a composition for treating or preventing infectious diseases, e.g., avian influenza virus infection	AVIR Green Hills Biotechnology Research Development Trade AG,Wien,AT
US20100166769A1	Preparing influenza virus-like particle used as vaccine, by inserting recombinant DNA with influenza hemagglutinin and neuraminidase sequences into Vero cell with influenza M1 and M2 sequences and culturing obtained coexpression cell	Academia Sinica,Taipei,TW
US20100189745A1	Reassortant influenza virus useful as vaccine for eliciting immune response comprises internal gene segment derived from first influenza virus A subtype, and hemagglutinin and neuraminidase genes from the influenza virus subtype	BAXTER INTERNATIONAL INC.,Deerfield,IL,US | BAXTER HEALTHCARE S.A.,Glattpark (Opfikon),CH

US20100221349A1	New nucleic acid construct, comprises chimeric promoter sequence, coding sequence, non-translated leader sequence, and enhancer sequence, for inducing an immune response against influenza virus hemagglutinin (HA) antigen	Powderject Vaccines Inc. | Powdermed Limited
US20100291146A1	Eliciting or inducing a protective immune response in a subject against a pandemic subtype of influenza virus, comprises administering to the subject a composition comprising an immunogen of an endemic influenza subtype	CSL Limited,Victoria,AU
US20110097418A1	Immunogenic composition, useful for treating influenza, comprises types A and B influenza hemagglutinin proteins	VARIATION BIOTECHNOLOGIES INC.,Gatineau,QC,CA
US20110129497A1	Manufacturing a composition comprising directed-sequence polymers (DSPs) comprises selecting an amino acid sequence of an epitope of an antigen associated with a disease, and synthesizing a cassette of the DSPs	Peptimmune Inc.,Cambridge,MA,US
US20110150912A1	New live attenuated avian influenza virus useful in vaccine for preventing epidemic and pandemic influenza, comprises basic 2 protein gene and basic 1 protein gene	
US20110180430A1	New immunogenic composition comprising an influenza virus antigen, an oil-in-water emulsion adjuvant and a cytokine-inducing agent, useful in raising an immune response against influenza virus infection in a patient	NOVARTIS VACCINES AND DIAGNOSTICS SRL,Siena,IT,IT
US20110229518A1	Use of nucleotides encoding influenza proteins e.g. haemagglutinin with few or no glycosylation sites for manufacturing immunogenic composition or vaccine component against present day and coming influenza A infections in humans and pigs	Statens Serum Institut,Copenhagen S,DK
US20110262481A1	New reassortant influenza-A virus comprising gene segments of seasonal or pandemic strain origin, a polymerase basic protein-1 gene segment, and a polymerase gene segment, useful e.g. as vaccine to prevent influenza virus infection	AVIR GREEN HILLS BIOTECHNOLOGY RESEARCH DEVELOPMENT TRADE AG,Vienna,AT

US20110287054A1	Immunogenic composition for preparing vaccines against e.g. influenza virus comprises influenza antigen from at least two influenza virus strains and at least one strain associated with pandemic outbreak and oil-in-water emulsion adjuvant	GlaxoSmithKline Biologicals s.a.
US20110305748A1	Composition for immunizing subject against pre-pandemic influenza virus comprises recombinant hemagglutinin from pre-pandemic influenza virus, and adjuvant comprising disaccharide having reducing/non-reducing terminus e.g. glucosyl	IMMUNE DESIGN CORP.,Seattle,WA,US
US20120009215A1	New hemagglutinin and/or neuraminidase variant, useful for stimulating an immune response against influenza virus, or for prophylactic or therapeutic treatment of a viral infection	
US20120034264A1	New 6:2 reassortment influenza virus, useful as a vaccine for stimulating the immune system of an individual or for treating or preventing a viral infection in a subject	MedImmune LLC,Gaithersburg,MD,US
US20120064110A1	Dosage form, useful e.g. for the prophylaxis of influenza virus infection, preferably influenza A virus infection, comprises synthetic nanocarriers coupled to peptides that are obtained from human influenza A virus hemagglutinin	Selecta Biosciences Inc.,Watertown,MA,US
US20120064115A1	Recombinant virus-like particle used as vaccine comprises at least two different epitopes/proteins containing epitopes selected from different viral strains/serotypes of same virus and/or different viral strains specific for different hosts	
US20120207786A1	Use of influenza virus like particle comprising specified influenza virus protein and specified influenza virus hemagglutinin and neuraminidase proteins in the preparation of vaccine for inducing substantial immunity to influenza virus	NOVAVAX INC.,Rockville,MD,US

US20120219584A1	Immunogen comprises nucleic acid molecule encoding a protein with influenza A subtype H1 hemagglutinin glycan-shielded receptor binding domain A region and influenza A subtype H1 hemagglutinin antigenic site, where site is not within region	THE UNITED STATES OF AMERICA as represented by THE SECRETARY DEPARTMENT OF HEALTH,Bethesda,MD,US
US20120219586A1	Adjuvanted influenza vaccine formulation, useful for prophylaxis of influenza infection or disease in subject, comprises peptidoglycan microparticles, and influenza virus antigen or its antigenic preparation	
US20120244185A1	New chimeric adenoviral expression vector comprising an expression cassette containing promoters useful for eliciting an immune response (mucosal immune response) against H1N1 influenza in mammals in mammals (human)	Vaxart Inc.,San Francisco,CA,US
US20120269852A1	Influenza vaccine for immunizing patient against influenza virus infection comprises combination of detoxified or non-toxic mutant of subunit A of AB type exotoxin, aluminum salt, and influenza-specific antigen	
US5948410A	New influenza surface antigen vaccine propagated on animal cell culture used to produce e.g. human, swine, equine and avian influenza vaccines avoids disadvantages associated with culturing on embryonated chicken eggs	Duphar International Research B,Weesp,NL
US6800288B2	Recombinant NS gene of an influenza A virus comprising a functional RNA binding domain and a gene sequence modification after nucleotide position 400 of the NS1 gene segment, useful for producing a live attenuated influenza virus vaccine	Polymun Scientific Immunbiologische Forschung GmbH,Vienna,AT
US7238349B1	New monovalent influenza vaccine, useful particularly for preventing infection by pandemic strains, contains low dose of egg-derived antigen	SmithKline Beecham Biologicals s.a.,Rixensart,BE | Saechsisches Serumwerk Dresden,Dresden,DE

US7521220B2	Producing an influenza virus or influenza viral protein for use as a vaccine by providing a cell with a sequence encoding a gene product of an adenoviral E1 gene and harvesting the influenza virus from the suitable medium or the cell	Crucell Holland B.V.,Leiden,NL
US8119337B2	Preparing an influenza vaccine from influenza virus grown in a culture of a mammalian cell line by testing the vaccine or culture for an infectious agent that can grow in the cell line but that does not grow in embryonated hen eggs	GREGERSEN JENS-PETER
US8163545B2	New recombinant adenovirus vector comprises a polynucleotide encoding at least one antigen of an avian influenza strain, useful for producing vaccines for eliciting an immune response against avian or pandemic influenza	United States of America as represented by the Secretary of the Department of Health and Human Services Centers for Disease Control and Prevention,Washington,DC,US | Purdue Research Foundation,West Lafayette,IN,US
US8288090B2	Preventing or treating infection caused by influenza A H1N1, H1, H2, H3, H5 or H7, involves delivering nucleic acid molecule encoding hemagglutinin or neuraminidase from pandemic influenza to subject	Statens Serum Institut,Copenhagen S,DK
VN22532A	New immunogenic influenza composition, comprises an influenza virus antigen or antigenic preparation in combination with an oil-in-water emulsion adjuvant, useful for treating or preventing diseases caused by influenza infection	
VN23203A	New monovalent influenza vaccine composition comprises low amount of influenza virus antigen from an influenza virus strain that is associated with a pandemic, useful for protecting a human from influenza infection	

WO2007065967A1	New vaccine composition containing HN antigen pairs of influenza A virus targeted against recombinant H5N2 type of influenza virus, useful for vaccinating against influenza A virus	REMEDAL OY,FI | HEINO Pekka,FI
WO2011138032A3	Immunogenic composition useful for inducing a protective immune response to an influenza infection in a mammal, comprises one or more peptides	MAKSYUTOV Amir,RU | ARTEMEV Timur,GB | ANTONETS Denis,RU | BAKULINA Anastasia,RU | MAKSYUTOV Rinat,RU
WO2012114323A1	Improving protective effect of seasonal or pandemic influenza vaccine, comprises vaccination of subject, prior to, or together with, administration of seasonal or pandemic vaccine, with synthetic or recombinant multimeric polypeptide	BEN-YEDIDIA Tamar,IL | BIONDVAX PHARMACEUTICALS LTD.,IL | LOWELL George H.,IL
Supporting Technologies Category		
AU2011202991A8	New influenza hemagglutinin or neuraminidase variant polypeptide, useful in preparing a composition for treating or preventing infection caused by influenza virus	US GOVERNMENT | MEDLMMUNE LLC
AU2011253998A1	Replicating virus, e.g. adenoviruses, hepadnaviruses, or herpes viruses, in avian embryonic derived stem cells Ebx, useful as vaccine, comprises infecting cells with the virus, culturing infected cells, and harvesting the virus	VIVALIS
AU733191B2	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	PROTEIN SCIENCES CORP
CN101560503B	New influenza A virus Vero cell adapted strain named A/Yunnan/1/2005Va (H3N2), where the preserving number of the strain is CCTCC No: V200514, useful for preparing a Vero cell adapted strain of the epidemic strain	INST MEDICAL BIOLOGY CHINESE ACAD MEDICA,CN

CN101897966A	Cynomorium songaricum immunological adjuvant useful in influenza vaccine, comprises Cynomorium songaricum extract and a carrier	Chinese Academy of Sciences Kunming Institute of Botany,CN | Institute of Medical Biology Chinese Academy of Medical Sciences
CN101899418A	New isolated avian influenza virus comprising RNA in its genome, useful in vaccine for preventing avian influenza virus	Shanghai Centre for Animal Disease Control and Prevention,CN
CN101926994B	Immunoadjuvant used in influenza vaccine, comprises turtle shell extract and carrier, and has low side effect and is prepared in simple, cost-effective and eco-friendly manner	Institute of Medical Biology Chinese Academy of Medical Sciences,CN | Chinese Academy of Sciences Kunming Institute of Botany,CN
CN101926995A	Immunoadjuvant used in influenza vaccine, comprises Asparagus extract and carrier, and is safe and prepared in simple, cost-effective and eco-friendly manner	Chinese Academy of Sciences Kunming Institute of Botany,CN | Institute of Medical Biology Chinese Academy of Medical Sciences
CN102038949A	Inactivated quad vaccine useful for pharmaceutical applications comprises inactivated Newcastle disease virus, chicken infectious bronchitis virus, chicken egg drop syndrome virus, bird flu virus (H9 subtype), and adjuvant	Qingdao Yebio Bioengineering Co. Ltd.,CN
CN102068695B		Qingdao Yebio Bioengineering Co. Ltd.,CN
CN102078605A	Influenza vaccine produced using infected Vero cell by preparing virus liquid vaccine by cleaning Vero cells, adding virus into maintenance medium, adding pancreatin to obtain virus supernatant and purifying liquid vaccine	Jilin Yatai Bio-pharmaceutical Co. Ltd.,CN
CN102139104A	Inactivated trivalent vaccine, useful for Newcastle disease virus, avian influenza and infectious bursal disease virus causing diseases, comprises e.g. inactivated LaSota strain of Newcastle disease virus and YBF003 strain	Qingdao Yebio Bioengineering Co. Ltd.,CN

CN102293743A	Lipid microsphere emulsion useful for treating pandemic influenza virus in children, comprises pharmaceutical grade oil, zwitterionic/non-ionic surfactant composition, antigen associated with pandemic influenza and aqueous solution	Liaoning Chengda Biotechnology Co. Ltd.,CN
CN102397540A	A type avian influenza recombinant phage vaccine, comprises recombinant T7 phage as antigen	Jiangsu Academy of Agricultural Sciences,CN
CN102406931A	Preparing pandemic influenza virus split vaccine comprises culturing NIBRG-14, inactivating by adding an inactivator containing e.g. an alkylating agent, filtering and concentrating virus liquid, purifying and freeze-drying vaccine product	Chengdu Kanghua Biological Products Co. Ltd.,CN
CN1313605C	Gene recombinant fowl influenza virus D3/F-R2/6 and its construction method	Yangzhou University
CN1644686B	High yield strain of mammalian influenza virus, useful in preparing vaccine strains of influenza A	INST BEIJING VIRAL DISEASE CONTROL & PRE
EP1534845A1	Rescuing attenuated and/or recombinant orthomyxovirus, useful for the manufacture of live, attenuated vaccine, comprises delivering the resulting recombinant baculovirus genome to a mammalian host cell by transduction	Polymun Scientific Immunbiologische Forschung GmbH,1190 Wien,AT,01690530
EP2484757A1	Producing alpha-Gal expressing virus, e.g. influenza viruses, by introducing alpha 1,3-galactose transferase gene into cell, inoculating virus into cell system and culturing viral infected cell system to obtain virus	National University Corporation Obihiro University of Agriculture and Veterinary Medicine,Obihiro-shi, Hokkaido 080-8555,JP,100825962 | Incorporated Administrative Agency National Agriculture and Food Research Organization,Ibaraki 305-8517,JP,101317142
EP2491117A1	Preparing virus e.g. rotavirus, used e.g. as vaccine, comprises transfecting culture of host cells with expression construct encoding viral RNA molecule, adding cells to the transfected cells, and culturing mixture of cells to produce virus	Novartis AG,4056 Basel,CH,101062816
GB660109A		AMERICAN CYANAMID CO

IN201001689P4	Producing influenza virus, useful for producing vaccine against influenza, comprises administering a vaccine against influenza to chickens, activating embryogenesis in eggs of chicken, infecting eggs with influenza and harvesting virus	
IN201005447P4	Stabilizing influenza vaccine composition comprises diluting liquid bulk composition, subjecting regular droplets to freezing to form frozen regular spherical micropellets or particles, and drying	
IN201104719P2	Host cell useful for producing recombinant virus strains comprises expression construct encoding viral RNA molecule, where expression of the RNA molecule is controlled by pol I promoter which is not endogenous to host cell's taxonomic order	
JP03918949B2	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	PROTEIN SCI
JP2007314538A	Recombinant influenza haemagglutinin produced in baculovirus system avoids problems of growing virus in eggs and produces stable, un-cleaved protein useful in vaccines	PROTEIN SCIENCES
KR1998081114A	New influenza surface antigen vaccine propagated on animal cell culture used to produce e.g. human, swine, equine and avian influenza vaccines avoids disadvantages associated with culturing on embryonated chicken eggs	
KR593235B1	New influenza surface antigen vaccine propagated on animal cell culture used to produce e.g. human, swine, equine and avian influenza vaccines avoids disadvantages associated with culturing on embryonated chicken eggs	DUPHAR INTERNATIONAL RESEARCH B.V.

MX2009009565A	New recombinant protein comprising hemagglutinin of influenza virus A H1N1-2009 expressed in Escherichia coli, used as a vaccine or the main active ingredient of a vaccine against influenza A H1N1-2009	ITESM
MX207194B	New influenza surface antigen vaccine propagated on animal cell culture used to produce e.g. human, swine, equine and avian influenza vaccines avoids disadvantages associated with culturing on embryonated chicken eggs	
RU2031941C1	Strain of virus A(H1N1) for prodn. of live intranasal influenza vaccine based on the epidemic virus A/Leningrad/92/89 (H1N1)	NII GRIPPA RAMN
RU2033424C1	Strain of influenza A (H3N2) virus used in prodn. of live intranasal vaccine for children and adults	NII GRIPPA RAMN
RU2065498C1	Strain Shangdong for prodn. of live influenza intranasal vaccine for children is useful in public health for prevention of influenza epidemics in children of age 3-14	NIIEX MEDITSINY RAMN
RU2078818C1	Viral strain used in preparation of active influenza vaccine is polymorphic strain used in intranasal influenza vaccine for adults	NIIEX MEDITSINY RAMN
RU2078820C1	Strain A/47/Peking/92/3 (H3N2) GISK No. 104 is polymorphic and used for live intranasal influenza vaccine used by children	NIIEX MEDITSINY RAMN
RU2084524C1	Influenza A virus strain A/17 Texas/91/1/3(H1N1) Gisk No. 102 is used in the manufacture of live, intranasal influenza vaccine for adults	NIIEX MEDITSINY RAMN
RU2159812C1	Influenza virus strain a/17/sydney/97/76 (h3n2) for production of live influenzal intranasal vaccine for adults	NII EHKSPERIMENTAL | NOJ MEDITSINY RAMN
RU2285723C2	Influenza virus strain A/Wyoming/3/03 (H3N2) for production of living influenza intranasal vaccine for infants and adults	GU NII EHKSPERIMENTAL NOJ MEDI
RU2307161C2	Influenza virus strain for living influenza intranasal vaccine for infants and adults	GU NII EHKSPERIMENTAL NOJ MEDI
RU2307162C1	Influenza virus strain for influenza intranasal vaccine for infants and adults	GU NII EHKSPERIMENTAL NOJ MEDI

RU2413765C1	Vaccine strain of flu virus a/17/california/2009/38 (h1n1) for profuction of live influenza intranasal vaccine for adults and children	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM
RU2428476C1	Reassortant rn a9-swine a(h7n1) influenza virus strain for neuraminidase antibody assay in influenza infection and vaccination	UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII EHKSPERIMENTAL NOJ MEDITSINY SEV ZAP OTDEL RAMN NIIEHM
RU2457243C1	Cultivated hybrid cell strain of mouse mus. Musculus-1e7 producer of monoclonal antibody immunoresponsive to haemagglutinin protein of pandemic influena virus a/iiv-moscow/01/09(h1n1)sw1	FEDERAL NOE G BJUDZHETNOE UCHREZHDENIE NII VIRUSOLOGII IM D I IVANOVSKOGO MIN ZDRAVOOKHRANENIJA I SO
RU2457245C1	Reassortant rem8-vaccine strain of suptype h1n1 influenza a virus What is offered is a vaccine strain of A ReM8 (H1N1) virus deposited in the State Collection of Viruses No. 2632	FEDERAL NOE G BJUDZHETNOE UCHREZHDENIE NII VIRUSOLOGII IM D I IVANOVSKOGO MIN ZDRAVOOKHRANENIJA I SO
RU2458124C2	New strain of influenza A virus subtype H3N2 useful for producing composition containing inactivated influenza virus for treating influenza	FEDERAL NOE G BJUDZHETNOE UCHREZHDENIE NII GRIPPA MIN ZDRAVOOKHRANENIJA I SOTSIAL NOGO RAZVITIJA RF
SU1003539A1	Influenza virus strain A-17-42-3 H3N2 is used for prodn. of live influenza vaccine	POLEZHAEV F I | ALEKSANDROVA G I | BUDILOVSKIJ G N | GARMASHOVA L M | KOVAL T A | GRUNIS A M | KLIMOV A I | SLEPUSHKIN A N | MEDVEDEVA T E | GENDON YU Z
SU1219644A1	Influenza virus strain a-f-59-1 is used for prepn. of inactive anti-influenza vaccine.	NIIEX MEDITSINY | MO NII VIRUSNYKH PREPARATOV | LE NII VAKTSIN SYVOROTOK
SU1838404A3	Influenza A virus strain H3N2 is used for the prodn. vaccines for children which are administered nasally, is useful for the prevention of influenza epidemics in children	NIIEX MEDITSINY AMN SSSR
SU833260B	Prodn. of vaccine strain of influenza virus by crossing virulent and heat sensitive viral strains for high biological stability and immunogenic activity	

TW570803A	New influenza surface antigen vaccine propagated on animal cell culture used to produce e.g. human, swine, equine and avian influenza vaccines avoids disadvantages associated with culturing on embryonated chicken eggs	
US20090202589A1	Fermenter vessel for culturing cells and for preparation of virus vaccine, comprises view port provided in outside wall for inspecting processes within vessel volume, and heating device on transparent member of view port	
US20090326978A1	Combination anti-viral therapy stockpiling method for e.g. pandemic influenza, involves coordinating storage of therapeutic doses of antiviral agents to enable shipment of therapeutic doses within preset hours for each other	
US20110177121A1	New composition comprises an immunogenic epitope of influenza that is not immunodominant as in a wild type virus, useful for inducing an immune response against influenza	BIOLOGICAL MIMETICS INC.,Frederick,MD,US
US20110212129A1	Producing influenza virus, useful for producing vaccine against influenza, comprises administering a vaccine against influenza to chickens, activating embryogenesis in eggs of chicken, infecting eggs with influenza and harvesting virus	SANOFI PASTEUR S.A.,Lyon,FR | MERIAL LIMITED,Duluth,GA,US
US20110217330A1	Degrading host cell nucleic acids associated with virus or its viral antigen produced by cell culture, useful to e.g. treat influenza infection, comprises degrading the nucleic acids with an endonuclease or a DNA alkylating agent	
US20110243987A1	Immunizing a human against influenza virus infection by selecting a human who was previously vaccinated with a monovalent first vaccine composition, and administering a second vaccine composition comprising an influenza virus antigen	GlaxoSmithKline Biologicals s.a.

US20120189656A1	Host cell useful for producing recombinant virus strains comprises expression construct encoding viral RNA molecule, where expression of the RNA molecule is controlled by pol I promoter which is not endogenous to host cell's taxonomic order	
US20120219587A1	Producing split influenza virus preparation used for pharmaceutical composition for preventing and/or treating diseases caused by influenza, by fractionating preparation, adding Triton X-100 to preparation and filtering preparation	
US20120294879A1	New polypeptide comprising lysosome-associated membrane protein-1 (LAMP-1) luminal sequence, a segment of influenza A protein, and LAMP transmembrane and cytoplasmic tail, useful in e.g. immunizing human against human influenza A virus	NATIONAL UNIVERSITY OF SINGAPORE,Singapore,SG | THE JOHNS HOPKINS UNIVERSITY,Baltimore,MD,US
US4206287A	Influenza virus mutant repeated culture and isolation immuno vaccins against future virus mutants	Agence Nationale de Valorisation de la Recherche (ANVAR),Neuilly sur Seine,FR
US6245532B1	Expressing a protein e.g. recombinant influenza virus hemagglutinin comprising using a vector encoding a polypeptide comprising a baculovirus signal peptide and a baculovirus expression system is useful as a multivalent influenza vaccine	Protein Sciences Corporation,Meriden,CT
US8148132B2	Replicating virus, e.g. adenoviruses, hepadnaviruses, or herpes viruses, in avian embryonic derived stem cells Ebx, useful as vaccine, comprises infecting cells with the virus, culturing infected cells, and harvesting the virus	Vivalis,Roussay,FR
US8163545B2	New recombinant adenovirus vector comprises a polynucleotide encoding at least one antigen of an avian influenza strain, useful for producing vaccines for eliciting an immune response against avian or pandemic influenza	United States of America as represented by the Secretary of the Department of Health and Human Services Centers for Disease Control and Prevention,Washington,DC,US | Purdue Research Foundation,West Lafayette,IN,US

US8282937B2	New reassortant influenza virus, useful in preparing a vaccine comprising the reassortant influenza virus for preventing influenza virus infection	The Regents of the University of Michigan,Ann Arbor,MI,US
VN24155A	Producing influenza virus, useful for producing vaccine against influenza, comprises administering a vaccine against influenza to chickens, activating embryogenesis in eggs of chicken, infecting eggs with influenza and harvesting virus	
WO2008138120A1	Assessing the anti-influenza effect of an agent of interest by incubating the particles with cells capable of infection, and comparing the infection rate of the virus-like particles in the presence and absence of the agent	UNIVERSITY OF MANITOBA,CA | HER MAJESTY THE QUEEN IN RIGHT OF CANADA AS REPRESENTED BY THE MINISTER OF HEALTH,CA | YAO Xiojian,CA | AO Zhujun,CA | KOBINGER Gary,US | KOBASA Darwin,CA
WO2011133997A1	Use of gamma-irradiated influenza virus comprising Chalmers strain backbone of specific proteins for treating influenza virus infection, and for inducing cross-protective immunity against multiple influenza virus subtypes in a subject	GAMMA VACCINES PTY LIMITED,AU | MULLBACHER Arno,AU | ALSHARIFI Mohammed,AU | HIRST Tim,AU
WO2012009790A1	Use of second unique hemagglutinin and pathogen e.g. HIV1 protein for inducing a cross-protective antibody response in a subject that has been previously subjected to a first unique hemagglutinin and pathogen protein	SCHRADER John W.,CA
WO2012050229A1	New recombinant vaccinia virus used in pharmaceutical composition for preventing and/or treating H5N1 virus and H1N1 virus, comprises expression promoter and complementary DNA encoding highly pathogenic avian influenza A (H5N1) virus	TOKYO METROPOLITAN INSTITUTE OF MEDICAL SCIENCE,JP | KIDA Hiroshi | MURAKAMI Toshio,JP | YASUI Fumihiko,JP | KOHARA Michinori,JP | NATIONAL UNIVERSITY CORPORATION HOKKAIDO UNIVERSITY,JP | THE CHEMO-SERO-THERAPEUTIC RESEARCH INSTITUTE,JP | SAKODA Yoshihiro

WO2012088428A1	New virus-like particle comprising a recombinant influenza virus hemagglutinin protein, useful for inducing substantial immunity to an influenza virus infection, and for treating and/or preventing influenza infection	NOVAVAX INC.,US | SMITH Gale,US | LIU Ye,US | MASSARE Michael,US | SINGHVI Rahul,US
ZA201001480A	Producing influenza virus, useful for producing vaccine against influenza, comprises administering a vaccine against influenza to chickens, activating embryogenesis in eggs of chicken, infecting eggs with influenza and harvesting virus	
ZA201006225A	Stabilizing influenza vaccine composition comprises diluting liquid bulk composition, subjecting regular droplets to freezing to form frozen regular spherical micropellets or particles, and drying	

GenomeQuest findings

The ITTI team used genome quest for this patent landscape report according to the methodology previously described. Find sequences from PubMed proved to be an arduous task as many of the relevant articles did not disclose sequence that we could use for a GenomeQuest search. As such, few sequences were found through PubMed.

Additionally the ITTI team pulled sequences directly from patents whenever they were disclosed within the document. However, the occurrence of sequences disclosure within a patent document was quite rare and as such many of the GenomeQuest searches were not performed from sequences acquired in this manner.

For this report, the second approach of acquiring sequences from a relevant database proved to be the main source of sequences used in GenomeQuest searches. The main database used was the influenza research database.[124] Both genetic and protein sequences were acquire from the database for GenomeQuest searches. The sequences acquired were from influenza viruses that were found in birds or pigs and additionally with hemagglutinin or Nneuraminidase subtypes of interest.

124 http://www.fludb.org/brc/influenza_sequence_search_segment_display.do?method=ShowCleanSearch&decorator=influenza.

With the sequences found, GenomeQuest searches were used on these sequences. For sequences acquired from patent documents, the search results, when sorted by the percentage of conformity to the sequenced searched, the relevant results were patents generally from the same company or a subsidiary of the company. For sequences from the database, many relevant patents were found at all levels of conformity. While GenomeQuest did find many relevant patents, these patents were already identified through keyword searches in either Thomson Innovation or Total Patent.

Analysis

Categories of Analysis

Analysis is presented for the two major relevant categories, Vaccines and Supporting Technologies. The subcategories under each of these major headings were pooled together and analyzed as a group in order to present a large enough dataset for generating meaningful results. Parallel analytics were generated for the two major categories, and comparisons are given. The exceptions were the analysis for multi-jurisdictional filings, which was performed for only vaccine documents, and the analysis of top assignees, which was performed with both major groups pooled together. Platform technologies were not analyzed.

ThemeScape Map of Derwent Data

A graphical representation of the results was generated using ThemeScape, a tool within the Aureka platform initially developed by Aurigin Systems, Inc., and now available through Innovation.[125] ThemeScape creates a virtual "map" of patent data by extracting keywords from the documents and plotting those topics in relation to one another. "Islands" are formed by closely related topics and "mountains" are formed when a large number of documents all contain the same or similar keywords. Gaps between distantly related topics represent an "ocean." ThemeScape is a powerful tool which can reveal relationships within a large dataset that are not otherwise apparent.

ThemeScape provides options for the sources of keywords within each document. The maps presented below were derived from the DWPI title, DWPI abstract, and claims in English from one representative of each INPADOC family. Extracting data only from representative documents prevents large patent families from skewing the results and gives equal weight to each invention. Not all references had this DWPI data in their records, so the maps represent a subset of the entire datasets.

The map in Figure 10 shows the topics found with documents coded to the vaccine category. Many of the topics agree with the coding criteria. At the center right of the map is a mountain labeled "split influenza" and "pandemic combination," which would represent subunit vaccines for a combination of pandemic and seasonal influenza. The bottom center of the map has a mountain labeled "live, intranasal, embryos" which would indicate live virus vaccines where the virus is grown in eggs (chicken embryos) and then administered intranasally. Since pandemic influenza strains cannot be propagated in eggs because the viruses are lethal to the embryos, the viruses must be attenuated or recombinant (reasserted) so they do not kill the embryos. A peak

[125] http://www.intellogist.com/wiki/Report:Thomson_Innovation/Viewing_Results/Analyzing_Results/ThemeScape.



Figure 10. ThemeScape map of the representative documents from 570 influenza vaccine patent families.

indicating as much is immediately adjacent to the whole virus vaccine mountain. Other methods of avoiding this problem of lethality is to express subunits in plants (upper center) or insect cells (center left). Antigens could also be expressed as polypeptides, possibly in bacteria or mammalian cells, although these expression systems are not indicated.

The center right and upper right portion of the map has keywords related to the formulation of vaccines, such as "solution, mixing, adding," and "oil-in-water emulsion." Carriers such as "lipid vesicles" are also represented in the upper center of the map. The center and upper left of the map represents DNA constructs, or "vectors," used to generate recombinant viruses or recombinant subunits. The topics in the upper left such as "plasmid," "chimeric promoter," and "[nucleic] acid molecule encoding," along with ""delivery device," most likely indicates DNA vaccines.



Figure 11. ThemeScape map of the representative documents from the 750 vaccine supporting technology families.

The map of the vaccine documents can be contrasted to the map of the supporting technologies shown in Figure 11. The supporting technologies map contains more "islands," representing the broader range of technologies in this category as compared to vaccine documents. The upper left and upper center sections of the map have keywords related to the subcategory of methods of making vaccines, such as "harvesting" virus from "eggs" and purifying the virus by "filtration," "centrifugation" of the "allontoic fluid" to isolate the virus, and "treating virus-containing fluid" and then adding "cationic detergent." Just below those peaks are other methods of preparing vaccines such as "lyophilization" and "isolated" virus from "serum-free medium."

The bottom left section of the map is an island which indicates methods of producing virus or viral subunits, such as "producing negative strand RNA" viruses, "cDNA transcription," and "nucleic acid vectors." Novel viruses useful in vaccines are represented by the "attenuated/cold adapted" peak in the center of the map. Most of the Russian documents in this subcategory mentioned use of the viruses to immunize children. The "amino acid/peptide" peak at lower right would correspond to recombinant subunits, and the "coding/noncoding" peak just beneath would represent DNA constructs used to produce the recombinant subunits. At extreme lower left are veterinary vaccines, such as for "equine" influenza. Tetanus toxin is an adjuvant in some

of these vaccines. "Canarypox virus" is used as a carrier for influenza antigens in some bird vaccines.

In summary, the two maps are very different which would be expected if the coding of the documents successfully placed the majority of the documents in the correct subcategories. The labels on the peaks also correspond to the subcategories. These maps not only reveal the relationships between the different technologies in each group but they also validate the document coding protocol which is the basis for the further analytics presented below.

Priority Country v. Document Count

Important questions to ask in the analysis of patent data is "where does the technology come from?" and "where is the technology being used?" The first question can be answered by analyzing the priority country, which is the country in which the priority patent document is filed. Further data can be gleaned from the country in which the top assignees are based, which is presented below. The second question can be answered by analyzing the multi-jurisdictional filings, which also follows below.

Although information regarding the priority country is useful, it does not necessarily indicate the source of the technology. For example, publications HK1154041A0 and HK1156969A0 are assigned to Medicago, Inc., a Canadian company. However, Medicago[126] tends to file applications first in the U.S., and the priority documents for both of these references are U.S. applications. Also, IN200503876P1 is assigned to a group of French entities - CNRS, the Pasteur Institute, and the University of Paris - but the priority document is a Canadian application. Thus, some assignees file first in other jurisdictions, perhaps to take advantage of that country's patent laws or because the patent will be practiced primarily in that country. For example, Medicago has a manufacturing plant in the U.S., although its research facility is apparently in Canada.

Most documents have priority data recoded in the Innovation database, but a few do not. In the majority of cases, priority data can be found through patent family members. When possible, priority information was added to the data. Such manually corrected data is indicated by highlighted cells in the files presented in Appendices C and D.

The priority country information for vaccine patent documents is presented in Figure 12. The United States (US) is by far the largest source of priority documents. China (CN) and Great

[126] http://www.medicago.com/.

Britain (GB) are secondary sources, followed by Russia (RU) and the former Soviet Union (SU), the European Patent Office (EP), Japan (JP), and Korea (KR).

The priority country information for the supporting technologies documents, shown in Figure 13, is very similar to that of vaccine documents. All the countries listed above were also the source of supporting technologies. The major difference is that France (FR) is a more prominent source of supporting technologies than complete vaccines.

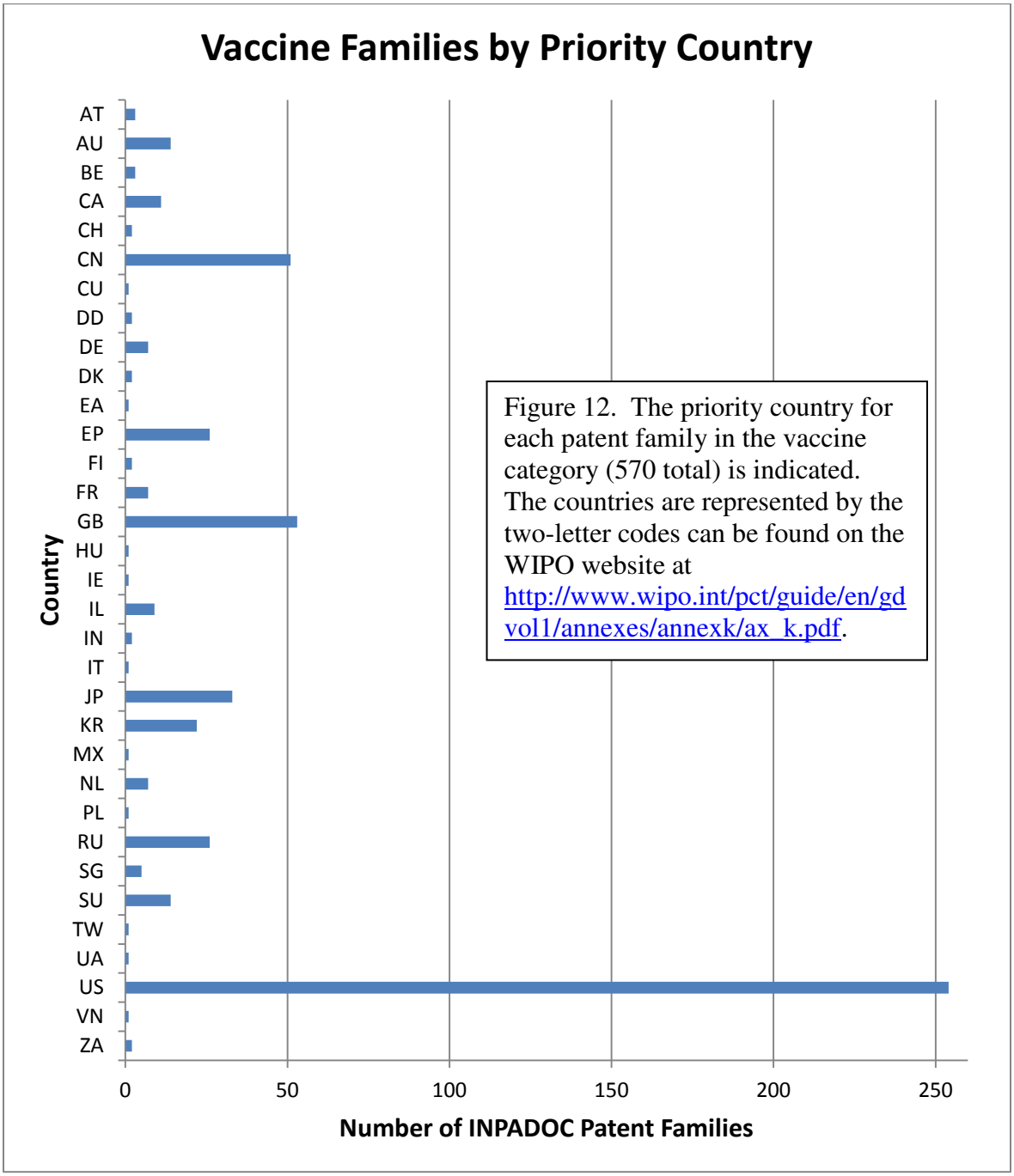


Figure 12. The priority country for each patent family in the vaccine category (570 total) is indicated. The countries are represented by the two-letter codes can be found on the WIPO website at http://www.wipo.int/pct/guide/en/gdvol1/annexes/annexk/ax_k.pdf.

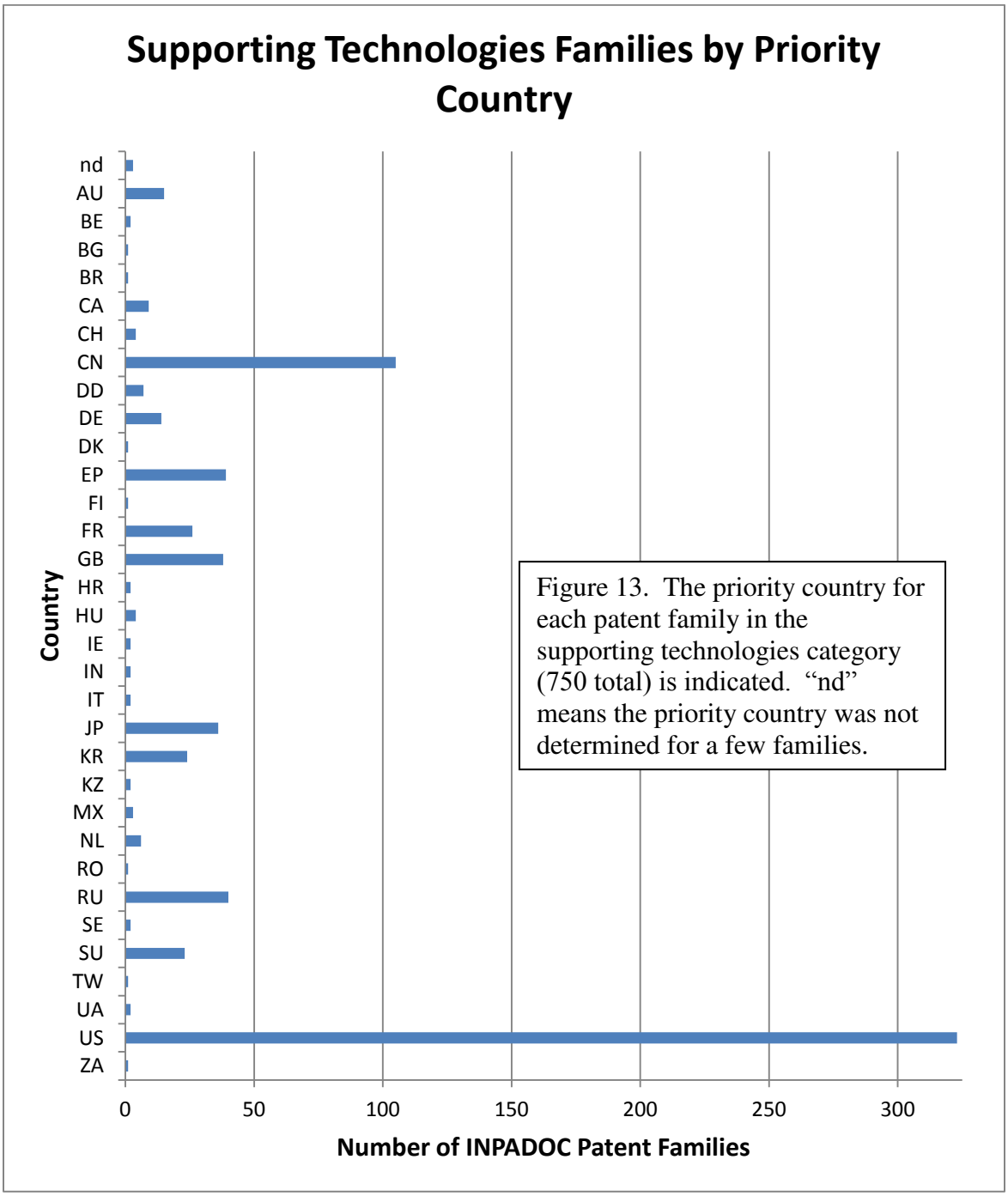


Figure 13. The priority country for each patent family in the supporting technologies category (750 total) is indicated. "nd" means the priority country was not determined for a few families.

Top Vaccine Families for Multi-Jurisdictional Filings

Vaccine technologies that have been transferred to the most other countries were calculated by first determining the size of each INPADOC family within the vaccine document dataset. This data may be slightly skewed because applications filed in certain jurisdictions are not recorded as

being members of INPADOC families.[127] These jurisdictions include Hong Kong, India, Mexico, the Philippines, Portugal, Tawain, and Viet Nam. For this reason, the TotalPatent Extended Family was also retrieved for each of the largest INPADOC families to try to capture family members from these jurisdictions. It is still possible these jurisdictions remain under-represented in the dataset. The extended family was not retrieved for all documents because the export functions of TotalPatent do not allow this data to be captured in a convenient manner. The number of jurisdictional filings was determined by combining the INPADOC, DWPI, and TotalPatent families for each representative document.

Twenty-one representative family members had INPADOC families with 29 or more members. The top family was represented by US20110180430A1, a relatively recent document whose family already contains 90 members. However, the INPADOC family represented by US5948410A has been filed in 32 different jurisdictions, which is the most of this group. Four families are assigned to GlaxoSmithKline and two to Novartis. No other assignee is represented multiple times. The oldest family is represented by US3953592A, which was filed in 1973. Three applications published in 2012 are also on the list. These families are shown in Table III, and the details of each family can be found in Appendix E.

Table III. Top Multi-Jurisdictional Filings per INPADOC Family in the Vaccine Category.

Publication Number	Assignee	Size of INPADOC Family	Filing Jurisdictions	Total Number of Jurisdictions
US20110180430A1	CHIRON SRL | NOVARTIS	90	AT | AU | BR | CA | CN| DE | DK | EA | EP | ES | JP | KR | NZ | PL | PT | SI | US | WO | IN	19
US20110287054A1	GLAXOSMITHKLINE	76	AR | AU | BR | CA | CN | EA | EP | GB | IL | JP | KR| MA | MX | NO | NZ | PE | SG | US| WO | ZA| IN | TW	22
US20120207786A1	NOVAVAX	69	AT | AU | BR | CA | CN | DK | EP | ES | HK | IL | JP| KR | MX | NZ | PT | RU | SG | US | WO | IN | TW	21
US20100221284A1	GLAXOSMITHKLINE | Saech-Sisches Serumwerk Dresden	54	AR | AT | AU | BR | CA | CN | CO | CZ | DE | DK | EP | ES | GB | HK | HU | IL | JP| MX | MY | NO | NZ | PL | PT | SI | TW | US | WO | ZA | KR | IN | PH	31

[127] See also Notes on Patent Families in Appendix M.

US8309099B2	St. Jude Children's Research Hospital	54	AT | AU | BR | CA | CN | DE | DK | EA | EP | ES | HK | HU | IL | JP | KR | MX | NO | NZ | PL | PT | SI | US | WO | ZA | IN	25
US4140762A	SANDOZ SA	53	AT | AU | BE | CA | CH | CS | DE | DK | ES | FI | FR | GB | HK | HU | IE | IL | JP | MY | NL | NO | PH | PL | SE | SU | US | YU | ZA | PT	28
US7850956B2	Univ. Massachusetts Medical Center; St. Jude Children's Research Hospital	51	AT | AU | CA | DE | DK | EP | ES | JP | PT | US | WO	11
US20110293650A1	MEDICAGO INC	49	AU | CA | CN | CR | EA | EP | IL | IN | IS | JP | KR | MA | MX | NZ | RU | US | WO | VN | HK	19
US5948410A	DUPHAR INTERNATIONAL RESEARCH B.V.	47	US | AR | AT | AU | BR | CA | CN | CZ | DE | DK | DZ | EP | ES | GR | HK | HR | HU | ID | IL | JP | MX | NO | NZ | PL | PT | RU | SI | SK | TR | TW | ZA | KR	32
US6716823B1	The UAB (Univ. of Alabama, Birmingham) Research Foundation	45	AT| AU | CA | CN| DE | EP | ES | HK | JP | KR | MX | US | WO | ZA | IN	15
US20080038294A1	ABBOTT BIOLOGICALS BV | SOLVAY BIOLOGICALS BV	39	AR | AT | AU | BR | CA| CN | DE | DK | EA | EP | ES | HR | IL | JP | KR| MX | MY | NO | PT | SI | TW | US | WO | ZA | IN | VN	26
US8119337B2	CHIRON BEHRING GMBH & CO | NOVARTIS	39	AT | CA | DE | DK | EP | ES | HK | HR | JP | PT | RS | SI | US | WO	14
US20120034264A1	MEDIMMUNE | US NAT INST OF HEALTH	36	AU | CA | EP | ES | JP | US | WO	7
US20110129497A1	PEPTIMMUNE INC	34	AP | AU | CA | CN | EP | IL | JP | KR | MX | NZ | US | WO	12
US20120219575A1	PEPTCELL LTD	34	AP | AT | AU | BR | CA | CN | DK | EA | EP | ES | GB | IL | JP | KR | MX | NO | NZ| PL | PT | SG | US | WO| ZA |	24

			IN	
US20040087521A1	MERCK & CO INC	33	US | AU | BG | BR | CA | CN | CZ | DZ | EP | FI | HR | HU | IL| JP | NO | NZ | PL | RO | SG| SI | SK | WO | ZA | ID | TH	25
US6024963A	CONNAUGHT LAB LTD	32	AT | AU | CA | DE | DK | EP | ES | FI | GR | IL | JP | NO | PT | US | ZA	15
US7238349B1	GLAXOSMITHKLINE | Saech-Sisches Serumwerk Dresden	32	AT | AU | BR | CA | DE | DK | EP | ES | GB | HK | JP | PT | US | WO	14
US20080260781A1	GLAXOSMITHKLINE	31	AT | AU | CA | DE | EP | ES | HK | IL | JP | NO | US | WO	12
US20030124145A1	MERIAL	29	AR | AU | BR | CA | CN | CO | DE | EP | ES | FR | HU | ID | JP | MA | NZ | US | WO | MX | KR | IN	20
US3953592A	Recherche et Industrie Therapeutiques (R.I.T.)	29	US | AT | AU | BE | CA | CH | CS | DE | DK | ES | FI | FR | GB | HU | IE | IL | JP | LU | NL | NO | SE| ZA | PT	23

Global Filing Trends for Influenza A Virus Vaccines

The previous section assessed filing trends for individual family trends. The entire vaccine category was analyzed to determine the jurisdictions in which the entire vaccine population were filed. The INPADOC and DWPI patent families were combined for each reference document, and each jurisdiction was counted only once per family. For example, if a representative document had three European Patent Office applications, the EPO was counted once for that family. The TotalPatent families were not incorporated into this dataset, due to the difficulties with exporting such data. Thus, certain jurisdictions such as India, Taiwan and the Philippines may be under-represented.

Of over 230 possible different jurisdictions in which patent applications could potentially be filed, influenza vaccine families were filed in a total of 68 jurisdictions. As shown in Figure 14, North America and Europe are popular locations for assignees to seek protection for influenza vaccine inventions. Of Asian countries, China, India, Japan, South Korea (i.e. the Republic of Korea), Vietnam, Singapore, and Hong Kong were targets for filing. Most families were also filed Australia and New Zealand. However, Central and South America, other than Brazil, were

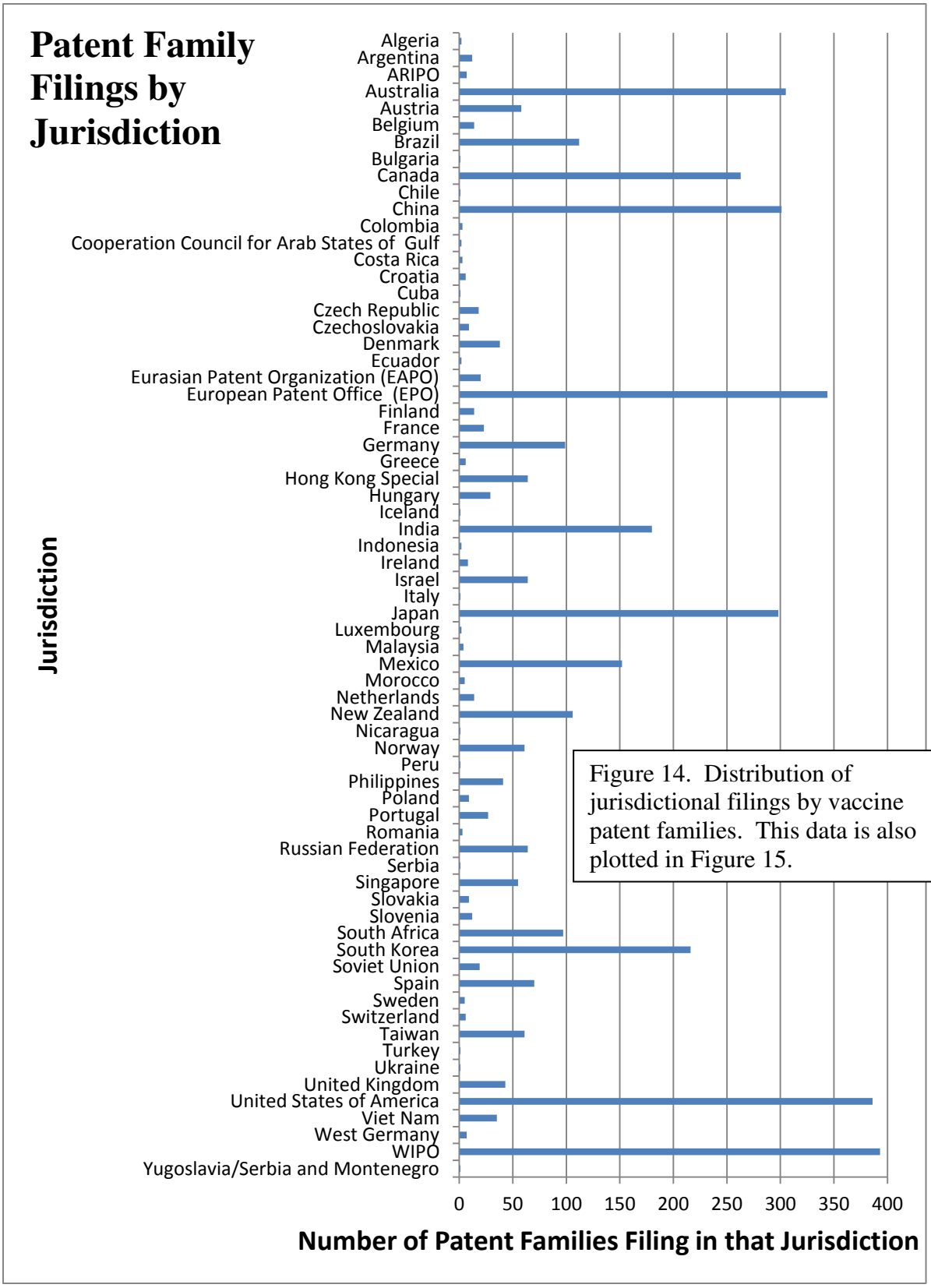


Figure 14. Distribution of jurisdictional filings by vaccine patent families. This data is also plotted in Figure 15.

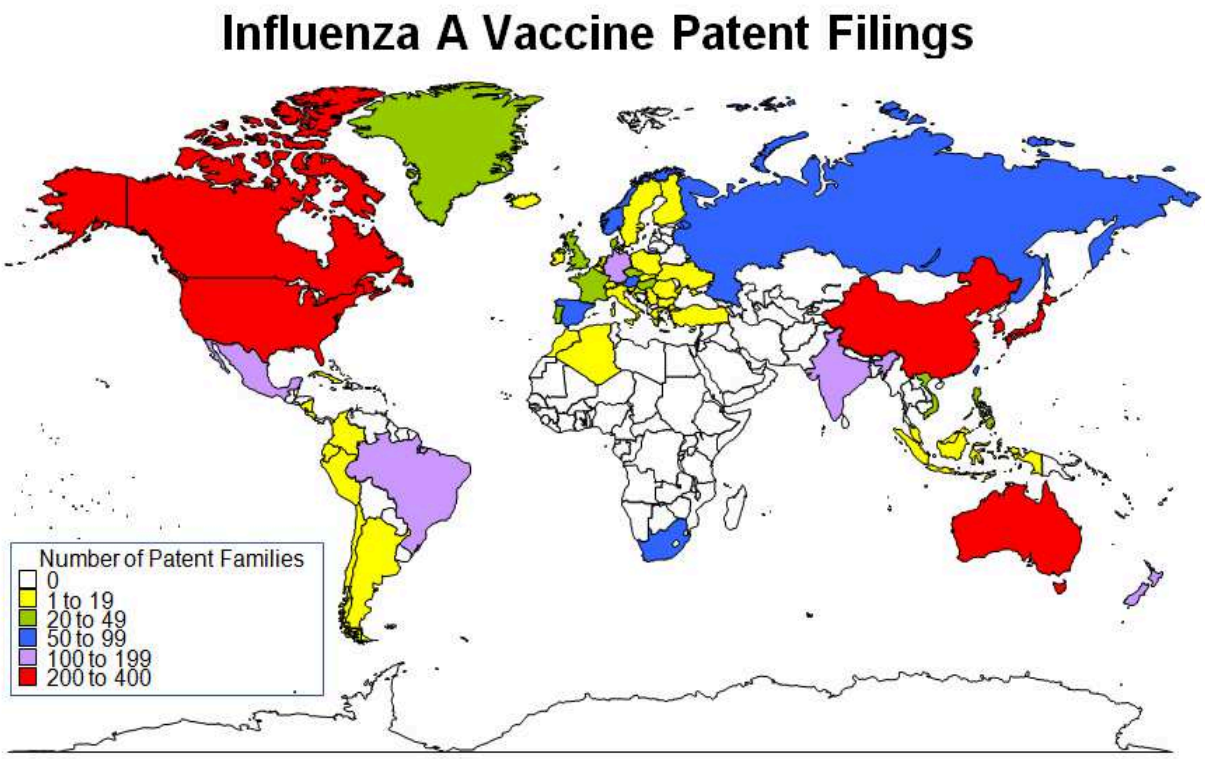


Figure 15. Global filing trends by country. The number of patent families that have sought protection in a given country are indicated by colors. Countries shown in white have no identified filings among the 570 influenza vaccine patent families. Multijurisdictional agencies, such as WIPO and the EPO, are not indicated.

poorly represented, and no filings were done in any African country other than South Africa. Countries are only shown in Figure 14 if at least one filing occurred in that country.

The jurisdictions where each patent family chose to seek patent protect was also plotted on a world map (see Fig. 15, above). Each jurisdiction is indicated once per family. For example, if a given patent family filed three U.S. applications, the United States was counted once for that family. Greenland was considered part of Denmark for this analysis. Also, the former Yugoslavia was indicated under Serbia and Montenegro, the former Czechoslovakia under the Czech Republic, and the former Soviet Union under Russia. Multijurisdictional agencies were not plotted. Nearly 70% of patent families had filed PCT applications with WIPO, so excluding PCT filings probably did not skew the results, as each country was affected equally. Also, since the map only indicates countries where PCT applications entered the national phase, the map gives a more accurate portrayal of the jurisdictions in which assignees are most interested. However, exclusion of filings at the European Patent Office (EPO), probably does leave some European countries slightly underrepresented on the map. Other multijurisdictional agencies not

indicated on the map are the Eurasian Patent Office (EAPO)[128] which consists of countries belonging to the former Soviet Union and in which 20 patent families filed, the African Regional Intellectual Property Organization (ARIPO)[129] which currently represents 18 nations and in which seven patent families filed, and the Cooperation Council for the Arab States of the Gulf (GCC)[130] which represents six nations on the Arabian peninsula and in which two patent families filed. Due to the time-consuming nature of this analysis, only influenza vaccines patent families were analyzed and plotted as above.

The map demonstrates that the majority of patent families file in just a few countries. The top nations for filings, indicated in red, are Australia, Canada, China, Japan, the Republic of Korea (South Korea), and the United States. Secondary target nations, indicated in purple, are Brazil, Germany, India, Mexico, and New Zealand, followed by a group (in blue) that includes Austria, Norway, Russia, Spain, and South Africa. A final group (in green) includes the Philippines, Vietnam, and several European nations. No other nation had more than 20 patent family filings. Filings were particularly sparse in South America and Africa.

Top Assignees by Patent Document Count

Assignee data for patent documents is often inaccurate. The patent rights could be sold to another assignee, who does not record the assignee. Also, a company holding the rights changes its name or is sold *in toto* and new assignments are not recorded. Some companies do not record an assignment until a patent is allowed, so published applications that are later abandoned or rejected do not have assignment data. Outside of the U.S., university faculty members retain rights in their inventions so the name of the university is not given on the patent document. None of the patent databases maintain accurate updates for such changes or account for such missing data.

Correction of patent assignee information must be performed manually. While this represents a burden on clinic members' time, such information would is invaluable to the use of the clinic report. Accurate assignee information is essential in order for the report data to be updated, and so the correct owners of the technologies can be contacted for licensing inquiries.

The main protocol for correcting assignee names is to use Google, searching for the company website or new releases about the company. Business Week[131] is a great source of information, as are technology-specific business reporters such as Fierce Biotech[132]. These sources reveal the

[128] http://www.eapo.org/en/.
[129] http://www.aripo.org/.
[130] http://www.gcc-sg.org/eng/.
[131] http://www.businessweek.com/.
[132] http://www.fiercebiotech.com/.

current accurate name of the company listed as the assignee or whether the company is now a wholly-owned subsidiary of a larger company.

If no information was readily obtainable, the assignee was searched using Innovation, restricting the date field to after the publishing date of the known document. The Derwent Assignee field may have another assignee commonly listed with the company being researched. A Google search of the two names together sometimes revealed a link between the two, such as a name change or an acquisition. The Derwent assignee code[133] is another source of assignee information. Other companies may be linked to the same code, such as ASTR being used for both AstraZeneca and its acquired company MedImmune.

If the only information available is the inventor name(s), then the document was located on Google Patent[134]. This website has hyperlinks to other patent documents by the same inventor which may have assignee data recorded. The name of the inventor was also searched on Google to find an association between the inventor and a particular company. To make the search more accurate, the search includes both the inventor's name and some keywords from the patent document. LinkedIn[135] and other networking websites are another source of information, and can be especially useful if an inventor is associated with multiple companies. Typically the date of the application can be associated with a date range for when the inventor was working for one company rather than another. Since patent applications can be filed months if not years after the date of the invention, this latter method was used with caution.

Using the above methodology, the assignee information for each relevant document in the vaccine and supporting technologies categories was manually corrected as accurately as possible. The results were then sorted on assignee names to reveal the number of patent families associated with each assignee. The two categories were analyzed together so a single list of assignees was generated, which is presented in Table IV.

Twenty-one assignees had seven or more patent families each. While the top four assignees – Novartis, GSK, Pfizer, and U.S. Merck - are for-profit companies, half of the assignees (12) are government agencies or non-profit institutions. More assignees (7) are based in the United States than any other country. Three institutions are located in China, and two each are based in Great Britain, Japan, Korea, and Russia. Switzerland, Germany, and France have one assignee each.

[133] http://ip-science.thomsonreuters.com/support/patents/dwpiref/reftools/companycodes/lookup/.
[134] www.google.com/patents.
[135] http://www.linkedin.com.

Table IV. Assignees with the Most INPADOC Patent Families in the Vaccines and Supporting Technologies Categories Combined (1,320 Families).

Standardized Assignee	Number of Families	Home Country
Novartis	33	CH
GlaxoSmithKline	25	GB
Pfizer	25	US
Merck and Co. (Merck Sharpe & Dohme)	23	US
Nauchno-issledovatel'skij institut ehksperimental'noj meditsiny RAMN (Scientific Research Institute of Experimental Medicine, RAMS)	23	RU
Sanofi	21	FR
AstraZeneca	20	GB
University of Wisconsin	18	US
US Department of Health	16	US
Baxter International	15	US
Saint Jude's Hospital	15	US
Chinese Academy of Agricultural Sciences	14	CN
Chinese Academy of Sciences	11	CN
Kaketsuken	9	JP
Institute of Medical Biology Chinese Academy of Medical Sciences	8	CN
Ministry for Food Agriculture, Forestry and Fisheries (Korea)	8	KR
Mount Sinai Hospital	8	US
Boehringer Ingelheim	7	DE
Choong and Vaccine Laboratory	7	KR
Ministry of Health, Labour and Welfare (Japan)	7	JP
Vsesoyuznyj Nauchno-Issledovatelskij Institut Grippa (Union Scientific Research Institute of Influenza)	7	RU

Top Inventors by Patent Document Count

Of all patent data, inventor names are probably the most error-prone. Inventor names do not change as assignee names tend to do, but inventor names are listed in a number of different ways. The inventor name may include a middle initial or not, or the middle name may be spelled

out entirely.[136] Names may be misspelled.[137] Last names may be hyphenated or the hyphen may be absent.[138] First and last names may even be switched.[139]

Because of these errors, analysis of inventors using the databases is extremely inaccurate, as those calculations treat each variant of a name as a different inventor. Thus, inventor names were reviewed manually and corrections made when possible. The DWPI Inventor field lists alternative versions of inventors' names, although sometimes more research is needed to determine which one of those variants is the correct name. The most accurate source of inventor names is the scientific literature, which, unlike patents, is carefully edited prior to publication.

Table V lists 30 inventors who each was an inventor of four or more patent families with the vaccines category. The assignees associated the inventors are also given. Curiously, this list of top inventors does not match the top assignee data, as only one Novartis inventor appears on the list and no GSK inventors are present. The top five inventors are all Russian. Complete inventor data for the vaccine category are given in Appendix H.

Table V. Top Inventors of Vaccine Patent Families.

Standarized Inventor Name	Number of Documents	Assignee - DWPI
Aleksandrova, Galina Ibragimovna	27	A MED EXPER MED RES INST
Rudenko, Larisa Georgievna	24	A MED EXPER MED RES INST
Klimov, Aleksandr I	16	A MED EXPER MED RES INST
Kiseleva, Irina Vasil Evna	15	A MED EXPER MED RES INST
Romanova, Julia	8	A MED EXPER MED RES INST| AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG | POLYMUN SCI IMMUNBIOLOGISCHE FORSCHUNG
Egorov, Andrej	7	POLYMUN SCI IMMUNBIOLOGISCHE FORSCHUNG | AVIR GREEN HILLS BIOTECHNOLOGY RES AG
Barrett, P. Noel	6	BAXTER HEALTHCARE SA
Kistner, Otfried	6	BAXTER HEALTHCARE SA
Webster, Robert G.	6	WYETH | ST JUDE CHILDREN'S RES HOSPITAL
Arnon, Ruth	5	YEDA RES & DEV CO LTD
Kawaoka, Yoshihiro	5	WISCONSIN ALUMNI RES FOUND

[136] An example from the vaccine inventor list is Galina Ibragimovna Aleksandrova, who is also listed as Galina I. Aleksandrova and G. I. Aleksandrova.
[137] RU2319744C2 misspells Aleksandrova's middle name by dropping the "A" at the end.
[138] For example, Derwent information shows at least five different versions of Wilson Romero Capparros-Wanderley's name. See US20120219575A1.
[139] Compare Robert G. Webster's name on US8293247B2 and CA813864A.

O'Hagan, Derek	5	CHIRON CORP | NOVARTIS VACCINES&DIAGNOSTICS INC
Polezhaev, Fial I	5	EXPER MEDICAL RES | KALIN SANITARY EPIDEMY | VIRUS MEDICAMENTS RES
Sambhara, Suryaprakash	5	AVENTIS PASTEUR LTD | CONNAUGHT LAB LTD | PURDUE RES FOUND
Seong, Baik Lin	5	BIOTRION CO LTD | PROTHEON CO LTD
Ben-Yedidia, Tamar	4	YEDA RES & DEV CO LTD | BIONDVAX PHARM LTD
Chatfield, Steven Neville	4	ARCHIMEDES DEV LTD | DANBIOSYST UK LTD | MEDEVA HOLDINGS BV | WEST PHARM SERVICES DRUG DELIVERY & CLIN
Dorner, Friedrich	4	BAXTER HEALTHCARE SA
Ferko, Boris	4	POLYMUN SCI IMMUNBIOLOGISCHE FORSCHUNG | AVIR GREEN HILLS BIOTECHNOLOGY RES AG
Galarza, Jose M.	4	AMERICAN CYANAMID CO | WYETH HOLDINGS CORP | TECHNOVAX INC
Kemble, George	4	MEDIMMUNE INC
Larionova, Natalja Valentinovna	4	AS SIBE MED EXPERIMENTAL MED RES INST
Medvedeva, Tamilla E	4	AMS EXP MED RES INS | INFLUENZA RES INST | MED BIOLK PREP STANDARD | MOSC VIRUS PREPD RES INST
Nabel, Gary J.	4	US DEPT HEALTH&HUMAN SERVICES
Ohkuma, Kunio	4	CHEMO SERO THERAPEUTIC RES INS |NAT INST OF HEALTH JAPAN
Osterhaus, Albert D.M.E.	4	ABBOTT BIOLOGICALS BV | SOLVAY BIOLOGICALS BV | UNIV ROTTERDAM ERASMUS CENT MEDICAL
Wei, Chih-Jen	4	US DEPT HEALTH&HUMAN SERVICES
Wolschek, Markus	4	AVIR GREEN HILLS BIOTECHNOLOGY RES AG
Yang, Chin-Fen	4	MEDIMMUNE INC
Yang, Zhi-Yong	4	US DEPT HEALTH&HUMAN SERVICES

The same analysis was performed with supporting technologies documents, as shown in Table VI. There were more inventors (47) with four or more patent families, but number of patent documents per inventor was lower than that with the vaccine documents. For example, G.I. Aleksandrova was the top inventor on both lists, but this inventor had 27 patents documents in the vaccines category but only 15 in the supporting technologies category. Overall, this agrees with the previous determination that the supporting technologies category represents a more diverse pool of documents than the documents in the vaccines category. Many of the vaccine inventors also appear on the supporting technologies list, which was probably to be expected. The assignees associated with these inventors are surprisingly different from the vaccine inventors list. GSK is represented on the supporting technologies list of inventors but Pfizer and

Merck are not. Non-profit entities are more represented, with 34 of the 47 inventors working for such institutions. Russian and Chinese inventors were prominent on the top of the supporting technologies inventor list. A prominent person on this list is Dr. Peter Palese,[140] of Mount Sinai School of Medicine in New York, USA. Dr. Palese uses reverse genetics as a tool to modify and study pandemic influenza strains.[141]

Complete inventor data for the supporting technologies category are given in Appendix I.

Table VI. Top Inventors of Supporting Technologies Patent Families.

Standardized Inventor Name	Number of Documents	Assignee - DWPI
Aleksandrova, Galina Ibragimovna	15	A MED EXPER MED RES INST
Kawaoka, Yoshihiro	15	ST JUDE CHILDREN'S RES HOSPITAL | US DEPT HEALTH & HUMAN SERVICES
Rudenko, Larisa Georgievna	14	A MED EXPER MED RES INST
Klimov, Aleksandr I	11	A MED EXPER MED RES INST
Chen, Hua-lan	10	CHINESE ACAD AGRIC SCI HARBIN VETERINARY MEDICINE INST
Smith, Gail Eugene	9	MG-PMC LLC | MICROGENESYS INC | PROTEIN SCI CORP
Bu, Zhi-gao	8	CHINESE ACAD AGRIC SCI HARBIN VETERINARY MEDICINE INST
Gendon, Yury Zakharovich	8	NIZHEGOROD EPIDEMICS MICROBIOLOG INST | VEKTOR VIROLOGY & BIOTECH RES CENTRE
Palese, Peter M.	8	MOUNT SINAI SCHOOL MEDICINE
Webster, Robert G.	8	ST JUDE CHILDREN'S RES HOSPITAL
Garcia-Sastre, Adolfo	7	ISIS INNOVATION LTD | UNIV NEW YORK MT SINAI SCHOOL MEDICINE
Polezhaev, Fial I	7	
Yoon, In Joong	7	CHOONG ANG VACCINE LAB | VACCINE LEADER
LI, Ying-bo	6	CHINESE ACAD SCI KUNMING INST ZOOLOGY
Seo, Sang Heui	6	CHOONG ANG VACCINE LAB | VACCINE LEADER
Chen, Qin-qin	5	CHINESE ACAD SCI KUNMING INST ZOOLOGY
LI, Hui	5	
Neumann, Gabriele	5	WISCONSIN ALUMNI RES FOUND
Shin, Yeun-Kyung	5	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI

[140] See e.g. http://www.mountsinai.org/profiles/peter-palese.
[141] See e.g. http://www.sciencemag.org/content/310/5745/77.short.

Song, Jae Young	5	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND
Akopova, Irina Ivanovna	4	NIZHEGOROD EPIDEMICS MICROBIOLOG INST | VEKTOR VIROLOGY & BIOTECH RES CENTRE
Andre, Bruno, Rene	4	GLAXOSMITHKLINE
Audonnet, Jean-Christophe Francis	4	MERIAL | MERIAL SAS | RHONE MERIEUX SA
Cao, Yong-chang	4	UNIV SUN YET-SEN
Champluvier, Benoit Paul Suzanne	4	GLAXOSMITHKLINE
Choi, Young Ki	4	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND
Couture, Manon	4	MEDICAGO INC
Egorov, Andrej	4	A MED EXPER MED RES INST
Garmashova, Lyudmila M	4	
Gou, Hong-ying	4	LIAONING TIANCHENG INST BIOLOGICAL MEDIC | TIANCHENG INST BIOLOGICAL PHARMACY LIAON
Jiang, Yong-ping	4	HARBIN VETERINARY RES INST CAAS
Jin, Hong	4	MEDIMMUNE LLC | MEDIMMUNE VACCINES INC
Kim, Hyun Soo	4	CHOONG ANG VACCINE LAB | VACCINE LEADER
Kwon, Hyuk Il	4	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND
Larionova, Natalja Valentinovna	4	A MED EXPER MEDICINE RES INST
Liu, Da-cai	4	UNIV SUN YET-SEN
Markushin, Stanislav Georgievich	4	NIZHEGOROD EPIDEMICS MICROBIOLOG INST | VEKTOR VIROLOGY & BIOTECH RES CENTRE
Medvedeva, Tamilla E	4	
Murphy, Brian R.	4	ST JUDE CHILDREN'S RES HOSPITAL
O'Hagan, Derek	4	CHIRON CORP | NOVARTIS VACCINES & DIAGNOSTICS INC
Pushko, Peter M.	4	NOVAVAX INC
Song, Min Suk	4	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND
Vezina, Louis-Philippe	4	MEDICAGO INC
Wang, Cheng-yu	4	LIAONING TIANCHENG INST BIOLOGICAL MEDIC | TIANCHENG INST BIOLOGICAL PHARMACY LIAON
Xue, Chun-yi	4	UNIV SUN YET-SEN
Yoon, So Ra	4	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND
Yoon, Soon Seek	4	REPUBLIC KOREA MANAGEMENT MIN AGRIC&FI | UNIV CHUNGBUK NAT IND ACAD COOP FOUND

Publication Year v. Patent Document Count

Trends in publication of patent documents were analyzed for the two major categories. Publication date was chosen as the parameter for analysis, which indicates publication of applications generally 18 months after filing and publication of patents after allowance. In the few cases in which the publication date was not recorded, the year of publication could usually be found in DWPI data such as the DWPI update information.

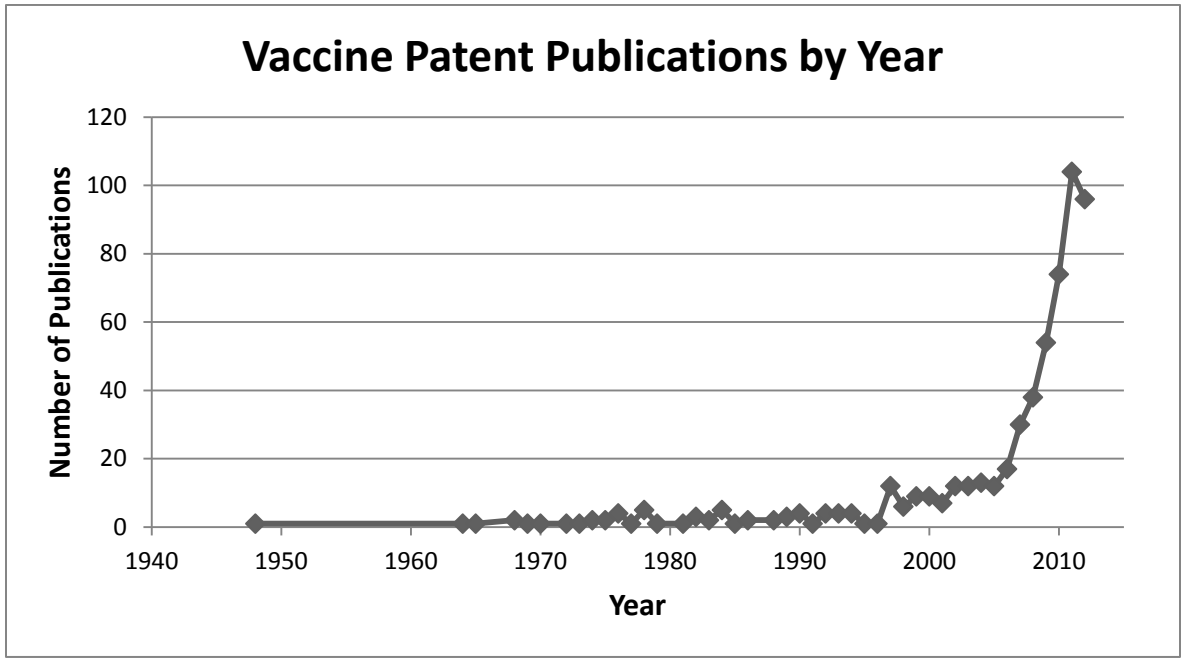


Figure 16. Publication trends for patent families in the influenza vaccine category. The year of publication of each representative document of the 570 families is shown.

The earliest representative family member in the vaccine category was a U.S. patent issued in 1948, as shown in Figure 15. The second place document was published 16 years later in 1964. From the mid 1960s until the mid 1990s, only one or two patents were published, on average. In 1997, the average number of publications leapt to 10, possibly because the TRIPS Agreement took effect in 1996 and patent applications began to be published 18 months after filing. In 2006, the number of influenza vaccine-related publications began to steadily climb, up to 104 in 2011. The number of publications in 2012 was approximately equal to that peak, especially considering this report includes a thorough search of patent only up to early October 2012, and thus the search did not cover the entire calendar year.

The increase in filing of patent applications also correlates with the H5N1 (bird flu) epidemic that began in 1997, and was probably driven even higher following the 2009 H1N1 (swine flu) pandemic.

The data may be somewhat skewed because the representative family member was chosen as the latest publication from the U.S., or the latest document from another jurisdiction if there was no U.S. family member. However, the trend still indicates an increased interest in influenza vaccine technologies in the last case.

Supporting technology publication trends present a similar story, as shown in Figure 16. Only three such documents were published before 1966. In the 1970s, there was a higher average level of patent publication than that for vaccine patents, but this average dropped to only two documents per year in the late 1980s and early 1990s. There was a small increase when applications began to be published. However, since at least 2004 there has been a steady increase in publication of supporting technology documents. In fact, even though the data is not complete 2012, there were still 151 publications in that partial year, which represents a substantial increase over the 102 publications in 2011. Again, this increase in patent filings is likely driven by a response to the 1997 H5N1 epidemic and the 2009 H1N1 pandemic.

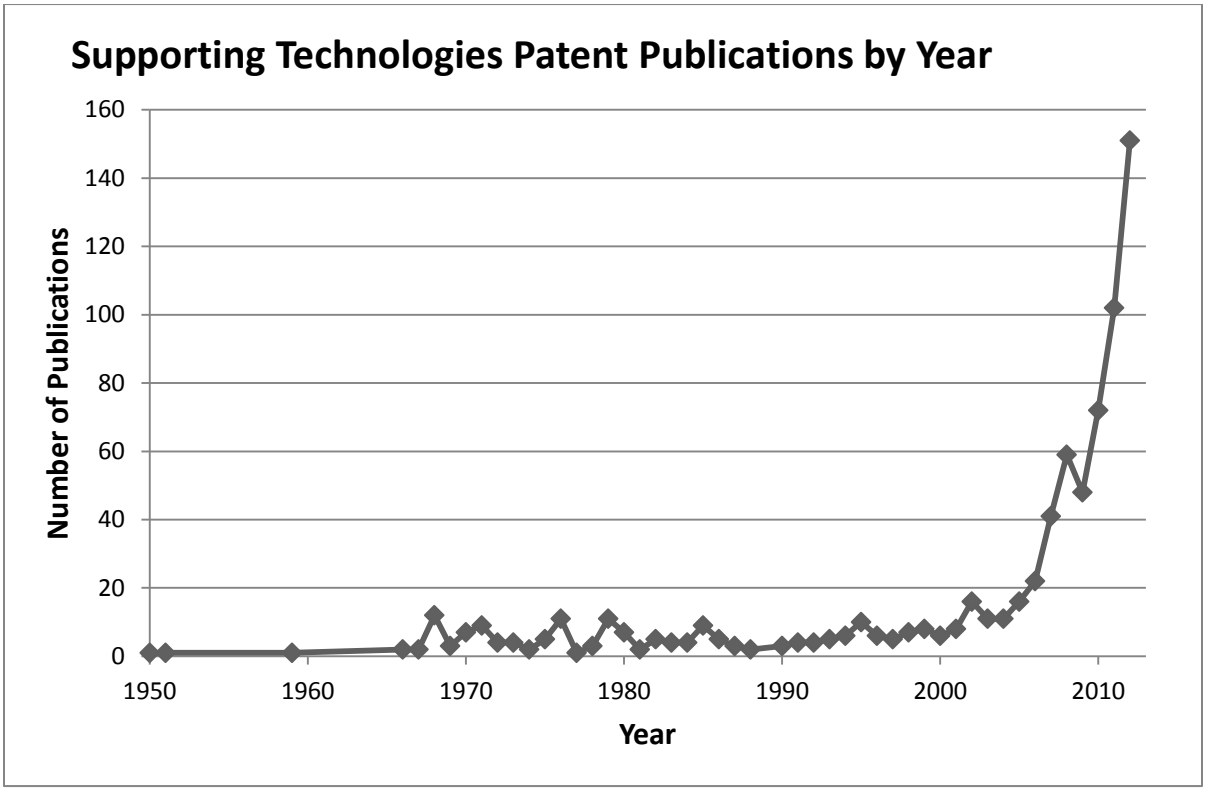


Figure 17. Publication trends for patent families in the supporting technologies category. The year of publication of each representative document of the 750 families is shown.

U.S. Classification by Patent Document Count

Every patent application submitted to the U.S.P.T.O. receives a preliminary classification which determines the art unit in which that application is examined. The patent examiner assigns other classes to the application as she feels appropriate to indicate the technologies important the particular invention disclosed by the application. The U.S. Patent Classification System (USPC) " is a system for organizing all U.S. patent documents and many other technical documents into relatively small collections based on common subject matter."[142] The USPC groups similar patent documents together into small classes which can be searched. For example, once a relevant document is identified, an interested person could search the U.S. class of that document for other relevant references. This represents an alternative to keyword searching for relevant documents, and this system may help identify relevant documents when specific keywords are difficult to ascertain. Certainly, class searching should supplement any keyword search to ensure all relevant documents are identified.

The U.S.P.T.O. is currently revising its classification system to bring the USPC into harmony with the European Classification System (ECLA) to facilitate identification of relevant documents from multiple jurisdictions.[143] While the USPC is being revised, it is useful to present an analysis of the current USPC since complete harmonization has not been achieved to date.

Figure 17 shows the 53 different classes that have been assigned to influenza vaccine documents by the U.S.P.T.O. Most documents were assigned to Class 424, particularly the subclasses 209.1, 210.1, 206.1, and 186.1. The definitions for each of the top classes are given in Table VII. Class 424 is related to vaccines, and subclasses 209.1, 206.1, and 210.1 are specifically limited to influenza vaccines. Class 424/450 is directed to liposomes as carriers in vaccines. Classes 514/044R and 435/320.1 are directed to DNA sequences, probably as used in DNA vaccines or in the production of recombinant viruses and subunits.

As indicated before, the supporting technologies category contains a broader range of inventions so there are 74 different classes assigned to documents in this category, as shown in Figure 18. Many of the top classes are the same between the two categories, including the number one class on both lists, 424/209.1. The list of top classes for supporting technologies did have three classes that were not prominent with vaccine documents. Class 435/239 contains technologies related to virus purification, which would describe the subcategory of methods of making vaccines. Additionally, Classes 435/069.3 and 435/069.1 contains recombinant peptides, which could include novel subunits useful in vaccines. Table VIII lists the definitions of these classes.

[142] http://www.uspto.gov/patents/resources/classification/overview.pdf.
[143] http://www.uspto.gov/patents/resources/classification/index.jsp.

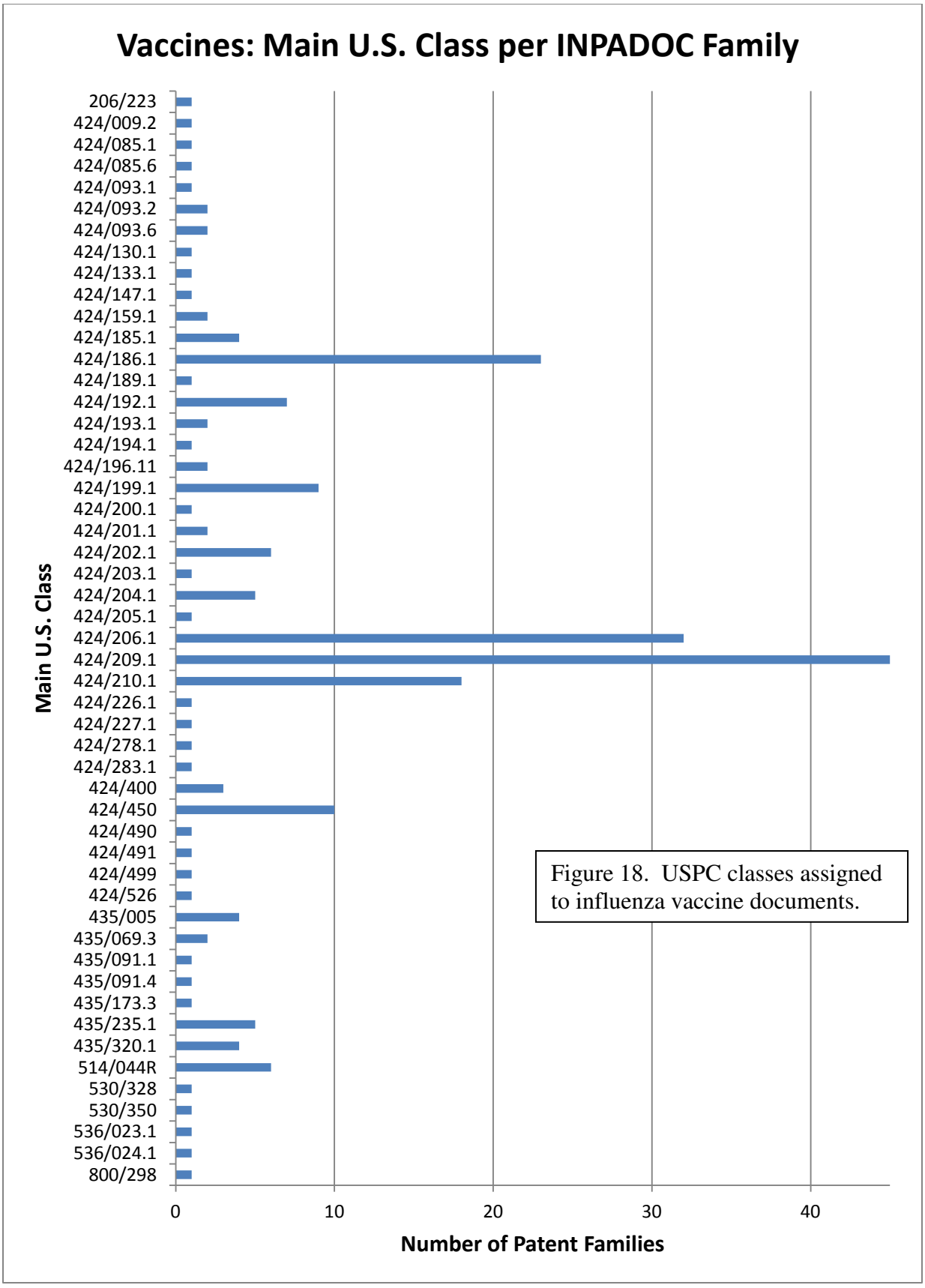


Figure 18. USPC classes assigned to influenza vaccine documents.

Table VII. Top U.S. Classes for Vaccine Documents.

US Class - Main	# Docs	Class Title
424/209.1	45	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Orthomyxoviridae (e.g., influenza virus, fowl plague virus, etc.)
424/206.1	32	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Reassortant or deletion mutant virus (205.1): Influenza virus
424/186.1	23	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Amino acid sequence disclosed in whole or in part; or conjugate, complex, or fusion protein or fusion polypeptide including the same (185.1): Disclosed amino acid sequence derived from virus
424/210.1	18	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Orthomyxoviridae (209.1): Subunit vaccine containing hemagglutinin or neuraminidase
424/450	10	PREPARATIONS CHARACTERIZED BY SPECIAL PHYSICAL FORM (400): Liposomes
424/199.1	9	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Recombinant virus encoding one or more heterologous proteins or fragments thereof
424/192.1	7	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Fusion protein or fusion polypeptide (i.e., expression product of gene fusion)

424/202.1	6	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Combination of antigens from multiple viral species (e.g., multivalent viral vaccine, etc.)
514/044R	6	DESIGNATED ORGANIC ACTIVE INGREDIENT CONTAINING (DOAI) (001): Carbohydrate (i.e., saccharide radical containing) DOAI (023): N-glycoside (042): Nitrogen containing hetero ring (043): Polynucleotide (e.g., RNA, DNA, etc.)
424/204.1	5	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof
435/235.1	5	VIRUS OR BACTERIOPHAGE, EXCEPT FOR VIRAL VECTOR OR BACTERIOPHAGE VECTOR; COMPOSITION THEREOF; PREPARATION OR PURIFICATION THEREOF; PRODUCTION OF VIRAL SUBUNITS; MEDIA FOR PROPAGATING
435/005	4	MEASURING OR TESTING PROCESS INVOLVING ENZYMES OR MICRO-ORGANISMS; COMPOSITION OR TEST STRIP THEREFORE; PROCESSES OF FORMING SUCH COMPOSITION OR TEST STRIP (004): Involving virus or bacteriophage
424/185.1	4	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Amino acid sequence disclosed in whole or in part; or conjugate, complex, or fusion protein or fusion polypeptide including the same
435/320.1	4	VECTOR, PER SE (E.G., PLASMID, HYBRID PLASMID, COSMID, VIRAL VECTOR, BACTERIOPHAGE VECTOR, ETC.)

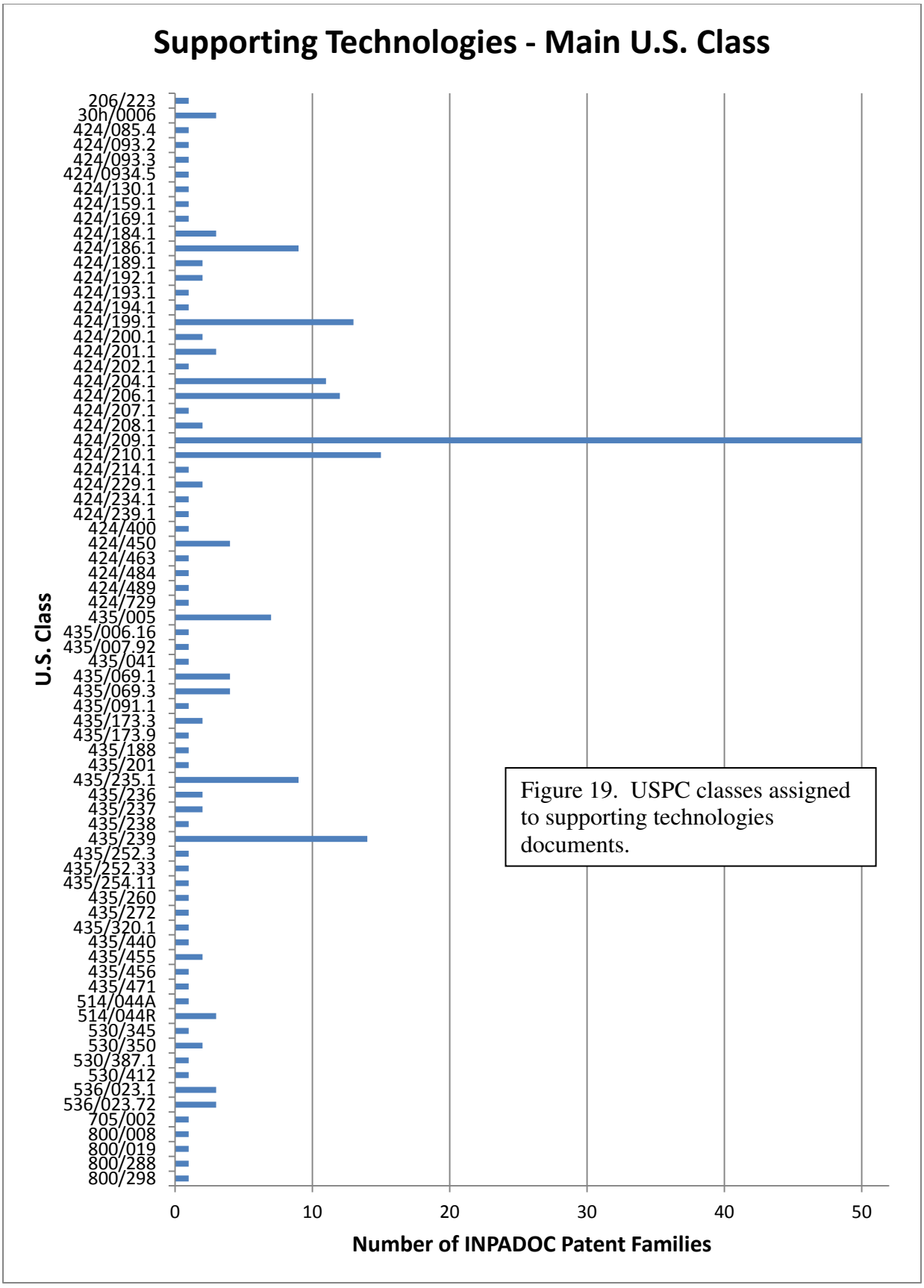


Figure 19. USPC classes assigned to supporting technologies documents.

Table VIII. Top U.S. Classes for Supporting Technology Documents.

US Class - Main	# Docs	Class Title
424/209.1	50	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Orthomyxoviridae (e.g., influenza virus, fowl plague virus, etc.)
424/210.1	15	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Orthomyxoviridae (209.1): Subunit vaccine containing hemagglutinin or neuraminidase
435/239	14	VIRUS OR BACTERIOPHAGE, EXCEPT FOR VIRAL VECTOR OR BACTERIOPHAGE VECTOR; COMPOSITION THEREOF; PREPARATION OR PURIFICATION THEREOF; PRODUCTION OF VIRAL SUBUNITS; MEDIA FOR PROPAGATING (235.1): Recovery or purification
424/199.1	13	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Recombinant virus encoding one or more heterologous proteins or fragments thereof
424/206.1	12	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof (204.1): Reassortant or deletion mutant virus (205.1): Influenza virus
424/204.1	11	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Virus or component thereof
435/235.1	9	VIRUS OR BACTERIOPHAGE, EXCEPT FOR VIRAL VECTOR OR BACTERIOPHAGE VECTOR; COMPOSITION THEREOF; PREPARATION OR PURIFICATION THEREOF; PRODUCTION OF VIRAL SUBUNITS; MEDIA FOR PROPAGATING

424/186.1	9	ANTIGEN, EPITOPE, OR OTHER IMMUNOSPECIFIC IMMUNOEFFECTOR (E.G., IMMUNOSPECIFIC VACCINE, IMMUNOSPECIFIC STIMULATOR OF CELL-DIATED IMMUNITY, IMMUNOSPECIFIC TOLEROGEN, IMMUNOSPECIFIC IMMUNOSUPPRESSOR, ETC. (184.1): Amino acid sequence disclosed in whole or in part; or conjugate, complex, or fusion protein or fusion polypeptide including the same (185.1): Disclosed amino acid sequence derived from virus
435/005	7	MEASURING OR TESTING PROCESS INVOLVING ENZYMES OR MICRO-ORGANISMS; COMPOSITION OR TEST STRIP THEREFORE; PROCESSES OF FORMING SUCH COMPOSITION OR TEST STRIP (004): Involving virus or bacteriophage
435/069.3	4	MICROORGANISM, TISSUE CELL CULTURE, OR ENZYME USING PROCESS TO SYNTHESIZE A DESIRED CHEMICAL COMPOUND OR COMPOSITION (41): Recombinant DNA technique included in method of making a protein or polypeptide (69.1): Antigens
435/069.1	4	MICROORGANISM, TISSUE CELL CULTURE, OR ENZYME USING PROCESS TO SYNTHESIZE A DESIRED CHEMICAL COMPOUND OR COMPOSITION (41): Recombinant DNA technique included in method of making a protein or polypeptide
424/450	4	Recombinant DNA technique included in method of making a protein or polypeptide

Top IPC (Current) Classifications

The International Patent Classification (IPC) system, established in 1971, is administrated by the World Intellectual Property Organization (WIPO). The IPC "provides for a hierarchical system of language independent symbols for the classification of patents and utility models according to the different areas of technology to which they pertain."[144] The IPC contains eight core sections with approximately 70,000 subdivisions, called advanced levels. WIPO continuously revises the IPC, with the core levels being updated every three years and the advance levels being reviewed a few times each year. The current version of the core levels was released in 2012.

The IPC (Current) codes were analyzed for each patent family. Some families had more than one code, and each was counted. For the vaccine category, 15 codes represented more than 20 families each, as shown in Figure 19. The two classes that represented the most families were A61K 39/145, which contains preparations of influenza antigens such as a vaccine, and A61P 31/16, which contains pharmaceutical compositions used to treat influenza infections. The definitions of the top IPC classes for vaccine documents are given in Table IX.

[144] World Intellectual Property Organization, *Preface to the International Patent Classification (IPC)*, WIPO IP SERVICES, http://www.wipo.int/classifications/ipc/en/general/preface.html (last visited Apr. 18, 2012).

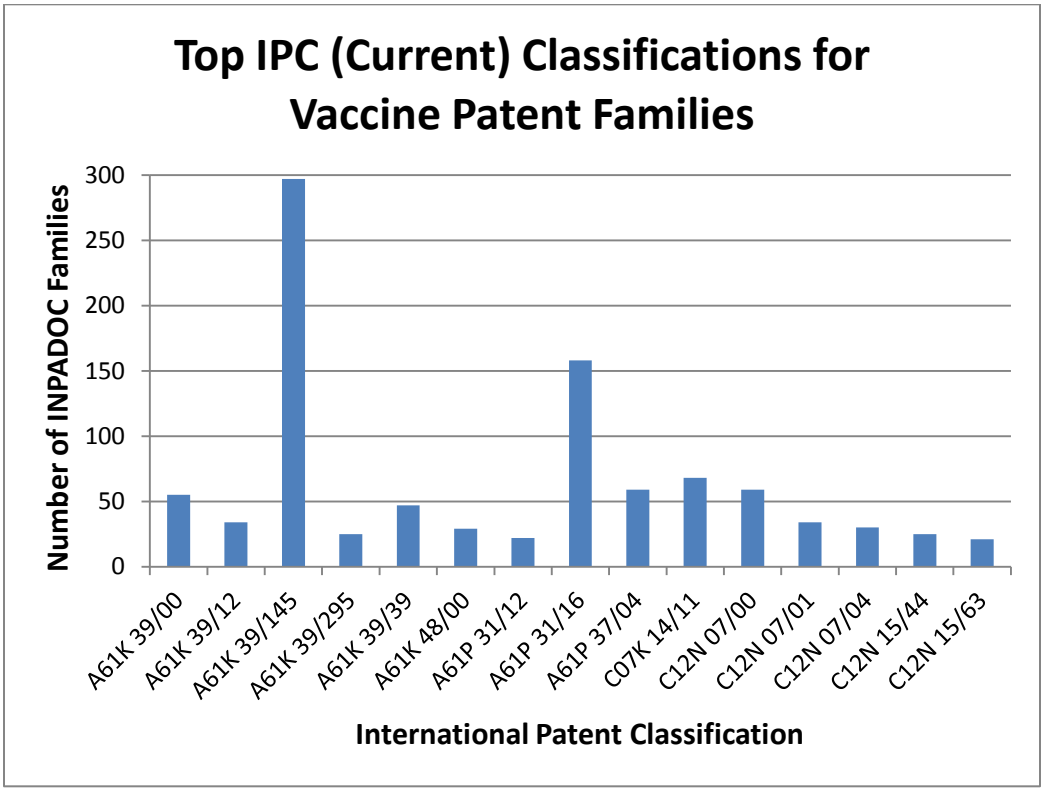


Figure 20. Top IPC (Current) Classification of Vaccine Families. Each class represented at least 21 different families.

Table IX. Definitions of the Top IPC (Current) Classifications of Vaccine Documents.

IPC - Current	# Docs	Class Description
A61K 39/00	55	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies
A61K 39/12	34	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens
A61K 39/145	297	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens (39/12): Orthomyxoviridae, e.g. influenza virus
A61K 39/295	25	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens (39/12): Polyvalent viral antigens; Mixtures of viral and bacterial antigens
A61K 39/39	47	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): characterised by the immunostimulating additives, e.g. chemical adjuvants

A61K 48/00	29	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy
A61P 31/12	22	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics (A61P 31/00): Antivirals
A61P 31/16	158	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics (A61P 31/00): Antivirals (31/12): for RNA viruses (31/14): for influenza or rhinoviruses
A61P 37/04	59	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Drugs for immunological or allergic disorders (A61P 37/00): Immunomodulators (37/02): Immunostimulants
C07K 14/11	68	ORGANIC CHEMISTRY (C07): Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof (C07K 14/00): from viruses (14/005): RNA viruses (14/08): Orthomyxoviridae, e.g. influenza virus
C12N 07/00	59	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof
C12N 07/01	34	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (C12N 07/00): Viruses, e.g. bacteriophages, modified by introduction of foreign genetic material
C12N 07/04	30	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (C12N 07/00): Inactivation or attenuation; Producing viral sub-units
C12N 15/44	25	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology (15/09): DNA or RNA fragments; Modified forms thereof (15/11): Genes encoding microbial proteins, e.g. enterotoxins (15/31): Genes encoding viral proteins (15/33): Proteins from RNA viruses, e.g. flaviviruses (15/40): Orthomyxoviridae, e.g. influenza virus

C12N 15/63	21	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology (15/09): Introduction of foreign genetic material using vectors; Vectors; Use of hosts therefor; Regulation of expression

Again, the supporting technologies category had a broader spectrum of top classes, with 20 different classes each representing at least 21 families, as shown in Figure 20. However, the top two classes, A61k 39/145 and A61P 31/16, were the same as with the vaccine category. Two of the five additional classifications, C12N 15/09 and A61P 31/14 were merely higher level classifications of previously identified, more narrow classes. The three new classes were C12N 05/10, which concerns culture of transformed cell lines such as for the production of viruses or viral subunits, C12N 07/02, which concerns methods of purifying viruses, and C12N 15/86, which concerns DNA constructs such as for producing recombinant polypeptides. Complete definitions are located in Table X.

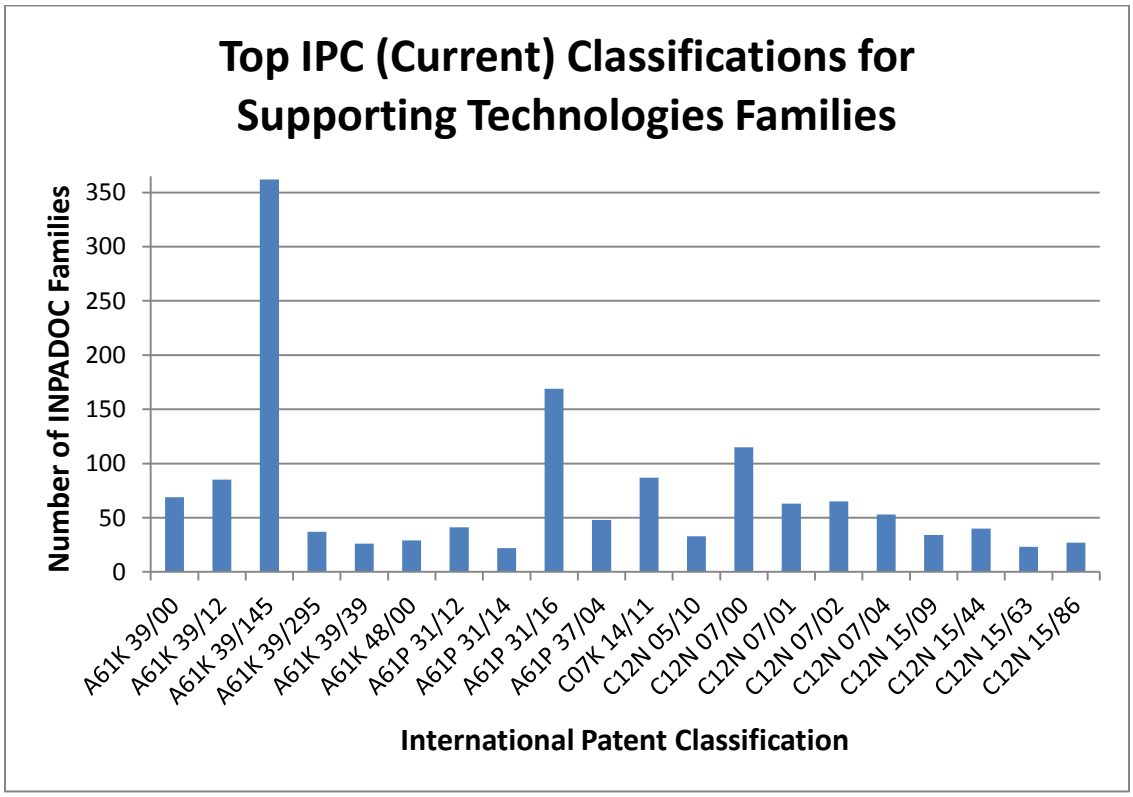


Figure 21. Top IPC (Current) Classification of Supporting Technology Documents. Each class represented at least 21 different families.

Table X. Definitions of the Top IPC (Current) Classifications of Supporting Technology Documents.

IPC - Current	# Docs	Class Definitions
A61K 39/00	69	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies
A61K 39/12	85	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens
A61K 39/145	362	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens (39/12): Orthomyxoviridae, e.g. influenza virus
A61K 39/295	37	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): Viral antigens (39/12): Polyvalent viral antigens; Mixtures of viral and bacterial antigens
A61K 39/39	26	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing antigens or antibodies (A61K 39/00): characterised by the immunostimulating additives, e.g. chemical adjuvants
A61K 48/00	29	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy
A61P 31/12	41	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics (A61P 31/00): Antivirals
A61P 31/14	22	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics (A61P 31/00): Antivirals (31/12): for RNA viruses
A61P 31/16	169	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics (A61P 31/00): Antivirals (31/12): for RNA viruses (31/14): for influenza or rhinoviruses
A61P 37/04	48	MEDICAL OR VETERINARY SCIENCE; HYGIENE (A61): Drugs for immunological or allergic disorders (A61P 37/00): Immunomodulators (37/02): Immunostimulants
C07K 14/11	87	ORGANIC CHEMISTRY (C07): Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof (C07K 14/00): from viruses (14/005): RNA viruses (14/08): Orthomyxoviridae, e.g. influenza virus

C12N 05/10	33	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor (C12N 5/00): Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells
C12N 07/00	115	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof
C12N 07/01	63	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (C12N 07/00): Viruses, e.g. bacteriophages, modified by introduction of foreign genetic material
C12N 07/02	65	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (C12N 07/00): Recovery or purification
C12N 07/04	53	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (C12N 07/00): Inactivation or attenuation; Producing viral sub-units
C12N 15/09	34	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology
C12N 15/44	40	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology (15/09): DNA or RNA fragments; Modified forms thereof (15/11): Genes encoding microbial proteins, e.g. enterotoxins (15/31): Genes encoding viral proteins (15/33): Proteins from RNA viruses, e.g. flaviviruses (15/40): Orthomyxoviridae, e.g. influenza virus

C12N 15/63	23	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology (15/09): Introduction of foreign genetic material using vectors; Vectors; Use of hosts therefor; Regulation of expression
C12N 15/86	27	BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING (C12): Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (C12N 15/00): Recombinant DNA-technology (15/09): DNA or RNA fragments; Modified forms thereof (15/11): Vectors or expression systems specially adapted for eukaryotic hosts (15/79): for animal cells (15/85): Viral vectors

Top DWPI Classification v. Patent Document Count

The DWPI classification system uses a simple way of categorizing patent documents. This system was developed by Thomson Scientific to facilitate searching of a particular area of a given technology by providing a smaller initial pool of documents to search. As per this system, patents are broadly divided into three areas: Chemical, Engineering, and Electronic and Electrical Engineering. Each of these is then further divided into Sections and Classes which describe the technical area, or areas, covered by the patent.

The pattern of top DWPI codes was similar for the vaccine category and the supporting technologies category, as shown in Figure 21. Among codes representing at least 10 families each, the top three codes for both categories was B04, which covers polymers such as polypeptides, D16, which covers cultures of cell lines or yeast, and C06, which covers production of recombinant proteins in plants and veterinary vaccines. Full definitions of the codes are given in Table XI.

There were only minor differences between the two categories, perhaps because the DWPI codes represent fairly broad areas of technology and cannot distinguish among the various categories used to delineate the results presented herein. Overall this particular analysis was very useful.

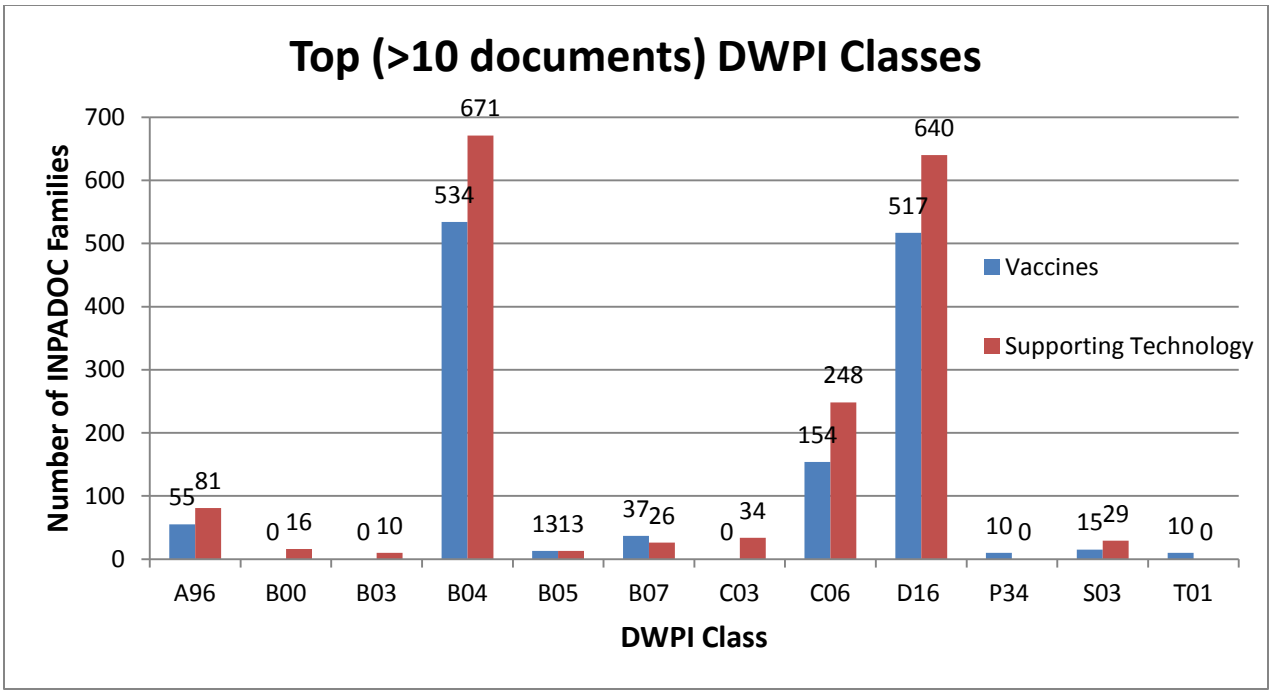


Figure 22. Top DWPI Classes for Both Vaccines and Supporting Technology Documents.

Table XI. Definitions of the Top DWPI Classes.

DWPI Class	Vaccines	Supporting Technology	Class Definition
A96	55	81	Polymers and Plastics: Medical, dental, veterinary, cosmetic
B00	0	16	Pharmaceuticals
B03	0	10	Pharmaceuticals: Other heterocyclics
B04	534	671	Pharmaceuticals: Natural products and polymers. Including testing of body fluids (other than blood typing or cell counting), pharmaceuticals or veterinary compounds of unknown structure, testing of microorganisms for pathogenicity, testing of chemicals for mutagenicity or human toxicity and fermentative production of DNA or RNA. General compositions.
B05	13	13	Pharmaceuticals: Other organics - aromatics, aliphatic, organo-metallics, compounds whose substituents vary such that they would be classified in several of B01 - B05.
B07	37	26	Pharmaceuticals: General - tablets, dispensers, catheters (excluding drainage and angioplasty), encapsulation etc, but not systems for administration of blood or saline or IV feeding etc.
C03	0	34	Agricultural Chemicals: Other organic compounds, inorganic compounds and multi-component mixtures. Polymers and proteins.
C06	154	248	Agricultural Chemicals: Biotechnology - including plant genetics and veterinary vaccines.

D16	517	640	Food, Detergents, Water Treatment and Biotechnology: Fermentation industry - including fermentation equipment, brewing, yeast production, production of pharmaceuticals and other chemicals by fermentation, microbiology, production of vaccines and antibodies, cell and tissue culture and genetic engineering.
P34	10	0	General Engineering: HEALTH, AMUSEMENT: Sterilising, syringes, electrotherapy
S03	15	29	Instrumentation, Measuring and Testing: Scientific Instrumentation (G01J, K, N, T-W) Photometry, calorimetry. Thermometers. Meteorology, geophysics, measurement of nuclear or X-radiation. Investigating chemical or physical properties.
T01	10	0	Computing and Control: Digital Computers (G06C-F) Electronic data processors, interfaces and programme control. Mechanical digital computers.

Top Derwent Manual Codes v. Patent Document Count

The Derwent Manual Code represents a further level of classification that provides more specificity to the DWPI Codes.[145] Again, patent families often had multiple different Manual Code associated with them, and each code was taken for analysis. Among vaccine documents, 24 different Manual Codes each represented more than 50 INPADOC families, as shown in Figure 22. The top three codes were D05-H07, which concerns production of vaccines, B14-S11D3, which concerns genetically engineered vaccines, and B14-A02B2, which concerns orthomyxoviruses. The definition of top Manual Codes are given in Table XII.

Once again, the supporting technologies category was covered by more Manual Codes than the vaccine category was. Thirty-six different Manual Codes were applied to 50 or more INPADOC families, as shown in Figure 23. D05-H07 and B14-A02B2 were again among the top three codes, but the second most prominent code for the supporting technologies was B14-S11A, which concerns antiviral vaccines. Additional Manual Codes appearing in association with supporting technology documents was B04-F0100E, D05-H08, and D05-H14, which all concern transformed cell lines such as those used to produce recombinant viruses or subunits, and B14-S12, which concerns veterinary pharmaceuticals such as vaccines. In general the supporting technologies documents had more Manual Codes in the C04 and C14 classes, which cover veterinary uses of pharmaceuticals. Thus, the differences in the Manual Codes represent the different subcategories under the vaccine and supporting technology headings.

[145] http://www.stn-international.de/dwpi_manual_codes/A.html.

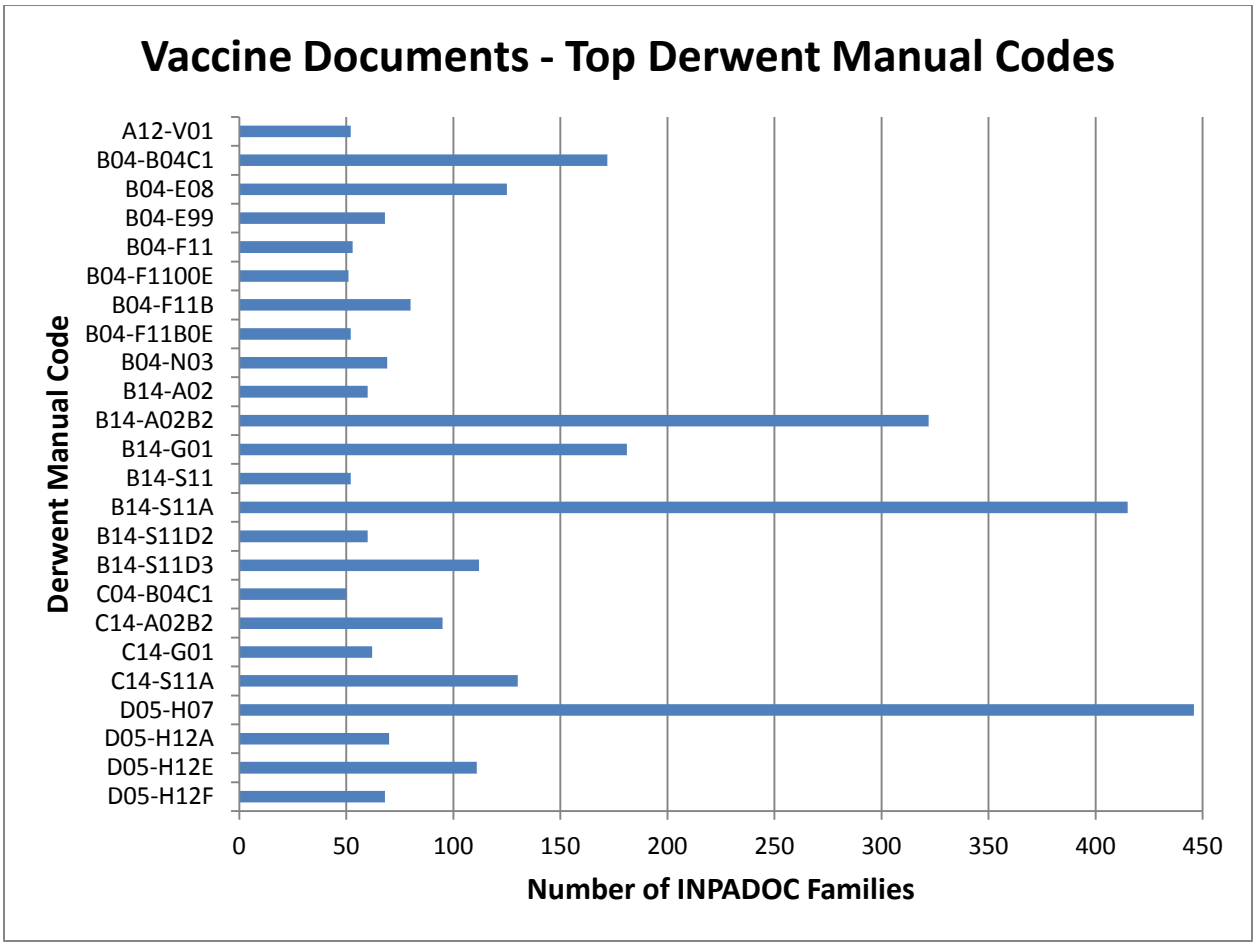


Figure 23. Top Derwent Manual Codes representing at least 50 vaccine documents.

Table XII. Definitions of Top Derwent Manual Codes for Vaccine Documents.

DWPI Manual Codes	# Docs.	Code Description
D05-H12F	68	Food, Detergents, Water Treatment and Biotechnology: RECOMBINANT VIRUSES [EXCLUDING VIRAL VECTORS]
D05-H12E	111	Food, Detergents, Water Treatment and Biotechnology: VECTORS
D05-H12A	70	Food, Detergents, Water Treatment and Biotechnology: WILD-TYPE CODING SEQUENCES
D05-H07	446	Food, Detergents, Water Treatment and Biotechnology: PRODUCTION OF VACCINES, ANTIGENS
C14-S11A	130	Agricultural Chemicals: ANTIVIRAL VACCINE
C14-G01	62	Agricultural Chemicals: IMMUNOSTIMULANT GENERAL AND OTHER
C14-A02B2	95	Agricultural Chemicals: (PARA/ORTHO)MYXOVIRUS
C04-B04C1	50	Agricultural Chemicals: MICROBIAL ANTIGEN
B14-S11D3	112	Pharmaceuticals: SYNTHETIC/GENETICALLY ENGINEERED VACCINE
B14-S11D2	60	Pharmaceuticals: LIVE-ATTENUATED (WEAKENED) VACCINE

B14-S11A	415	Pharmaceuticals: ANTIVIRAL VACCINE
B14-S11	52	Pharmaceuticals: VACCINE [GENERAL]
B14-G01	181	Pharmaceuticals: IMMUNOSTIMULANT GENERAL AND OTHER
B14-A02B2	322	Pharmaceuticals: (PARA/ORTHO)MYXOVIRUS
B14-A02	60	Pharmaceuticals: ANTIVIRAL [GENERAL]
B04-N03	69	Pharmaceuticals: MICROORGANISM PROTEIN/POLYPEPTIDE (NO SEQUENCE)
B04-F11B0E	52	Pharmaceuticals: RNA VIRUS GENERAL (GENETICALLY ENGINEERED)
B04-F11B	80	Pharmaceuticals: RNA VIRUS GENERAL
B04-F1100E	51	Pharmaceuticals: VIRUSES (GENETICALLY ENGINEERED)
B04-F11	53	Pharmaceuticals: VIRUSES
B04-E99	68	Pharmaceuticals: PATENT WITH GENESEQ RECORD
B04-E08	125	Pharmaceuticals: VECTORS, PLASMIDS, COSMIDS, TRANSPOSONS
B04-B04C1	172	Pharmaceuticals: MICROBIAL ANTIGEN
A12-V01	52	Polymers and Plastics: MEDICINES, PHARMACEUTICALS

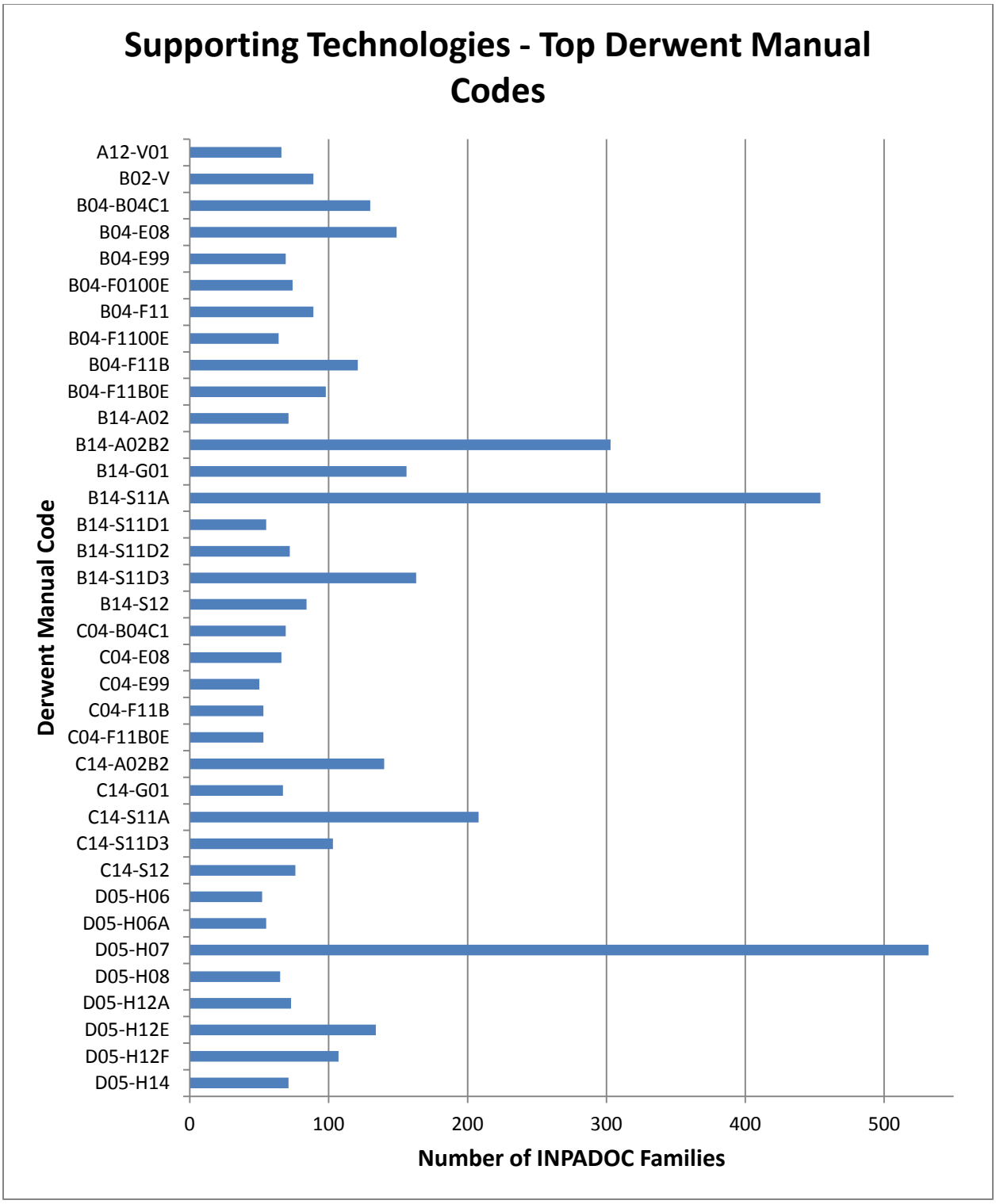


Figure 24. Top Derwent Manual Codes representing at least 50 supporting technology documents.

Table XIII. Definitions of Top Derwent Manual Codes for Supporting Technology Documents.

DWPI Manual Codes	# Docs	Code Description
D05-H14	71	Food, Detergents, Water Treatment and Biotechnology: RECOMBINANT CELLS
D05-H12F	107	Food, Detergents, Water Treatment and Biotechnology: RECOMBINANT VIRUSES [EXCLUDING VIRAL VECTORS]
D05-H12E	134	Food, Detergents, Water Treatment and Biotechnology: VECTORS
D05-H12A	73	Food, Detergents, Water Treatment and Biotechnology: WILD-TYPE CODING SEQUENCES
D05-H08	65	Food, Detergents, Water Treatment and Biotechnology: CELL OR TISSUE CULTURE
D05-H07	532	Food, Detergents, Water Treatment and Biotechnology: PRODUCTION OF VACCINES, ANTIGENS
D05-H06A	55	Food, Detergents, Water Treatment and Biotechnology: NEWLY DISCOVERED, TESTING OF, ISOLATION OF, IDENTIFICATION OF AND DETECTION OF VIRUSES
D05-H06	52	Food, Detergents, Water Treatment and Biotechnology: NEWLY DISCOVERED, TESTING OF, ISOLATION OF, IDENTIFICATION OF AND DETECTION OF VIRUSES AND OTHER
C14-S12	76	Agricultural Chemicals: VETERINARY
C14-S11D3	103	Agricultural Chemicals: SYNTHETIC/GENETICALLY ENGINEERED VACCINE
C14-S11A	208	Agricultural Chemicals: ANTIVIRAL VACCINE
C14-G01	67	Agricultural Chemicals: IMMUNOSTIMULANT GENERAL AND OTHER
C14-A02B2	140	Agricultural Chemicals: (PARA/ORTHO)MYXOVIRUS
C04-F11B0E	53	Agricultural Chemicals: RNA VIRUS GENERAL (GENETICALLY ENGINEERED)
C04-F11B	53	Agricultural Chemicals: RNA VIRUS GENERAL
C04-E99	50	Agricultural Chemicals: PATENT WITH GENESEQ RECORD
C04-E08	66	Agricultural Chemicals: VECTORS, PLASMIDS, COSMIDS, TRANSPOSONS
C04-B04C1	69	Agricultural Chemicals: MICROBIAL ANTIGEN
B14-S12	84	Pharmaceuticals: VETERINARY
B14-S11D3	163	Pharmaceuticals: SYNTHETIC/GENETICALLY ENGINEERED VACCINE
B14-S11D2	72	Pharmaceuticals: LIVE-ATTENUATED (WEAKENED) VACCINE
B14-S11D1	55	Pharmaceuticals: WHOLE-KILLED (INACTIVE) VACCINE
B14-S11A	454	Pharmaceuticals: ANTIVIRAL VACCINE
B14-G01	156	Pharmaceuticals: IMMUNOSTIMULANT GENERAL AND OTHER
B14-A02B2	303	Pharmaceuticals: (PARA/ORTHO)MYXOVIRUS
B14-A02	71	Pharmaceuticals: ANTIVIRAL [GENERAL]
B04-F11B0E	98	Pharmaceuticals: RNA VIRUS GENERAL (GENETICALLY ENGINEERED)

B04-F11B	121	Pharmaceuticals: RNA VIRUS GENERAL
B04-F1100E	64	Pharmaceuticals: VIRUSES (GENETICALLY ENGINEERED)
B04-F11	89	Pharmaceuticals: VIRUSES
B04-F0100E	74	Pharmaceuticals: CELLS, MICROORGANISMS, TRANSFORMANTS, HOSTS, CELL LINES, TISSUE [GENERAL] (GENETICALLY ENGINEERED)
B04-E99	69	Pharmaceuticals: PATENT WITH GENESEQ RECORD
B04-E08	149	Pharmaceuticals: VECTORS, PLASMIDS, COSMIDS, TRANSPOSONS
B04-B04C1	130	Pharmaceuticals: MICROBIAL ANTIGEN
B02-V	89	Pharmaceuticals: VACCINES AND ANTIBIOTICS BEGINNING WITH THE LETTER "V", GENERAL VACCINES
A12-V01	66	Polymers and Plastics: MEDICINES, PHARMACEUTICALS

Conclusions

A search of the patent literature for publications containing keywords related to the influenza virus returned approximately 33,500 total documents representing almost 3,800 patent families. However, only about one-half of those patent documents will actually be specific for prophylactic influenza A vaccines or for technologies that are used in the manufacture of vaccines. Of those relevant documents, approximately 10-15% are specifically related to pandemic influenza, although the remainder could probably be applied to pandemic strains. Thus, influenza vaccine technologies are disclosed in a fairly small set of patent documents, especially considering that influenza virus infections have been a global threat to human health for at least century.

However, filing of applications related to influenza have been steadily increasing in the last decade, so there are many new technological advances that have yet to be fully tested in the clinic for effectiveness against influenza. Much of the increase in filings is in response to recent influenza outbreaks: the H5N1 (bird flu) epidemic that began in 1997 and continued for a decade, and the H1N1 (swine flu) pandemic that was first diagnosed in 2009.

Influenza virus technologies appear to originate from a small set of countries, mostly the United States, Great Britain, France, China, Japan, Korea, and Russia. Protection for influenza vaccine intellectual property has been sought worldwide. However, except for Brazil coverage in South America is quite minimal, and except for South Africa protection for these technologies is sparse in Africa.

Top assignees for the relevant families were mostly large pharmaceutical companies, with the majority of patent families coming from Novartis, followed by GlaxoSmithKline, Pfizer, U.S. Merck (Merck, Sharpe, & Dohme), Sanofi, and AstraZeneca. Governmental and nonprofit institutes in China, Japan, Russia, South Korea and the United States also are contributing heavily to influenza vaccine research.

Progress is being made towards the development of an effective vaccine against pandemic influenza strains, but much work remains to be done, especially testing these novel vaccines in the clinic. Additionally, this much-needed technology is not adequately distributed to the least-developed nations. Once a new pandemic strain arises, infections could rapidly spread over an extensive area, so more thorough global preparedness is needed to prevent the health crisis this pathogen still poses.

Appendix Materials

APPENDIX A: Master Coding Spreadsheet (electronic version only).

This Excel file describes coding of representative INPADOC family members, with notes on the basis of the coding decisions. The first sheet is organized by publication number, and the second sheet shows the publication numbers which fell in each category. The third sheet shows the consolidated major categories.

APPENDIX B: Platform Technologies Documents: Full Records (electronic version only).

This Excel file has detailed information of each relevant patent family in this category. The full records, containing all available information extracted from Thomson Innovation, are given for each representative family member. Documents are organized alphabetically by publication number.

APPENDIX C: Vaccine Documents: Full Records (electronic version only).

This Excel file has detailed information of each relevant patent family in this category. The full records, containing all available information extracted from Thomson Innovation, are given for each representative family member. The first sheet has documents organized alphabetically by publication number. Subsequent sheets show the data manipulations used to determine priority countries, publications by year, major classifications, and family size. Analyses of assignees, inventors, and top multi-jurisdictional filers are shown in separate files, as given below.

APPENDIX D: Supporting Technologies Documents: Full Records (electronic version only).

This Excel file has detailed information of each relevant patent family in this category. The full records, containing all available information extracted from Thomson Innovation, are given for each representative family member. The first sheet has documents organized alphabetically by publication number. Subsequent sheets show the data manipulations used to determine priority countries, publications by year, and major classifications. Analyses of assignees and inventors are shown in separate files, as given below.

APPENDIX E: Top Multi-Jurisdictional Filings Spreadsheet (electronic version only).

This Excel file has representative family members ranked according the size (number of publications) of the INPADOC family each document represents. The top 21 largest families are then analyzed based on the total number of jurisdictions in which each family has been filed. Data is assembled from INPADOC, DWPI and TotalPatent family data. Note that this analysis was performed for vaccine documents only.

APPENDIX F: Assignees Analysis Spreadsheet (electronic version only).

Assignee data for each representative family member was manually corrected to reflect changing company names or the acquisition of an assignee by another company. This Excel file details assignee data first by publication number, and then assignees are shown by total number of families believed to be owned by that assignee. Both vaccines and supporting technology documents were pooled together to generate an assignee list covering all highly relevant documents. The website for each assignee is also given, if possible.

Appendix G: Alternative Assignee Names and Subsidiaries Spreadsheet (electronic version only).

The names of assignee companies can often change, particularly following mergers and acquisitions. This data has been manually assembled as much as possible, and this Excel file details the alternative names and subsidiaries under which a given assignee may appear.

Appendix H: Vaccine Inventors Spreadsheet (electronic version only).

This Excel file separates each representative family member by the individual inventors listed in the record. The top inventors who are listed on the most patent publications are then given. Note that inventor names are often misspelled, have variable middle names, or have first and last names switched. For those reasons, the accuracy of this data cannot be entirely assured.

Appendix I: Supporting Technology Inventors Spreadsheet (electronic version only).

This Excel file separates each representative family member by the individual inventors listed in the record. The top inventors who are listed on the most patent publications are then given. Note that inventor names are often misspelled, have variable middle names, or have first and last names switched. For those reasons, the accuracy of this data cannot be entirely assured.

Appendix J: PDF Files of Representative Patent Documents (electronic version only).

This folder contains the pdf files for each representative family member, if available. Subfolders are given for each of the Vaccine and Supporting Technologies categories, but not Platforms. Note that in a few instances a pdf file of the representative family member was not available. Thus these folders do not contain the complete number of representative documents.

Appendix K: PDF Files of Selected Non-Patent Literature (electronic version only).

This folder contains pdf files for selected non-patent literature relevant to prophylactic influenza A vaccines. An extensive search of NPL was not performed; rather the documents included in this folder are mostly review articles which reveal the general state of the art, summarize available technologies, or discuss strategic approaches to immunization. Given the rate at which influenza vaccine technologies have been changed, reviews were only selected from those published within the last five years in order to present only the most up-to-date articles.

Appendix L: PDF Files of This Report (electronic version only).

This folder contains separate pdf files of this report and the cover to the report. The ITTI Clinic wishes for this report to be as widely disseminated as possible, so that all interested parties may have access to the information presented herein. However, anyone is free to base a subsequent report on our work as long as proper attribution is given to ITTI.

Appendix M: Keywords Used in Searching.

The following represents the keywords used by the team members in patent database searching. Note that each team member used different combinations of these terms, and only a subset of terms was used for any particular search.

- Influenza
  - Pandemic
    - Swine
    - Avian
    - Bird
  - H5N1
  - H1N1
  - H{d}N{d} (TI)
  - Orthomyxovir* (TI) Orthomyxovir! (TP)
  - HPAI (Highly Pathogenic Avian Influenza)
  - Hemagglutinin (Haemagglutinin)
  - Neuraminidase
  - Epidemic
  - !Virulen! *Virulen*
  - highly pathogenic
  - Pathogen! Pathogen*
  - (negative strand RNA virus)

- Vaccine
  - Immun! (TP) Immun* (TI)
  - Immunologic! Immunologic*
  - Immunostimul! or immuno-stimul!
  - Immunomodul! or immuno-modul!
  - Immunologentic
  - Immunogen! Immunogen*
  - Immuniz! Immuniz
  - Vaccin! (TP) Vaccin* (TI)
  - Virotherap! Virotherap*
  - Prophyl! Prophyl*
  - Antigen! Antigen*
    - Epitope! Epitope*
    - Determinant
  - Antiinfective or anti-infective (sp?)
  - Antiviral or anti-viral or anti viral
  - Viricide or Virucide
  - Prevent! Prevent*
  - Phage

Appendix N: Notes on Patent Families.

If there are several applications or publications for an individual invention (in other countries) claiming the same priority or priorities and originating from the same inventors, those documents constitute a "patent family." All of the family members are related to one another by common priority publications with associated priority dates. INPADOC families are organized solely on priority data, whereas DWPI families focus on the inventions such that divisional applications of a single priority document are considered to be in different patent families. Further, Lexis TotalPatent reports "extended families" which are similar to INPADOC families but include more jurisdictions.

The concept of the patent family first emerged through the Paris Convention on the Protection of Intellectual Property in 1883, while automated systems enabling patent family searching became available through the establishment of the IIB in The Hague in 1947and INPADOC in Vienna in 1972. Since then, patent searching has evolved due to exponential improvements in computing and communication technology.

The term patent family can be defined in a number of ways depending on the relationship between a patent document and its priority or priorities within the meaning of the Paris Convention. The differences only become obvious when the structure of a patent application is complex, i.e. when applications are filed in several countries. Such applications may cite various earlier applications as priorities, or the different patent offices involved in the grant process may accept or refuse different patent claims. This results in patents which have different scopes of protection.

An important point when using any database to retrieve information on patent families is that there is never any guarantee that you will find all the corresponding patent documents that exist. Database producers do what they can to ensure completeness, but they can never guarantee it."[146]

<u>The "Extended" (INPADOC) Patent Family</u>

"The biobibliographic and legal status databases form the basis of the EPO's raw data resources (INPADOC). In February 2008 the bibliographic data included about 60 million bibliographic data sets from almost 80 different countries. The legal status database contains a collection of more than 50 million legal events from 48 countries.

From the beginning, the concept was to cover as many countries and as many publication levels as possible. One of the strongest motives for the integration of INPADOC into the EPO was the

[146] EUROPEAN PATENT OFFICE, *Patent Families* (Feb. 29, 2008), http://www.epo.org/patents/patent-information/about/families.html.

wish to combine the particular strengths of INPADOC with the EPO's existing in-house bibliographic database, "DOC-DB."

Following integration of the two databases in the 1990s, the raw data behind both databases is now the same. And since esp@cenet draws on the same pool of data as raw data resources (INPADOC) and DOC-DB, it contains the same documentation.

However, the philosophy of the "extended" (INPADOC) patent family is quite different, and so are the results of family searches. Unlike the "also published as" feature in esp@cenet, which only shows "equivalents," i.e. almost identical documents, an INPADOC family search should retrieve all documents relating in any way to the root document.

Features of INPADOC

When using INPADOC via one of the commercial database host services, it bears all the esp@cenet features, plus the following:

- Standardization of applicant and inventor names
- References to abstracts from Chemical Abstracts and Thomson Scientific Abstracts are made within the patent family
- By including the legal status database additional information is available and additional family links can be established
- National application numbers, international application numbers and domestic relations are included in the family search

For both of the EPO's raw data resources (INPADOC) and esp@cenet, even where no priority has been claimed by the patent application, artificial or "intellectual" links are built in systematic way for the complete PCT minimum documentation. The same is done for older documents (pre-1968) for which the priority information is not complete.

Definition of the "extended" (INPADOC) patent family

All the documents directly or indirectly linked via a priority document belong to one patent family. In the case shown below, documents D1 to D5 belong to the same patent family, P1.

FAMILY P1

Document D1	Priority P1		
Document D2	Priority P1	Priority P2	
Document D3	Priority P1	Priority P2	
Document D4		Priority P2	Priority P3
Document D5			Priority P5

As mentioned above, national patent application numbers, international application numbers and domestic relations are included in the family search.

In the “extended” (INPADOC) patent family, it does not matter where a search is started. It can be an application number, a priority application number or a publication number.
If the search starts with a publication number, all application numbers, domestic application numbers, priority numbers and international application numbers are used to retrieve additional documents. For all documents found in this step, step one is repeated. This iteration process ends only when no more new documents can be found.

Raw data resources (INPADOC) also use some additional sophisticated rules for certain countries, for example, if publication numbers are used instead of priority numbers in the original documents. This happened rather frequently for older documents, where the priority claims were not treated as carefully as they are now. The inclusion of legal status information in the patent search also sometimes retrieves additional links, e.g. for divisional applications, continuations, continuations in part or national publications of first filings of PCT (international) applications, where the priority links are often missing.

Limitations of the family search in raw data resources (INPADOC) have to rely on the correctness of the data supplied by the co-operating patent offices and the extent to which it is up to date. In particular, delays in the delivery of bibliographic data can vary significantly depending on the country concerned and the time period covered. Before relying on the completeness of a patent family, users should check where there are gaps or delays in certain areas. This kind of information can be found in the PFS and PRS statistics on the internet, which are updated weekly and contain indications of missing or delayed document series. See raw data resources (INPADOC) useful tables and statistics. To be absolutely sure about the actual status of a patent, users are recommended to contact the appropriate patent issuing authority direct. Particular care has to be taken in the case of European patents which have entered into the national phase. The completeness and accuracy of data can vary significantly from country to country. A good overview of the volume and kind of "post-grant" information available in raw data resources (INPADOC) can be found in the raw data resources (INPADOC) FAQ. For most of the EPO member states, information about the validation, lapse, etc., of European patents is

given as part of the legal status information, and as mentioned before is less consistent due to the different quality of data available. Starting from week 50/2007, additional post-grant information is taken from the fee administration system and included in the legal status part of the database.

Thomson Scientific WPI Patent Family (DWPI)

"Patent Families in the Thomson Scientific World Patents Index (WPI) draw together patents covering the same invention. Their relationship is defined by the priority or application details claimed by each document. Thus, in its simplest form, a new document (D1) claiming a unique priority (P1) will be assigned to be the basis of its own, new patent family in Thomson Scientific WPI.

Subsequently, if a second document (D2) also claiming priority P1 is received by Thomson Scientific this will be added (as an ―equivalent‖) to the patent family already containing document D1. Other documents claiming priority P1 will also be added to this family as ―equivalents as they are included in the database. Thus, a patent family may contain anything from a single document to 10 or more. Each patent family represents a single record in the Thomson Scientific WPI database.

The basic document is the first member of a patent family that appears in Thomson Scientific WPI, so it may not necessarily be the first one published for that invention. Differences in the speed that patenting authorities supply data to Thomson Scientific and in the processing time for documents from different countries may affect which document appears in Thomson Scientific WPI first and becomes basic.

Patents often claim more than a single priority and these must match before any equivalent is added to a family. This means that if a basic document (D3) claims priorities P2, P3 & P4, a subsequent document (D4) claiming priorities P2 & P3 will be added to the family as an equivalent, whereas patent D5 which claims priorities P2, P3 and a unique priority (P5) will form the basis of a new, but related patent family. In cases such as this, the accession number of any related family is included in the cross-reference field of each relevant Thomson Scientific WPI record.

Divisions and continuation patents maintain the same status as the original specification. This means that if GB1 is a basic, and GB2 is divisional to GB1, then GB2 will also be a basic (in its own family). However, if GB1 is equivalent to another document already in the Thomson Scientific WPI database, then GB2 will also join this family as an equivalent. It should be noted that family relationships will be defined by the order in which patents appear in Thomson Scientific WPI.

Thomson Scientific also puts a lot of resources into including patents in families even when no foreign priority is claimed, e.g. when an application has been made beyond the 12 months defined by the Paris Convention. Thomson Scientific identifies these "non-convention" equivalents by the presence of foreign nationals and addresses in the Inventor field in the absence of priority data other than the local filing details. Equivalency is determined through a time-consuming manual check of inventors, subject matter, etc.

In this way Thomson Scientific attempts to make patent families in Thomson Scientific PI as comprehensive as possible. However, because of the incidence of multiple priorities, and patent divisions and continuations (especially continuing applications in US documents), it is important to retrieve all related families through their common priorities in order to have a comprehensive overview of patent family relationships."[147]

APPENDIX O: Notes on Major Classifications.

US Classifications[148]

The U.S. Patent Classification System is a categorization of all U.S. patent and other technical documents by common subject matter. Each subject matter division includes a class and a subclass. The Manual of Classification is an ordered listing of all the valid classifications. Classes and subclasses have titles providing a general description of their contents, and definitions providing a more specific description. A definition may contain an explanation of the class or subclass, a glossary, search notes, references to subclasses within a class, and references to other classes and subclasses. The U.S. system contains about 450 classes and about 150,000 subclasses. The classification code is express with 2 numbers separated by a forward slash, for example, 435/134. The first number, 435, represents the class of the invention. The number following the slash, 134, is the subclass of the invention within the preceding class. Patents will always have both a class and a subclass. More explanation and definitions of U.S. patent classifications can be found at, http://www.uspto.gov/web/patents/classification/.

[147] *Id*.
[148] http://www.uspto.gov/web/patents/classification/.

International Patent Classification System[149]

- The World Intellectual Property Organization (WIPO) administers the International Patent Classification (IPC) system. IPCs are organized hierarchically and divide technology into eight sections (A through G) with approximately 70,000 subdivisions.
- An IPC is typically expressed as, for example, C12N 15/82, but may also appear as C12N001582.
    - The first letter, C, specifies a Section.
    - The number following the Section indicator, 12, specifies a Class.
    - The letter N specifies a Subclass.
    - The number 15 specifies a Main Group.
    - The number following the slash, 82, specifies a Subgroup.
- WIPO publishes the authentic IPCs versions in English and French languages. Chinese, Croatian, Czech, Dutch German, Hungarian, Japanese, Korean, Polish, Romanian, Russian, Serbian, and Spanish versions are also available.
- More information is available at the WIPO website, http://www.wipo.int/classifications/ipc/en/.

Description of Derwent Patent Classifications[150]

- The Derwent World Patent Index (DWPI) classification system categorizes patent documents using a simple classification system for all technologies; consistently applied to all patents by Thomson Scientific subject experts, enabling effective and precise searching in a particular area of technology.
- International Patent Classification (IPC) is an internationally recognized classification system controlled by the World Intellectual Property Organization (WIPO) and assigned to patent documents by various patent offices.
- Where possible Thomson indicated next to the class the equivalent IPC in an abbreviated form (e.g., A47, F23-5). However, this should be used only as a guide since there are areas where the DWPI classes are assigned intellectually by Thomson's subject experts, and no strict correspondence is claimed.

Appendix P: Authors' Resumes

Resumes for each of the four team members follow.

[149] WIPO, http://www.wipo.int/classifications/ipc/en/.
[150] *Derwent World Patent Index*, THOMSON CORPORATION, http://science.thomsonreuters.com/m/pdfs/mgr/derwentclass.pdf.

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Earned Patent Literature Searching Certificate (trained in patent database searching)
Relevant coursework includes: Patent Law, Patent Claim Drafting, Technology Licensing, Copyright Law, International Intellectual Property, Pharmaceutical Patent Law, Global IP Management, Patent Reexamination & Post-Grant Procedures, and Advanced Patent Law Seminar with retired Federal Circuit Judge Arthur Gajarsa
University of Kentucky, **Ph.D.**, Immunology, 1995, 3.9 GPA
Pennsylvania State University, **BS** with High Honors, Molecular & Cell Biology, 1987, 3.8 GPA

PROFESSIONAL EXPERIENCE

OFFICE of INNOVATION DEVELOPMENT & COMMERCIALIZATION, UNIVERSITY at ALBANY **January – August 2012**
In association with Heslin Rothenberg Farley & Mesiti, P.C.
- **Extern/Intern**

Analyzed invention disclosures: interviewed inventors, prepared patentability reports
Drafted response to International Search Report and assisted with USPTO Office Actions
Prepared Patent Landscape Report and US Provisional Patent Application

INTERNATIONAL TECHNOLOGY TRANSFER CLINIC, UNH SCHOOL OF LAW
Fall 2012 (Project Director): Preparing patent landscape report regarding pandemic influenza vaccines for the World Intellectual Property Organization;
Summer 2011: Refined and modified a protocol designed to assist developing nations in identifying patents encompassing drugs on the Essential Medicines List. Reported to WIPO.

Professional Tutor **2009 - 2011**
Provided standardized test preparation; Teaching subjects at high school & college level

CENTOCOR, A Johnson & Johnson Pharmaceuticals Company **2005 – 2008**
- **Research Scientist:**

Conducted biologics drug development in immunology and pulmonary biology
Provided expert scientific analysis of proposals for licensing and partnering opportunities

YALE UNIVERSITY SCHOOL OF MEDICINE **1995 – 2005**
- **Postdoc & Associate Research Scientist in Immunobiology & Orthopaedics**

PROFESSIONAL ACTIVITIES

American Intellectual Property Law Association, 2010 – present
Association of University Technology Managers (AUTM), 2011 - present
Licensing Executive Society, 2010 – present
President, LES student chapter at UNH School of Law
Patent Information Users Group, 2009 - present

COMMUNITY INVOLVEMENT & VOLUNTEER ACTIVITIES

Planning Commission, Caln Township, PA, 2008 – 2011
Inspector of Elections, Caln Township Precinct 1, Thorndale, PA, 2006, 2008, 2009
Justice of the Peace, State of Connecticut, 2005
Member of the Board of Education, City of Derby, CT, 2005 – 2006
President of the Board of Directors of Lincoln Senior Housing, Inc., 2004 – 2006
Founder of a 501(c)(3) non-profit organization. Personally managed a $3.8 million construction project that provided subsidized housing for senior citizens.

PUBLICATIONS

- M.C. Horowitz, A.L.M. Bothwell, D.G.T. Hesslein, **D.L. Pflugh**, and D.G. Schatz. 2005. B cells and osteoclast and osteoblast development. *Immunological Reviews 208:141*.
- M.C. Horowitz, Y. Xi, **D.L. Pflugh**, D.G.T. Hesslein, D.G. Schatz, J.A. Lorenzo, and A.L.M. Bothwell. 2004. Early onset osteopenia with increased osteoclast progenitors in Pax5 deficient mice. *Journal of Immunology 173:6583*.
- V. Giambra, S. Volpi, A.V. Emelyanov, **D. Pflugh**, A. Bothwell, P. Norio, Y. Fan, Z. Ju, A.I. Skoultchi, R.R. Hardy, D. Frezza, and B.K. Birshtein. 2008. Pax5 and linker histone H1 coordinate DNA methylation and histone modifications in the 3' regulatory region of the immunoglobulin heavy chain locus. *Mol. Cell. Biol. 28:6123.*
- K. Johnson, **D.L. Pflugh**, D. Yu, D.G.T. Hesslein, K.-I. Lin, A.L.M. Bothwell, A. Thomas-Tikhonenko, D.G. Schatz, and K. Calame. 2004. B-cell specific loss of histone 3 lysine 9 methylation in the V_H locus depends on Pax5. *Nature Immunology 5:853*.
- M.J. Fernandez-Cabezudo, C. Vijayasarathy, **D.L. Pflugh**, A.L.M. Bothwell, and B.K. al-Ramadi. 2004. Evidence for a dual pathway of activation in CD43-stimulated Th2 cells: Differential requirements for the lck tyrosine kinase. *International Immunology 16:1215*.
- D.G.T. Hesslein, **D.L. Pflugh**, D. Chowdhury, A.L.M. Bothwell, R. Sen, and D.G. Schatz. 2003. *Pax5* is required for recombination of transcribed, acetylated, 5' IgH V gene segments. *Genes & Dev. 17:37.*
- **D.L. Pflugh**, S.E. Maher, and A.L.M. Bothwell. 2002. Ly-6 Superfamily members Ly-6A/E, Ly-6C, and Ly-6I recognize two potential ligands expressed by B lymphocytes. *Journal of Immunology 169: 5130.*
- **D.L. Pflugh**, S.E. Maher, and A.L.M. Bothwell. 2000. Ly-6I, a new member of the murine Ly-6 superfamily with a distinct pattern of expression. *Journal of Immunology 165: 313.*
- S.E. Maher, **D.L. Pflugh**, N.J. Larsen, M.F. Rothschild, and A.L.M. Bothwell. 1998. Structure/function characterization of porcine CD59. *Transplantation 66: 1094.*
- J. S.Bryson, CD. Jennings, D.M. Lowery, S.L. Carlson, **D.L. Pflugh**, B.E. Caywood, and A.M. Kaplan. 1999. Rejection of an MHC class II negative tumor following induction of murine syngeneic graft-versus-host disease. *Bone Marrow Transplantation 23: 363.*
- J.S. Bryson, H. Lake-Bullock, **D.L. Pflugh**, C.D. Jennings, P.M. Stuart, B.E. Caywood, and A.M. Kaplan. 1995. *In vivo* reactivity of T cell clones isolated from mice with syngeneic graft-versus-host disease. *Transplantation 60: 171.*

JEREMY B. BARTON

USPTO Reg. 67,963
18A Charles Street ▪ Concord, NH 03301 ▪ jeremybarton19@gmail.com

BAR ADMISSIONS

United States Patent and Trademark Office (Reg. 67,963)

EDUCATION

University of New Hampshire School of Law (formerly Franklin Pierce Law Center), Concord, NH
Juris Doctor Candidate, May 2013
Top 10% of Class, Dean's Merit Scholar
Senior Editor, *IDEA: The Intellectual Property Law Review*
Faculty Assistant for Prof. John Orcutt's Contracts course (Fall 2011)

University of Utah, Salt Lake City, UT
Bachelor of Science, Biomedical Engineering, May 2007
Emphasis in Mechanical Engineering
Phi Theta Kappa Honor Society and Motor Board Honor Society

LEGAL EXPERIENCE

May to July 2012 **Oblon, Spivak, McClelland, Maier, and Neustadt, LLP**
Summer Associate:
Prepare responses to Office Actions, draft internal legal memos, and conduct legal research concerning pending litigation.

Jan. to May 2012 **Chief Judge Randall R. Rader, U.S. Court of Appeals for the Fed. Cir.**, Washington, DC
Judicial Clerk Extern
Researched and drafted bench memoranda, presented cases to Judge Rader at clerk meetings, and prepared preliminary opinion drafts.

June to Aug. 2011 **U.S. Patent and Trademark Office**, Alexandria, VA
Intern for the PCT Legal Office
Received patent examiner training. Worked on a major research project comparing the treatment of corresponding international patent applications by an International Searching Authority with the treatment in the national phase by the USPTO.

TECHNICAL EXPERIENCE

Aug. 2007 to July 2010 **ARUP Laboratories**, Salt Lake City, UT
Technologist II, ASCP (C)
Performed and analyzed laboratory testing in biochemical genetics—e.g., cell cultures, enzymatic reactions, electrophoresis, ion exchange chromatography, mass spectrometry, and spectrophotometer and solid-phase extraction.

June 2006 to **University of Utah—Keck Center for Tissue Engineering**, Salt Lake City, UT

Apr. 2007 *Research Assistant*
Studied the expression of cytokines in astrocytes cells under 2-D vibration. Presented research in a poster session and presented in the senior project symposium.

June to Aug. **Pacific Northwest National Laboratory**, Richland, WA
2004 *CCI Fellowship*
Investigated "ridge-" like structures using Rutherford backscattering spectrometry, scanning electron microscopy, energy dispersive x-ray emission, atomic force microscopy, and high-resolution transmission electron microscopy. Abstract of my research was published in the U.S. Dept. of Energy Journal of Undergraduate Research.

LEGAL PUBLICATION

Chico Gholz, Lisa Mandrusiak & Jeremy Barton, *Spoliation in Interferences*, IPToday Oct. 2012

VOLUNTEER WORK

Assistant Scoutmaster (Apr. 2008 to July 2010)
Missionary for the LDS Church in Santa Maria, Brazil (2000 to 2002)

LANGUAGES

Fluent in Portuguese

JEFF JANOVETZ
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EDUCATION

J.D. 2013 (expected). Franklin Pierce Law Center (currently The University of New Hampshire School of Law), Concord, NH

Ph.D. 2002. Division of Biological Sciences, University of Chicago, Chicago, IL

M.S. 1996. School of Biological Sciences, Washington State University, Pullman, WA

B.S. 1992. Department of Biology, University of Illinois, Champaign, IL, *cum laude*

LEGAL WORK EXPERIENCE

Toohey Law Group, LLC., Manchester, NH
Student Associate working exclusively for DEKA Research and Development, 2012 - current.

International Technology Transfer Clinic, Concord, NH
Project: Developing a patent landscape for pandemic influenza vaccines to assist the World Health Organization in the event of an outbreak.

Oliff and Berridge, PLC., Alexandria, VA
Intellectual property externship, spring semester 2013.

ACADEMIC WORK EXPERIENCE

Grand Valley State University, Allendale, MI
Assistant Professor, Biomedical Sciences Department, 2009 – 2010.

Centre College, Danville, KY
Assistant Professor, Department of Biology, 2006 – 2009.

Sweet Briar College, Sweet Briar, VA
Assistant Professor, Department of Biology, 2002 – 2006.

Each position involved designing and teaching courses as the sole instructor. Subjects taught include human anatomy and physiology, comparative anatomy, comparative physiology, genetics, general biology, and scanning electron microscopy. I established a research lab, conducted research as the principal investigator, and supervised student research. I wrote and received external grants, and published primary research in peer-reviewed journals. I directed the Scanning Electron Microscopy Center and administered the Center's budget.

SELECTED PUBLICATIONS and MEETING PRESENTATIONS

2005 Janovetz, J. *Functional Morphology of Feeding in the Scale-eating Specialist, Catoprion mento*. Journal of Experimental Biology 208: 4757 – 4768.

2005 Janovetz, J. Society of Integrative and Comparative Biology, San Diego, CA. *Functional Morphology of Prey Capture in Serrasalmine Fishes*. American Zoologist 44:30.10A.

2005 Lambert*, B., and J. Janovetz. Mid-Atlantic Regional Conference of Undergraduate Scholarship, Sweet Briar, VA. *Feeding Kinematics and Jaw Protrusion in the Creek Chub*, *Semotilus atromaculatus*.

2005 Janovetz, J. American Society of Ichthyologists and Herpetologists, Tampa, FL. *The Kinematics of Biting Prey Capture in Pacus, Silver Dollars, and Piranhas*.

2004 Janovetz, J. Society of Integrative and Comparative Biology, New Orleans, LA. *Functional Morphology of Feeding in the Scale-eating Piranha*, *Catoprion mento*. American Zoologist, 43:30.8A.

2003 McGuffey*, S., and J. Janovetz. Mid-Atlantic Regional Conference of Undergraduate Scholarship, Sweet Briar, VA. *The Effects of Pavlovian Conditioning on the Anti-predator Behavior of Hognose Snakes.*

2002 Janovetz, J. Society of Integrative and Comparative Biology, Anaheim, CA. *Biomechanics of Feeding in a Scale-eating Piranha: A Novel Feeding Behavior Using Extreme Jaw Rotation and Momentum Transfer.* American Zoologist 41:10.1A.

2002 Janovetz, J. Functional and Ecological Morphology of Feeding in Pacus, Silver Dollars, and Piranhas (Serrasalminae: Teleostei). Ph.D. thesis, University of Chicago.

2001 Alfaro, M.E., J. Janovetz, and M.W. Westneat. *Motor Control across Trophic Strategies: Muscle Activity of Biting and Suction Feeding Fishes*. American Zoologist 41(6):1266-1279.

1999 Janovetz, J. Society of Integrative and Comparative Biology, Regional Meeting, Athens, OH. *Evolution of Feeding Behavior in Serrasalmine Fishes*. Best Student Paper award.

* denotes undergraduate co-author

PROFESSIONAL ACTIVITIES

Include reviewing and editing manuscripts for *The Biological Journal of the Linnaean Society, Animal Behavior, Philosophical Transactions Royal Society London B, Behavioral Ecology and Sociobiology, Copeia, Oecologica, Functional Ecology.*

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Education

University of New Hampshire School of Law, Concord, NH
Juris Doctor Candidate, May 2014
Activities:

International Technology Transfer Clinic
Current member of Student Intellectual Property Law Association
Current parliamentarian of the Black Law Student Association

Hendrix College, Conway, AR
Bachelor of Arts in History and Biology, January 2011
Activities:

Teaching Assistant for Zoology Laboratory, fall term of 2009
Teaching Assistant for Botany Laboratory, spring terms of 2009 and 2010
Laboratory Assistant for Cell Biology, fall term of 2008

Experience

New Hampshire District Court Circuit Court Division –Internship June 2012 – Present

- Assisted in updating the New Hampshire judicial bench book, a manual containing the current New Hampshire jurisprudence designed to assist new judges in all areas of law.

Hendrix College - Assistant Laboratory Technician for Dr. Jennifer Dearolf May 2010 - December 2010

- Analyzed the percentage of different myosin isoforms present in the scalenus muscle of fetal guinea pigs.
- Responsible for gathering and interpreting data collected by eight former lab assistants necessary for publication of professor's findings.

Hendrix College- Summer Laboratory intern for Dr. Jennifer Dearolf, May 2009- May 2010

- Characterized the myosin profile of the rectus thoracis muscle collected from fetal guinea pigs.

Community Service

- Co-President of The Hendrix College chapter of Habitat for Humanity, 05/10 - 12/10

Presentations and Publications

- Co-author of presentation, *Effects of prenatal steroids on myosin heavy chain expression of breathing and locomotor muscles*. SE Regional IDeA Meeting - September 22-24, 2011, New Orleans, LA
- Oral Presentation of *The effects of glucocorticoids on myosin expression patterns of fetal Cavia porcellus hindlimb and ventilatory musculature* at the Society for Integrated and Comparative Biology 2011 Annual Meeting - January 3-7, 2011, Salt Lake City, Utah
- Poster Presentation of *The effects of betamethasone on myosin expression patterns of fetal Cavia porcellus rectus thoracis and scalenus muscles* at Third Biennial National IDeA Symposium - June 16-18, 2010, Washington DC, 2010
- Poster Presentation of *The effects of betamethasone on myosin expression patterns of fetal Cavia porcellus rectus thoracis muscle* at the Society for Integrated and Comparative Biology 2010 Annual Meeting - January 3-7, 2011, Seattle, WA, 2010