Patent Landscape Report on

Vaccines for Selected Infectious Diseases

2012

PATENT LANDSCAPE REPORTS PROJECT

WIPO
WORLD
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ORGANIZATION

The WIPO patent landscape report project is based on the Development Agenda project DA_19_30_31_01 "Developing Tools for Access to Patent Information" described in document CDIP/4/6, adopted by the Committee on Development and Intellectual Property (CDIP) at its fourth session held from November 16 to November 20, 2009.

The purpose of each report is three fold:

- It attempts to research and describe the patterns of patenting and innovation activity related to specific technologies in various domains such as health, food and agriculture, climate change related technologies, and others.
- WIPO attempts to collaborate for each report with institutional partners (IGOs, NGOs, public institutions of Member States) working in the respective field and having an interest in a specific topic. The collaborative work in the planning and evaluation phases may also serve as a vehicle for these institutions to familiarize themselves with the utilization and exploitation of patent information and related issues of patent protection. WIPO welcomes proposals for collaboration.
- Each report also serves as an illustrative example for retrieving patent information in the respective field and how search strategies may be tailored accordingly. It therefore includes detailed explanations of the particular search methodology, the databases used and well documented search queries that should ideally enable the reader to conduct a similar search.

Each report of this project is contracted out to an external firm selected in a tendering procedure. The tender is open to a limited number of bidders that were pre-selected based on their submission of an Expression of Interest (EOI). WIPO invites the submission of further EOIs by qualified providers.

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PATENT LANDSCAPE REPORT ON

VACCINES FOR SELECTED INFECTIOUS DISEASES

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World Intellectual Property Organization

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2012

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ACTIVE INGREDIENTS OF VACCINES AGAINST INFECTIOUS DISEASES

Methodology

The various patents and patent applications were extracted from the Patbase (Minesoft) and the FamPat (QUESTEL) and verified through Patentscope (WIPO), ESPACENET and USPTO databases or other databases provided by national patent offices. Patbase and FamPat group together patent applications into families of patents and cover all of the domains found in the documents published by 95 patent offices. Patbase and FamPat group respectively patent applications into INPADOC families and Fampat families (definition can be found in appendix “Terminology”).

The research methodology used for this study combines conventional Boolean operators (AND, OR and AND NOT) with more complex search operators such as word truncations (in the middle or at the end of the word), search of successions of words and search for several words in the same sentence or paragraph. Keyword searches may be carried out in the titles, abstract and claims of documents.

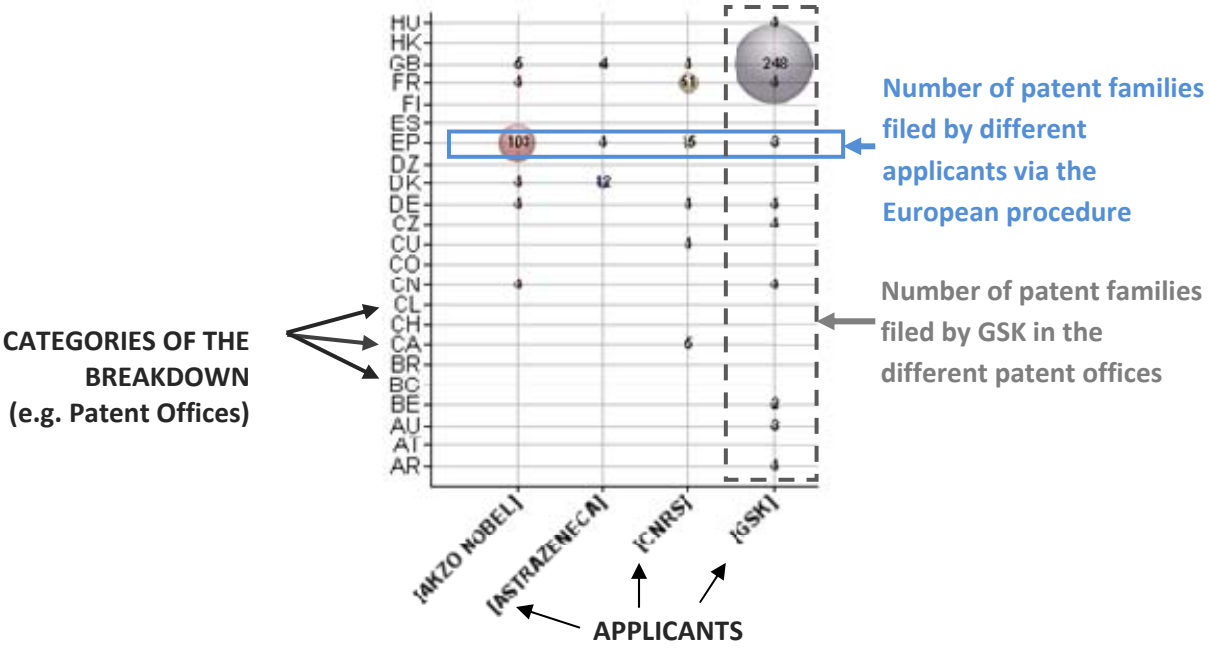
The patent search were limited or extended by the use of codes of the International Patent Classification (IPC), the European classification (ECLA), the US patent classification (USPC) or the Japan File-Index (Japan FI).

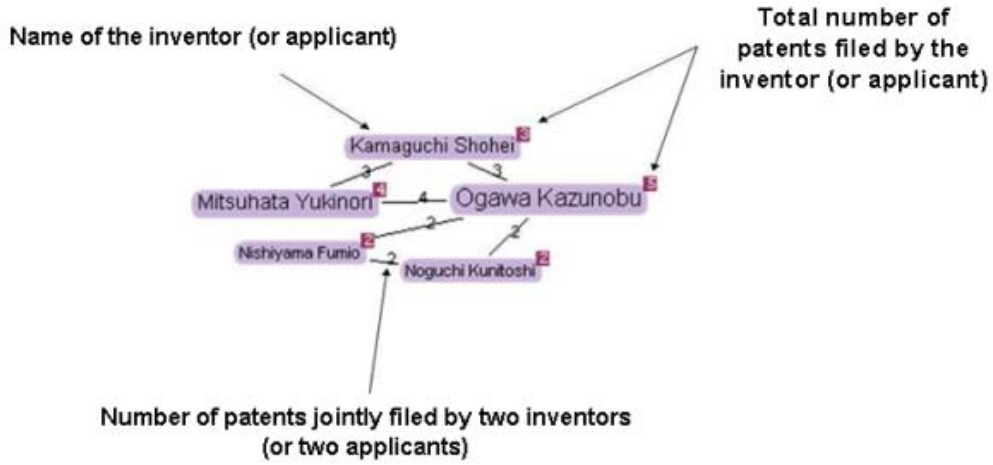
The patent searches were not limited by filing or priority dates.

Sets of data were validated and/or corrected by intellectual screening of the retrieved documents.

The processing of raw data and overall statistics was performed using Intellixir software (www.intellixir.com).

Guide to reading diagrams:





Executive summary

This patent landscape deals with active constituents of prophylactic vaccines against infectious diseases. It focuses specifically on three diseases: human pneumoccal conjugate vaccines, human conjugate typhoid vaccines and human influenza vaccines. It also focuses on patent filings in Brazil, India and China.

A vaccine is defined by the World Health Organization as any preparation intended to produce immunity to a disease by stimulating the production of antibodies. Vaccines include, for example, suspensions of killed or attenuated microorganisms, or products or derivatives of microorganisms. Vaccines are of public health importance since they prevent from major pandemics but not all. Therefore, the development of new vaccines is still required to combat diseases such as HIV or malaria, for exemple, but also to improve existing ones due to the emergence of new strains of pathogens such as for influenza.

After an explanation of the followed search methodology to retrieve relevant patent families, this report starts by the overall analysis of the datasets of patent families claiming active constituents of prophylactic vaccines against infectious diseases. This overall analysis led to the identification of more than 11800 patent families filed between 1921 and 2011 with an average of about 50% of these families including, at least, one grant of a patent in one jurisdiction and 60% including a PCT application. Historically, the United Kingdom and the United States have been the major patenting locations. Today, the United States are largerly dominating the area but is nevertheless challenged by China in the recent decade. Japan, Russia and European regional and national offices have been also active places of filings. The offices of second filings are mainly regional and national European offices as well as the United States. The most common applicants were identified as the US Government laboratories and GlaxoSmithKline (GSK). They are followed by Russian research institutes, other large pharmaceutical companies (e.g. Pfizer, Novartis) and other important research institutes specialized in infectious diseases (e.g. Pasteur Institute).

A deeper analysis of Brazilian, Indian, and Chinese filings shows a continuous increase of first filings in those three countries. However, Brazilian and Indian patent applications are still modest (about 70 patent families on the period). Indian data must however be taken with caution given the fact that patent information in this area is not yet fully available in worldwide database. Among these three countries, China is playing ahead in terms of filings. The record of Chinese patent application started in 1985, continuously increased since, to reach more than 180 first filings in 2010. A focus on Chinese first filings shows that these patenting activity is mainly due to Chinese academies of sciences and Chinese Universities. Hardly any Chinese industrial applicants are among the most active players.

The global patent landscape on active constituents of prophylactic vaccines against infectious diseases deals with a very large volume of patent families. It is important to keep in mind that many different types of inventions are in the dataset, leading sometimes to deal with apples and oranges. Information can only be relevant at a macro-level. In order to be able to draw more accurate focuses of technological sectors, it is convenient to analyse smaller volumes of patent families and therefore to focus on more specific fields.

This was the purpose of the three other patent landscapes that each focused only on one type of vaccines.

The first one focused on patent families claiming active ingredients of human pneumoccal conjugate vaccines. The dataset includes 165 patent families, the first one being filed in 1979. About 40% of these families included, at least, one grant of a patent in one jurisdiction and 70%, a PCT application. The United States and the United Kingdom have been the major patenting locations. China, with a recent but active patenting activity, is the third office of first filing in terms of number of patent applications. This field is mainly dominated by pharmaceutical companies and especially by large pharmaceutical corporations such as GSK, Novartis and Pfizer that tend to protect their inventions with a wide geographical coverage. The presence of some complex patent families, enlarging the protection of initial inventions, highlights an important patenting strategy developed by these companies to dominate this market. It is also interesting to note the recent active patenting activity of Novartis as well as the fact that contrary to GSK and Pfizer, this pharmaceutical corporation is not yet marketing pneumococcal conjugate vaccines.

The second one focused on patent families claiming active ingredients of human typhoid conjugate vaccines. The dataset includes 36 patent families filed between 1981 and October 2011. This low volume of filings is also marked by a low volume of granted patents since only 30% of them were issued by, at least, one patent office. The United States and the United Kingdom dominate as offices of first filing but India, despite a late arrival, comes third. Vaccines on the market were developed by a US government laboratory, the national institute of health (NIH) that may explain the dominant position of this player on this field. The typhoid sector is, here, well balanced between industrial and institutional applicants. The emergence of India is due to the very active research of Indian institutes to develop new conjugate typhoid vaccines for infants and especially the ALL India Institute.

The third and last focused on patent families claiming active ingredients of human influenza vaccines. The dataset includes 516 patent families filed between 1941 and October 2011. Half of them have a PCT member. The rate of granted patents was not very high, reaching barely 40%. The patenting activity is very high in the United States, Russia, China, the United Kingdom and Japan. The first efficient vaccine was developed in 1944 with the help of the American army which started an intense research in this field inside the US government laboratories. This analysis confirms the dominant position of the US even if Russian institutes and large pharmaceutical corporations such as Novartis and GSK are coming first. Of important economical importance, this sector led to the arrival of new players and to large geographical protections of inventions especially for those filed by players of the pharmaceutical industry.

To draw an even more detailed picture of these three focused field and, it would require integrating information from the patent landscape with market and pipeline data as well as an analysis of a technological breakdown of these datasets. This would enable a better understanding of companies' strategy and a more precise picture of the content of the patent portfolio of each player.

Introduction

The present patent landscape report is based on WIPO's Development Agenda project DA_19_30_31_01 ("Developing Tools for Access to Patent Information") described in document CDIP/4/6 adopted by the CDIP at its fourth session held from November 16 to November 20, 2009.

In the context of this approved project WIPO is preparing 12 patent landscape reports in the biennium 2010-2011. Patent landscape reports are envisaged to become in future a standard service of WIPO in the context of improved access to and exploitation of patent information.

The present landscape report was prepared in collaboration with WIPO and the WHO cluster on Innovation, Information, Evidence and Research (IER). It is intended to contribute to the implementation of several of the eight elements of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPOA) of WHO.

The intention of this patent landscape report on vaccine related patents is to detect patterns of patenting activity and innovation in the area of vaccine research and manufacturing in order to facilitate the sourcing of vaccine technologies that could potentially be used in developing countries, via a comprehensive study of the patents and patent applications filed in this field. A first part (part I) will cover vaccines against infectious human and animal diseases in general. This part aims at providing an overview of patenting activity in the area of vaccines by means of a statistical analysis. A second part (part II) will complement this broad picture by focusing separately on the patenting related to vaccines for three selected human infectious diseases of high economic and health burden importance: streptococcus pneumonia conjugate vaccines; typhoid conjugate vaccines; and influenza vaccines. In addition to describing the respective statistical patterns of patenting activity, this Part II of the report also aims at identifying all of the relevant patent families, and is complemented by respective databases including these patent families. Each part of the report also includes a special focus on the patenting activity in Brazil, China and India.

The scope of the present patent landscape report aims are patent families that claim inventions directly related to vaccines, i.e. any patents that protect any aspect like the active ingredient (antigen, antibody) as such, derivatives thereof, combinations, methods of production, uses, etc.

1. Active ingredients of vaccines against infectious diseases

1.1. Search methodology

1.1.1. Introduction

This section describes the search methodology developed to retrieve patents and patent applications claiming active constituents of vaccines against human and animal infectious diseases. The narrative of this search history shows how the search was performed. It describes specific tools, databases, and challenges encountered and methods of circumventing. This section also discusses the limits of the use of patent classification codes (IPC, ECLA…) when looking for patents and patent applications dealing with active constituents of vaccines. As the volume of patents and patent applications expected in the issued patent database is very large, it cannot be considered to be exhaustive and without noise. It is estimated to have 5 to 10 % of missing relevant patent families and 5 to 10% of irrelevant patent families which is the limit that does not affect the global trends, analysis and perspective of this part of the report that aims only at describing the general statistical patterns of patenting activity in this area.

1.1.2. Methodology and databases

A background study was first performed by looking at the literature on vaccines against infectious diseases in order to collect keywords to build the patent queries and especially to help us determine the relevancy of a patent family compared to another in relation to the fact that only patent describing “active constituents” had to be taken into account. General articles about vaccines against infectious diseases found on the Internet were useful to make a list of keywords[1].

Then, a review of patent classification was carried out to identify patent classification codes related to vaccines against infectious diseases.

With the list of keywords and patent classification codes established such as described, queries were built and run into Patbase database (Minesoft™).

[1] http://www.who.int/topics/vaccines/en/

http://en.wikipedia.org/wiki/Vaccine

see appendix 2

1.1.3. Background study

Review of the literature

A vaccine is a preparation of killed or inactivated microbes (parasites, viruses, batteria) or purified products derived from them used to elicit the immune system to a particular disease.

Prophylactic vaccines used to elicit the immune system to prevent future infections have to be distinguished from therapeutic vaccines that are used to treat a disease already present in the organism (such as cancers).

Different types of vaccines are produced or under development such as killed vaccines, attenuated vaccines, subunit vaccines, conjugate vaccines, toxoid vaccines, DNA vaccines, recombinant vectors or synthetic vaccines.

This analysis focuses on patents and patent applications claiming active constituents of prophylactic vaccines against infectious diseases. Following this definition, we excluded from this study patents and patent applications claiming purely diagnostic related technologies, therapeutic vaccines, general methods for large scale production of vaccines, as well as documents claiming only methods of administration of vaccines or vaccine adjuvants (however, if adjuvants or methods of administration were claimed in a patent were the active ingredients of vaccine is clearly described, these documents were included into the database).

From the background study, a list of keywords was established. This list was refined during the building of the search strategy by reading and analysing relevant patents and patent applications as well as patents and patent applications that were initially found by broader queries bu determined as unrelevant. The potential translations (vaccine-> vaccina), orthographic variations (immunise->immunize) and similar words (prevent->prevention) used in the refined queries are not mentioned in the lists below. These lists are thereby not considered as exhaustive.

Keywords potentially related to relevant patents and patent applications:

Vaccine: vaccine, immunise, immunogen, antigen, subunit, strain, adjuvanted, conjugate, attenuated, inactivated, killed, live, virulent, avirulent, recombinant, prophylactic

Active constituent: SEQ ID (peptide sequence)

Prevention of a disease and induction of the immune system: prevent, protect, elicit, generate, induce, trigger

Infectious diseases: infection, virus, bacteria, parasite, VLP (virus like particle)

Other: subject, host, patient, man, human, woman, animal

Keywords potentially related to irrelevant patents and patent applications:

Technologies related to vaccines but not active constituent: adjuvant, probiotic, stabilizer

Non infectious diseases: cancer, tumor, carcinoma, neoplasm, melanoma, cytokine, Crohn, Alzheimer, immune disease, autoimmune, inflammation, neurotoxicity, amyloid, arthritis, allergy, sclerosis, leukemia, lymphoma, diabetes, obesity, healing

Production of vaccines: cell line, culture, matrix, model, bioreactor, reactor, large scale, mass production, manufacture

Treatment and test: assay, diagnosis, detect, immunopotentiation, immunomodulation, immunostimulation, treatment, therapy, medicament, medicine, compound, monoclonal, graft, rejection, down regulation, xenograft, implant, transplantation, immunosuppressor

Delivering and formulation: deliver, cream, tablet, aqueous, solvent, gel, powder, oil, water, emulsion, dry

Review of relevant classification codes

By screening the international, European, American and Japanese patent classifications, there is no specific code for vaccines but a set of codes related to active constituent of vaccines such as antigens. However these codes are not specific to infectious diseases but also include antigens against other diseases. The codes corresponding to medicinal preparations containing antigens directed against infectious diseases were collected. The following codes were thereby identified:

International Patent Classification (IPC):

Selection of subgroups of subclass A61K39 corresponding to medicinal preparations containing antigens or antibodies directed against infectious diseases

Examples of selected subgroups of subclass A61K39: A61K39/02 (Bacterial antigens), A61K39/102 (Pasteurella; Haemophilus), A61K39/225 (Porcine transmissible gastroenteritis virus)

Examples of unselected subgroups of subclass A61K39: A61K39/35 (Allergens), A61K39/38 (Antigens from snakes), A61K39/385 (Haptens or antigens, bound to carriers)

The reason for not selecting certain IPC codes was they were not specific to infectious diseases. Although these codes were not included in the query, they can be present in the relevant and validated patents and patent applications of the final database.

US Patent Classification (USPC):

Selection of subgroups of subclass 424/184.1 corresponding to antigen, epitope, or other immunospecific immunoeffector specific to infectious diseases

Examples of selected subgroups of subclass 424/184.1: 424/193.1 (Conjugate or complex), 424/204.1 (Virus or component thereof), 424/254.1 (Bordetella pertussis)

Examples of unselected subgroups of subclass 424/184.1: 424/274.1 (Fungus, except allergen, or component thereof or substance produced by said fungus (e.g., Trichophyton, etc.)), 424/277.1 (Cancer cell or component thereof)

Subclasses 424/813 to 424/832 corresponding to viral vaccines or bacterial vaccines for some animal species such as bovine or fish species

Examples of subclasses 424/813 to 424/832: 424/817 (Viral vaccine for fish), 424/825 (Bacterial vaccine for porcine species (e.g., swine, etc.))

European classification (ECLA):

Selection of subclasses of subgroup A61K39 corresponding to medicinal preparations containing antigens or antibodies directed against infectious diseases

Examples of selected subclasses of subgroup A61K39: A61K39/00A (Archaeal antigens), A61K39/02T3 (Salmonella), A61K39/193 (Equine encephalomyelitis virus)

Examples of unselected subclasses of subgroup A61K39: A61K39/35 (Allergens), A61K39/395 (Antibodies; Immunoglobulins; Immune serum, e.g. antilymphocytic serum)

Japan File-Index (Japan FI):

Selection of subclasses of subgroup A61K39 corresponding to medicinal preparations containing antigens or antibodies directed against infectious diseases

Examples of selected subclasses of subgroup A61K39: A61K39/002 (Protozoa antigens), A61K39/17 (Newcastle disease virus), A61K39/295 (Polyvalent viral antigens (vaccinia virus or variola virus A61K 39/285); Mixtures of viral and bacterial antigens)

Examples of unselected subclasses of subgroup A61K39: A61K39/38 (Antigens from snakes), A61K39/39 (characterised by the immunostimulating additives, e.g. chemical adjuvants)

1.1.4. Search strategy

The patent search (see the corresponding appendix for the detailed strategy) started by building a pool of patents and patent applications retrieved by the classification codes selected (*pool 1* – queries 1 to 5). In a second step, within this *pool 1*, patent searches using a combination of keywords specific to vaccines were carried out to select patents and patent applications that clearly dealt with vaccines. The group of these selected patents from *pool 1* (i.e. patent dealing with vaccines) is now called *pool 2 (*queries 6 to 7 – see figure 1).

At this point of the search strategy, *pool 2* was split into two subgroups (*pool 2A* and *pool 2B*). Pool 2A was obtained by crossing *pool 2* with queries built from high relevant keywords (e.g. vaccine, queries 8 to 19). Pool 2B is constituted with the remaining documents (*pool 2* minus *pool 2A* – query 37). At this point, pool 2A and pool 2B contained respectively about 80% and 20% of relevant patents.

Pool 2A was then cleaned using queries built with keywords related to irrelevant patents (see lists above in section 1.1.3 and queries 20 to 36). A first group of relevant and validated patents and patent applications was thereby obtained.

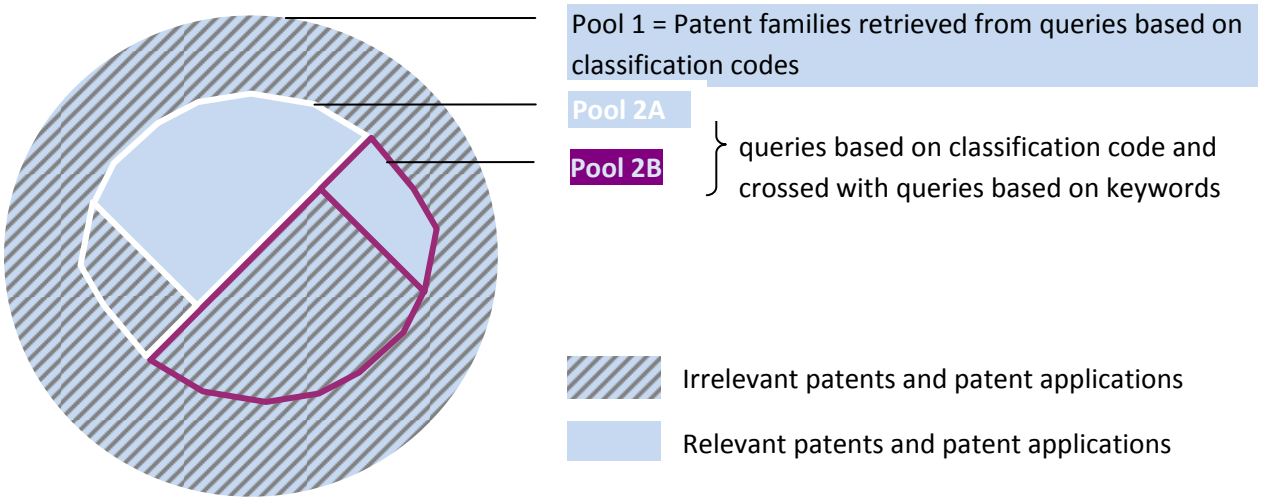


Figure 1 - Schematic view of the patent search strategy followed for this study

For Pool 2B, another approach was implemented consisting in an iteration of keyword search queries that either selected relevant documents or eliminated irrelevant ones, decreasing progressively the number of documents remaining in *pool 2B* (queries 38 to 48). A second group of relevant and validated patents and patent applications was thereby obtained.

Relevant patents from pool 2A and pool2B were gathered to constitute the final database.

Finally, to validate the fact that only a tiny fraction of relevant patents and patent applications were not covered by the selected classification codes (pool 1), other classification codes were investigated (queries 49 to 51).

1.2. Statistical analysis

1.2.1. General statistics of filings

The patent search resulted in 11818 INPADOC families of patents and patent applications published until November 2011. These 11818 patent families include 51476 patents or published applications. Among these 11818 patent families, 5950 included one or more granted patents.

Granted patents were identified by creating a query based on kind codes related to granted patents of all patenting authorities and applying it to the patent pool of active ingredients of human pneumococcal conjugate vaccines. Each patenting office has its own kind code system. For example, publications of the European Patent Office having a “B” kind code are granted patents, whereas publications having an “A1, A2, A3” kind code are applications. For the US Patent and Trademark Office, publications with an “A” kind code published before November 2000 and publications with kind code “B1, B2” are granted patent while publications with a “A1, A2” kind code published after November 2000 are applications.

Families having granted family members do not necessarily mean that protection has entered into force or the patent is still valid. Granted patents may not be in force for several reasons including that the patent term expired, that fees have not been paid, or that it did not survive opposition or revocation procedures.

Total number of patent families claiming active ingredients of vaccines	11818
Total different patents & patent applications	51476
Average INPADOC Family Size	4.4 patents or applications/family
PCT applications	54.6%
Granted patents	50.3%

Table 1 - General statistics of patent filings and grants

Figure 2 below describes patenting activity over time. The graph represents the number of patent families (Y axis) over the year of first filing (X axis). This year (priority year) was chosen rather than the publication year, as this is more indicative of patenting activities since they are less dependent on the varying publication policies and docket backlogs of patent offices.

Please note that for earlier years of filing, national publication policies and the evolution of national patent legislation have to be taken into account. For example, until November 2000, the US patent legislation published only granted US patents. Thereby, US applications that were not granted were in fact never published. For the coverage of national databases used in this study, please refer to corresponding appendix. In addition, because of the 18 months of publication delay after the date of patent filing, the data after 2009 are incomplete.

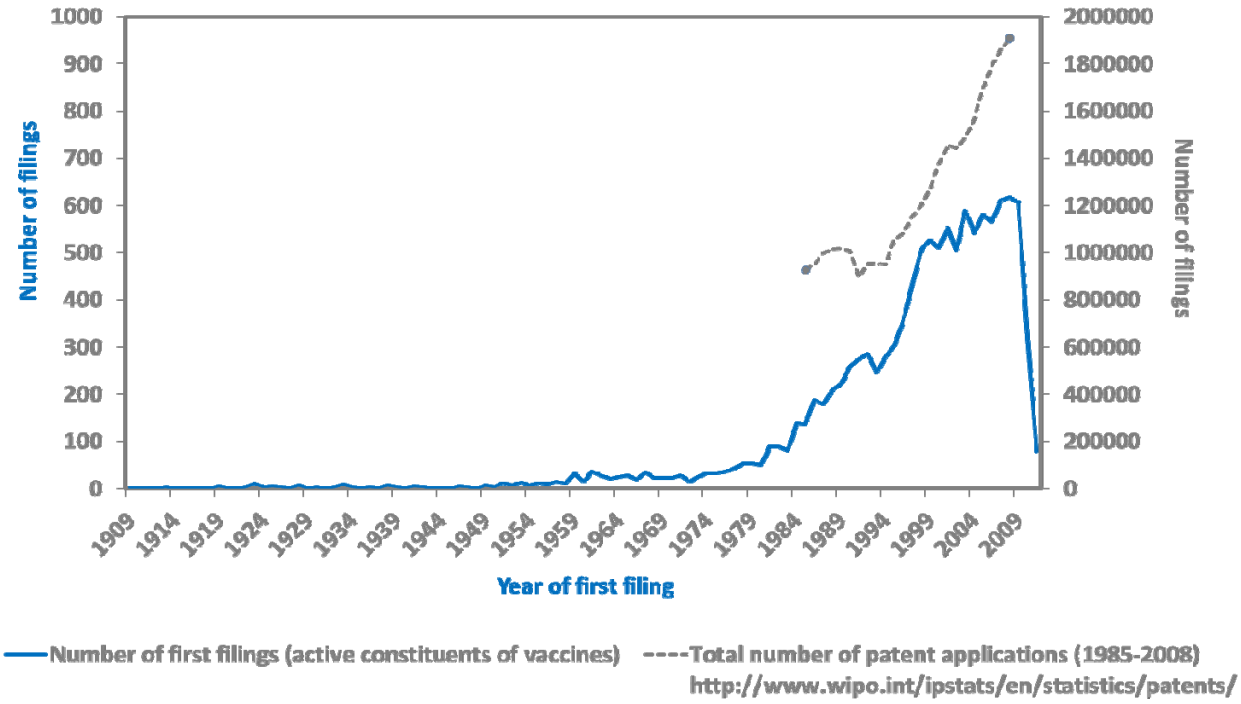


Figure 2 - Evolution of patent filings per year of first filing and comparison to global patenting activity per year of first filing

The graph shows a strong increase of filings from 1980 (50 filings) to 2000 (500 filings) reaching a plateau of 500-600 filings a year in the 2000-2010 period.

When comparing to global activities in patent filings (figure 1, dashed gray line) from 1985 to 2008, it can be seen that patent activities related to vaccines has more or less (less before 1995 and more after 1995) followed the trend of global increase in patenting.

The next figure further describes patent activity over time similar to Figure 2 but in more detail. The count of families for each year of first filing is split into two fractions according to whether families included a PCT application or not.

Starting 1991, PCT applications were widely used to reach over 60% of patent families.

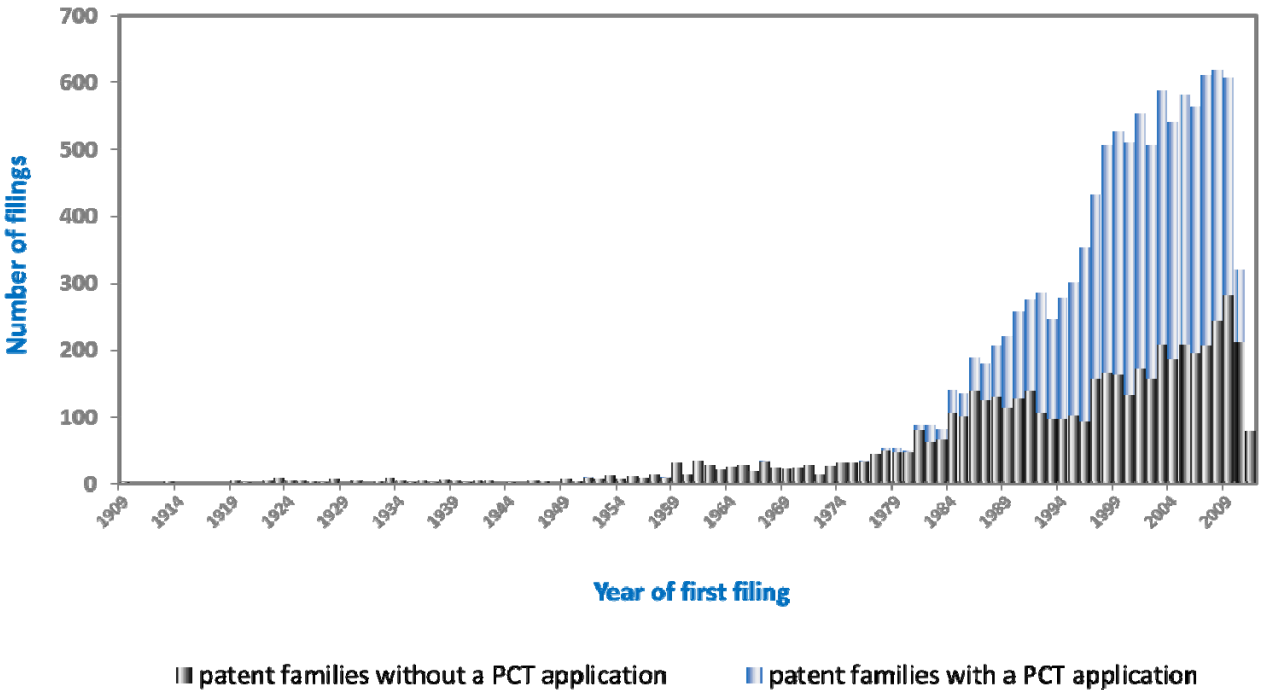


Figure 3 - Evolution of the number of patent families with and without PCT applications per year of first filing

The table below lists the office of origin of all PCT applications. This table was established by looking at the application number of a PCT filing that mentions the office of origin of the PCT (e.g. 2008WO-FR00687, this PCT application was filed via the French patent office).

This table shows that PCT applications were mainly filed via national or regional offices. Only few applications (5%) were filed directly via the international bureau.

Offices of filings	Number of PCT applications
UNITED STATES (US)	3117
EUROPE (EP)	881
UNITED KINGDOM (GB)	461
INTERNATIONAL BUREAU (WIPO)	333
FRANCE (FR)	280
CANADA (CA)	273
AUSTRIA (AU)	226
JAPAN (JP)	222
NETHERLANDS (NL)	91
SWEDEN (SE)	83
CHINA (CN)	72
KOREA (KR)	68
DENMARK (DK)	62
SPAIN (ES)	48
CUBA (CU)	41
INDIA (IN)	39
ISRAEL (IL)	37
BRAZIL (BR)	31
GERMANY (DE)	30

Table 2 - Origin of PCT applications

The next figure gives a view of patent grant rate in the field of active ingredients of vaccines against infectious diseases. The count of families for each year of first filing is split into two fractions according to whether families included at least one granted patent or not.

In the 1990s, up to 70% of patent families contained at least one granted patent while, after 2000, this rate has been continuously decreasing from 50% to barely 10% in 2009. The small fraction of grants in younger families (since 2005) reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO). For these families the examination of family members may still be pending or may not be requested yet.

For earlier years of filing, national publication policies and the evolution of national patent legislation have to be taken into account. For example, until November 2000, the US patent office only published granted US patents. Thereby, US applications that were not granted were in fact never published. For the coverage of national databases used in this study, please refer to corresponding appendix. In addition, because of the 18 months of publication delay after the date of patent filing, the data after 2009 are incomplete.

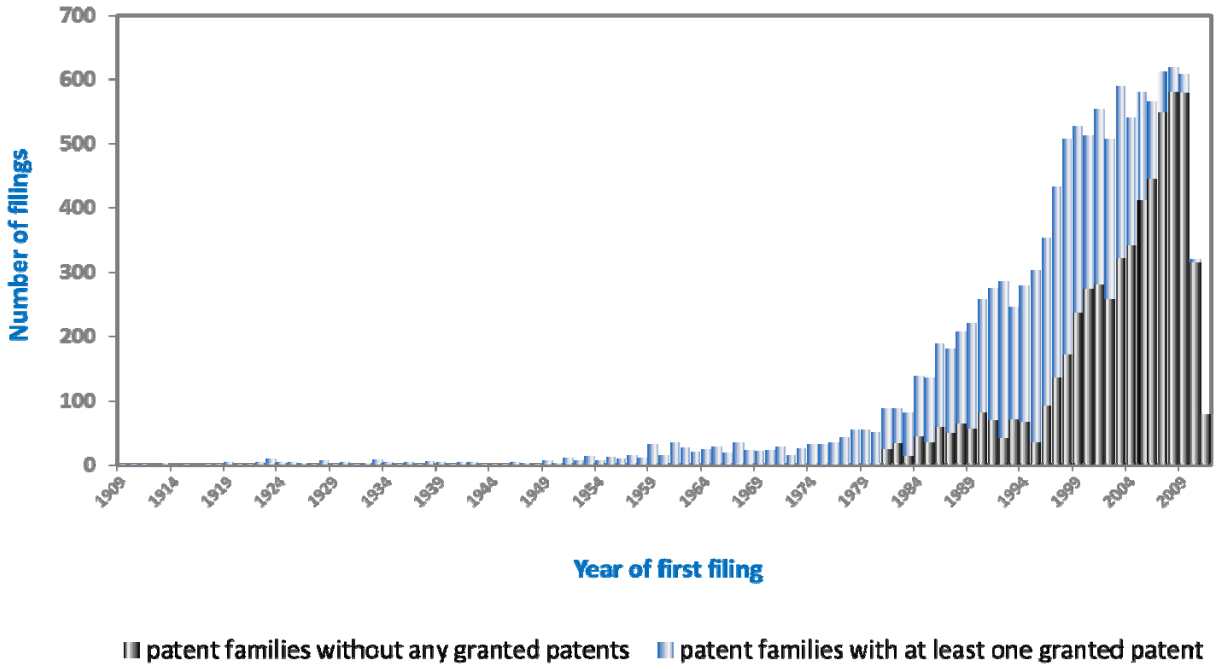


Figure 4 - Evolution of the number of granted and not granted patent families per year of first filing

1.2.2. Location of first filings

An analysis of the place of filing of priority patents results in the following tables. The location of first filings gives an indication of the country of origin of applicants and the dynamic of innovation in these countries. A map compiling these data can be found in the corresponding appendix.

Please note that 319 patent filings were not classified in the list below because of a lack of priority data in the database. It mainly concerns patent applications registered in Thailand and Taiwan as well as about 50 old patent applications registered in the UK, that seem to correspond to extensions not properly grouped within the patent family. As it concerns less than 2% of the dataset, it was unnecessary to perform manual corrections to improve statistics.

Offices of first filing	Number of filings
UNITED STATES (US)	5230
CHINA (CN)	1133
UNITED KINGDOM (GB)	942
JAPAN (JP)	632
RUSSIA (RU)	625
EUROPE (EP)	581
FRANCE (FR)	455
AUSTRALIA (AU)	245
KOREA (KR)	232
GERMANY (DE)	222
WIPO (WO)	148
DENMARK (DK)	89
CANADA (CA)	81
SPAIN (ES)	79
BRAZIL (BR)	75
SWEDEN (SE)	71
INDIA (IN)	69
UKRAINE (UA)	68
NETHERLANDS (NL)	56
CUBA (CU)	56
ITALY (IT)	51
HUNGARY (HU)	39
TAIWAN (TW)	36
SWITZERLAND (CH)	35
BULGARIA (BG)	33
NEW ZEALAND (NZ)	29
ISRAEL (IL)	27
ARGENTINA (AR)	26
AUSTRIA (AT)	23
SOUTH AFRICA (ZA)	20

Offices of first filing	Number of filings
CZECH REPUBLIC (CZ)	18
ROMANIA (RO)	18
IRELAND (IE)	17
POLAND (PL)	14
MEXICO (MX)	13
BELGIUM (BE)	13
NORWAY (NO)	12
FINLAND (FI)	11
SINGAPORE (SG)	6
MALAYSIA (MY)	5
CHILE (CL)	5
LATVIA (LV)	4
LUXEMBOURG (LU)	4
SLOVENIA (SI)	4
SLOVAKIA (SK)	3
PORTUGAL (PT)	3
CROATIA (HR)	2
KAZAKHSTAN (KZ)	2
GUATEMALA (GT)	2
GREECE (GR)	2
ALGERIA (DZ)	1
COLOMBIA (CO)	1
GULF COUNCIL (GC)	1
HONG KONG (HK)	1
MOLDOVA (MO)	1
MONGOLIA (MN)	1
MOROCCO (MA)	1
PHILIPPINES (PH)	1
TURKEY (TR)	1

Table 3 - Location of first filings

Table 4 - Evolution of first filings by offices (1/2)

		Total (1921-2011)	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	Total
PCT	WORLD	148																																																
AMERICA	UNITED STATES	5230				1																					3			2		1	2	4	3	4	4	5	6	6	9	17	10	8	11	16	6	11	11	13	153
	CANADA	81																																									1		1			1			3
	BRAZIL	75																																								1								1
	CUBA	56																																																
	ARGENTINA	26																																																
	MEXICO	13																																																
	CHILE	5																																																
	GUATEMALA	2																																																
	COLOMBIA	1																																																
EUROPE	EUROPE	581																																																
	UNITED KINGDOM	942	1	1	1			1		1			1	1	1			1	2									1						1	1			2	1	2	9		7	3	8	5		4	5	2	4	66
	FRANCE	449																																									1		1		1	1	5			9
	GERMANY	222																														1						1	1	1	1		2	4	2	1	3		2	3	2	24
	DENMARK	89																																																
	SPAIN	79																																														1			1
	SWEDEN	71																																																
	NETHERLANDS	56																																										1						1
	ITALY	51																																												1				1
	HUNGARY	39																																																
	SWITZERLAND	35																																							1			2						3
	BULGARIA	33																																																
	AUSTRIA	23																																																
	CZECH REPUBLIC	18																																																
	ROMANIA	18																																																
	IRELAND	17																																																
	POLAND	14																																																
	BELGIUM	13																																														1		1
	NORWAY	12																																																
	FINLAND	11																																																
	LUXEMBOURG	4																																														2		2
	SLOVENIA	4																																																
	PORTUGAL	3																																																
	SLOVAKIA	3																																																
	CROATIA	2																																																
	GREECE	2																																																
	TURKEY	1																																																
EURASIA	RUSSIAN FEDERATION	625																																																
	UKRAINE	68																																																
	LATVIA	4																																																
	KAZAKHSTAN	2																																																
	MOLDOVA	1																																																
ASIA	CHINA	1133																																																
	JAPAN	632																															1												1				1	3
	KOREA	232																																																
	INDIA	69																																																
	TAIWAN	36																																																
	SINGAPORE	6																																																
	MALAYSIA	5																																																
	HONG KONG	1																																																
	MONGOLIA	1																																																
	NORTH KOREA	1																																																
	PHILIPPINES	1																																																1
MIDDLE EAST	ISRAEL	27																																																
AFRICA	SOUTH AFRICA	20																																																
	ALGERIA	1																																																
	MOROCCO	1																																																
OCEANIA	AUSTRALIA	245																																														1	1			2
	NEW ZEALAND	29																																																
Total		11569	1	1	1	1		1		1			1	1	1			1	2									3	1		2		3	3	5	3	4	7	7	9	17	9	28	19	22	19	20	13	26	19	20	271

Table 4 - Evolution of first filings by offices (2/2)

		Total (1921-2011)	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	Total
PCT	WORLD	148															1	1				1				3	1	7	3	4	7	3	8	12	9	15	5	6	17	10	14	13	8		148
AMERICA	UNITED STATES	5230	10	10	6	12	10	12	10	14	18	28	23	38	45	38	49	63	88	88	86	96	133	155	129	141	132	170	194	220	272	237	228	251	226	257	235	248	246	268	270	247	73	1	5077
	CANADA	81		1				1	1	1	1	3	2	1	1			1	2			3		3	1	3	2	1	3	1	3	1	4	3	6	3	4	3	4	5	8		2	1		78
	BRAZIL	75																								1				12	1	1	3	1	2	2	5	10	7	10	6	10	3		74
	CUBA	56															2			1			2	2	1					3		2	4	4	3	12	5	6	4	4	1				56
	ARGENTINA	26											1							1													1	4	1	2	5		1	4	3	1	2		26
	MEXICO	13																													1	1		1		1	3	3	2			1			13
	CHILE	5																															1					2	1	1				5
	GUATEMALA	2																											1									1						2
	COLOMBIA	1																										1																1
EUROPE	EUROPE	581												1			2	1	5	1	7	8	10	14	16	16	21	13	22	27	27	34	37	27	31	44	24	32	33	52	41	23	12		581
	UNITED KINGDOM	942	2	3	2	6	4	4	1	4	8	6	1	4	4	6	7	6	11	13	10	26	23	17	31	15	27	24	31	28	71	101	64	57	41	29	35	40	28	31	21	25	9		876
	FRANCE	449	2	1	1	7	3	6	6	7	3	4	5	8	3	5	11	8	13	12	10	10	12	13	19	7	21	16	17	42	15	19	22	17	11	17	12	19	10	10	6	8	2		440
	GERMANY	222	3	5	3	4	4	3	2	2	1	1		3	4	1	4	3	6	8	4	8	9	11	6	3	11	6	12	5	6	8	9	10	13	6	5	4	2	1	1	1			198
	DENMARK	89										1			1		1	1	1	1	16			1	1	2		1	2	2	1	4	11	4	7	6	2	5	2	7	6	3			89
	SPAIN	79												2					1	1				2	1	2	3	4	4	1	4	1	2	3	2	4	5	9	6	9	6	6			78
	SWEDEN	71											1	1		1	1		2	3	2	2	5	3	4	1	3	4	8	5	5	6	6	2	1	1			1	2		1			71
	NETHERLANDS	56								1	2	2		1	2	3	1	3	4	6	6	3	10	2	1	2	2	1					1	2											55
	ITALY	51																	2	1	1	5	2	4	3	1	1	1		1	1		2	5	3		4		3	1	5	3	1		50
	HUNGARY	39										1		1	3	3	5		1	1	4	3			2		1			4	3	2	1	1			1		1			1			39
	SWITZERLAND	35		2			2	2		4	5	3		1			1	5		1	1		2	1		1						1													32
	BULGARIA	33							1					1	2	3	4	3	1	4		5	2	1					2	1							1	1		1					33
	AUSTRIA	23								1	1				1			2	1	1	2			1	1		2			1	1	1		4	1			1		1					23
	CZECH REPUBLIC	18																											2	1	5	2		2	1	1				1	1	2			18
	ROMANIA	18											1	1	4	1		4	2		5																								18
	IRELAND	17									1									1	1		2				1		2					3	1	2			1	1		1			17
	POLAND	14							1										1			1			1					1				4	1		1	1	1		1			14
	BELGIUM	13		1				3	1	1				1	2									1				1						1											12
	NORWAY	12																			1									1	2	3	2	1		1				1				12
	FINLAND	11																	1							1		1		1			2				2	2		1				11
	LUXEMBOURG	4																		1	1																							2
	SLOVENIA	4																									1	1											2				4
	PORTUGAL	3																1							1													1					3
	SLOVAKIA	3																								1	2																	3
	CROATIA	2																														1							1					2
	GREECE	2																																	1				1					2
	TURKEY	1																													1													1
EURASIA	RUSSIAN FEDERATION	625				1	3	1		1	1	8		3		3	9	1	8	4	10	7	10	14	21	11	11	18	15	24	30	44	25	50	52	35	37	43	32	16	34	24	19		625
	UKRAINE	68																											1			1				25	8	13	11	9					68
	LATVIA	4																														1		1		1					1			4
	KAZAKHSTAN	2																																								2			2
	MOLDOVA	1																																									1		1
ASIA	CHINA	1133																3	2		5	4	1		4	2	6	3	6	9	14	11	21	28	37	81	65	91	83	92	137	171	179	78	1133
	JAPAN	632	5	2	2		1	4	7	4	2	10	10	13	14	10	31	13	25	16	21	22	16	21	23	20	15	15	15	16	12	20	27	18	24	18	41	18	30	28	24	15	1		629
	KOREA	232									4	1	2		2					1	3		4	1	1	9	3	1	6	12	19	11	16	12	10	9	14	7	15	19	15	25	9	1	232
	INDIA	69					1														1	1						1	1	1	1	1	3	4		6	11	6	8	12	6	4	1		69
	TAIWAN	36																												1		1			2	3	3	3	2	6	7	8			36
	SINGAPORE	6																					1		1						1	1	1										1		6
	MALAYSIA	5																												1			1			1					1	1		5
	HONG KONG	1																											1															1
	MONGOLIA	1										1																																	1
	NORTH KOREA	1																						1																					1
	PHILIPPINES	1																																										
MIDDLE EAST	ISRAEL	27								2			2	2		1			2	3					3		2		2	3	2			1	1	1									27
AFRICA	SOUTH AFRICA	20	2								1	1		2																1	1		2	2		1	4			2	1			20
	ALGERIA	1																																									1		1
	MOROCCO	1																																1										1
OCEANIA	AUSTRALIA	245							1					2		3	9	7	7	3	8	13	10	4	9	3	10	12	6	10	10	12	15	15	10	11	13	9	10	8	6	5	2		243
	NEW ZEALAND	29	1								1			1						1	1		1		2	1	1	1	1	1	2	2	1	4	4	1				1		1			29
Total		11569	25	25	14	30	28	36	31	42	49	70	48	87	88	78	138	126	186	173	206	218	255	272	282	246	279	303	357	437	518	534	517	555	506	596	545	585	567	616	618	607	325	80	11298

Among the offices of first filings that gather the highest number of patent and patent applications, several countries have a long history and strong continuous filings all over the period such as the United States, the United Kingdom, Japan, Russia, France, Australia, Korea and Germany, and largely dominate as offices of first filing. On the contrary, China, that registered the second more important volume of filings over the period, has had an emerging filing activity over the last decade. The filings stemming from Brazil, Cuba, Argentina, Taiwan, India and South Africa, although not yet massive, are still worth noticing.

In order to have a better understanding of the country of origin and the innovation dynamic in these countries, it is more appropriate to take a look at the number of filings according to inventors' place of residence rather than the office of first filing.
To be able to make these statistics, the data related to Inventor's country (extracted from the address of the inventor), indexed in FamPat database (Questel^{TM}), was used. To do this, patent families of the database "Active Ingredients of Vaccines" were loaded into FamPat. The number of relevant patent families changes (12323 instead of 11818) because of the different definition of FAMPAT families compared to INPADOC families (FAMPAT families are built with patent applications having exactly the same priority whereas INPADOC families are built with patent applications having at least one priority patent application in common). The number of filings naming at least one inventor coming from a country in particular was then counted.
It should be noted that totals of the two categories of the table are different because the inventors indicated in an individual patent application may have different countries of residence; each country was counted once, e.g. an application with two inventors residing in Belgium and one inventor residing in the United Kingdom would result in one count for each country. In addition, these data should be taken with caution, since the country of inventors are not always stated in the databases (this is particularly true for Japanese and Chinese filings as well as ancient patents that do not systematically state this data). The number of inventors stemming from these two countries are therefore underestimated.

Based on these data, it was noted that Canadian innovation tends to be first protected through the US patent office and that European innovation tends to be first protected through UK patent offices and through European Procedure. Several reasons can co-exist to explain these differences:

- The interest in specific cases to use US provisional patents (even when the innovation do not stems from US inventors)
- The difference in location of patent officers and research team. For example, 414 applications filed by Belgian inventors vs. 13 first filings registered at the Belgian patent office. This is explained by the fact that GSK vaccine research team is located in Belgium but files in the United Kingdom where are located the headquarters. On the same way, NOVARTIS/CHIRON research team is located in Italy but files in the United Kingdom.
- The interest of filing directly in English to lessen future translation fees
- Some inventors are collaborating with foreign research teams and therefore do not file in their country of origin but in the country of their collaborators. This is for instance the case for Singaporeans that collaborate with many US companies, institutes or Universities.

		Number of filings in each patent authority	Number of filings according to inventors' place of residence
PCT	WORLD	148	/
AMERICA	UNITED STATES	5230	4384
	CANADA	81	545
	BRAZIL	75	53
	CUBA	56	59
	ARGENTINA	26	38
EUROPE	EUROPE	581	/
	UNITED KINGDOM	942	730
	FRANCE	455	699
	GERMANY	222	527
	DENMARK	89	91
	SPAIN	79	118
	SWEDEN	71	186
	NETHERLANDS	56	360
	ITALY	51	282
	HUNGARY	39	28
	SWITZERLAND	35	184
	BULGARIA	33	35
	AUSTRIA	23	107
	BELGIUM	13	414
EURASIA	RUSSIAN FEDERATION	625	347
	UKRAINE	68	34
ASIA	CHINA	1133	865
	JAPAN	632	425
	KOREA	232	231
	INDIA	41	98
	TAIWAN	36	88
	SINGAPORE	6	49
MIDDLE EAST	ISRAEL	27	84
AFRICA	SOUTH AFRICA	20	25
OCEANIA	AUSTRALIA	245	364
	NEW ZEALAND	29	35

Table 5 - Comparison between place of filings and origin of inventors (inventors named in 20 or more patents and patent applications)

1.2.3. Location of second filings

An analysis of the location of second filings results in the following table. A map compiling these data can be found in the corresponding appendix. Countries chosen for the extension of priority filings are an indicator of the markets and/or the production sites. The choice of countries may also be guided by company's competitors and potential infringers, even if there is no market in these corresponding territories. In Life Sciences, the choice can also be guided by usual locations of clinical trials (Poland, Hungary, Thailand, India…).
These data were established by looking at the publication numbers of each family without taking into account the publication number of the first filing. However, for patent and patent applications of European countries filed via the European Procedure, a different counting was carried out because of specificities of European procedures. According to the designated and chosen offices, a new patent application number is attributed by these offices or not. For instance, German patent office will deliver a number (DE123456) after an extension via the European procedure while France will use the EP number (EP654321). When looking at the patent families via the patent & patent application numbers, it therefore created, improperly, a higher number of German extensions compared to French ones. Consequently, when a patent family contained a patent application filed via the EPO, the numbers issued by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family.

Many second filings were performed via the PCT procedure (as seen in the previous section, it represented about 60% of the patent applications). The European Patent office (EPO), Australia, Canada, Japan and the United States also dominate as offices of second filings. Beware that the importance of Australia must be understood in relation to the policy of the Australian patent office which automatically delivered an Australian patent number when the PCT mentions Australia even if no extension was filed in Australia during the national phase.

Offices of second filings	Number of filings
WIPO (WO)	6303
EUROPE (EP)	4977
AUSTRALIA (AU)	4466
CANADA (CA)	4294
JAPAN (JP)	3670
UNITED STATES (US)	2293
CHINA (CN)	1713
KOREA (KR)	1148
BRAZIL (BR)	1089
SOUTH AFRICA (ZA)	1085
NEW ZEALAND (NZ)	1011
MEXICO (MX)	925
ISRAEL (IL)	905
INDIA (IN)	856
NORWAY (NO)	653
RUSSIA (RU)	428
TAIWAN (TW)	396
ARGENTINA (AR)	375
UNITED KINGDOM (GB)	310
HONG-KONG (HK)	285
GERMANY (DE)	216
FRANCE (FR)	210
BELGIUM (BE)	166
NETHERLANDS	158
EURASIA (EA)	132
SINGAPORE (SG)	122
DANEMARK (DK)	115
COLOMBIA (CO)	113
ARIPO (AP)	108
SPAIN (ES)	108
THAILAND (TH)	105
OAPI (OA)	101
SWITZERLAND (CH)	98
AUSTRIA (AT)	83
SWEDEN (SE)	80
MOROCCO (MA)	78

Offices of second filings	Number of filings
ITALY (IT)	74
PERU (PE)	60
IRELAND (IE)	55
PHILIPINNES (PH)	50
INDONESIA (ID)	40
COSTA RICA (CR)	38
FINLAND (FI)	38
ECUADOR (EC)	36
LUXEMBOURG (LU)	35
ICELAND (IS)	34
UKRAINE (UA)	30
HUNGARY (HU)	27
PORTUGAL (PT)	20
POLAND (PL)	19
ZIMBABWE (ZW)	18
CZECH REPUBLIC (CZ)	15
EGYPT (EG)	14
DOMINICAN REPUBLIC (DO)	12
GREECE (GR)	12
MALAYSIA (MY)	12
CHILE (CL)	11
ALGERIA (DZ)	8
ROMANIA (RO)	7
CUBA (CU)	6
CYPRUS (CY)	6
TURKEY (TR)	6
BULGARIA (BG)	5
KENYA (KE)	5
GUATEMALA (GT)	3
SLOVAKIA (SK)	3
EL SALVADOR (SV)	3
ZIMBABWE (ZW)	3
HONDURAS (HN)	2
MOLDOVA (MD)	2
NICARAGUA (NI)	1
SLOVENIA (SI)	1

Table 6 - Number of applications in the offices of second filings

1.2.4. Breakdown of filings by IPC codes

The figure below shows the most common relevant IPC codes present in the database.

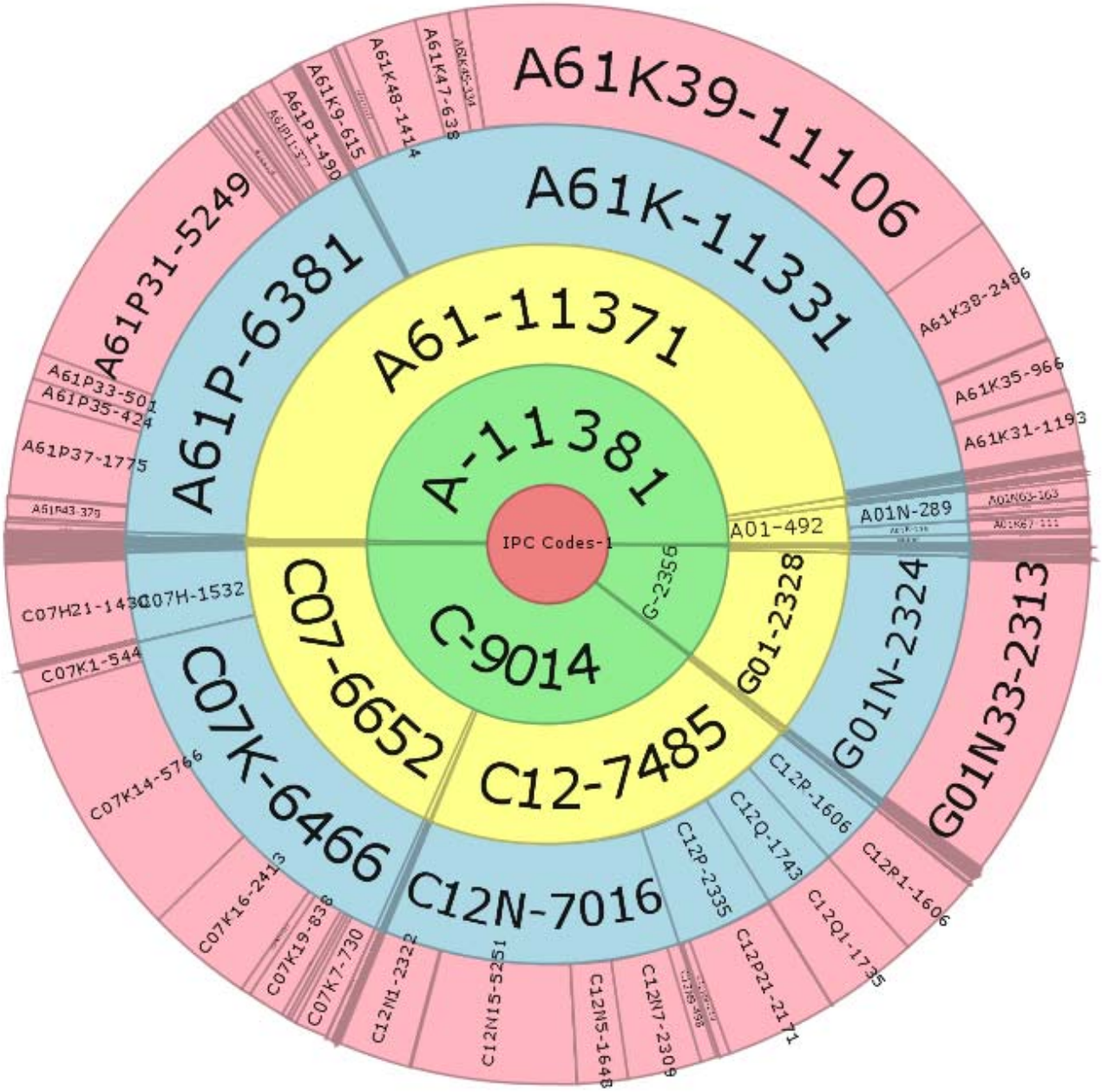


Figure 5 - Share of main IPC codes present in the whole database (IPC code – number of families in this class)

Details of the IPC codes can be found on the following webpage: http://www.wipo.int/ipcpub/

1.2.5. Analysis of applicants

The following graph shows the main applicants classified by the size of their patent portfolio.

Co-filings are counted for each co-owner. For instance, a patent application co-filed between US Government and GSK is counted once for US Government and once for GSK.

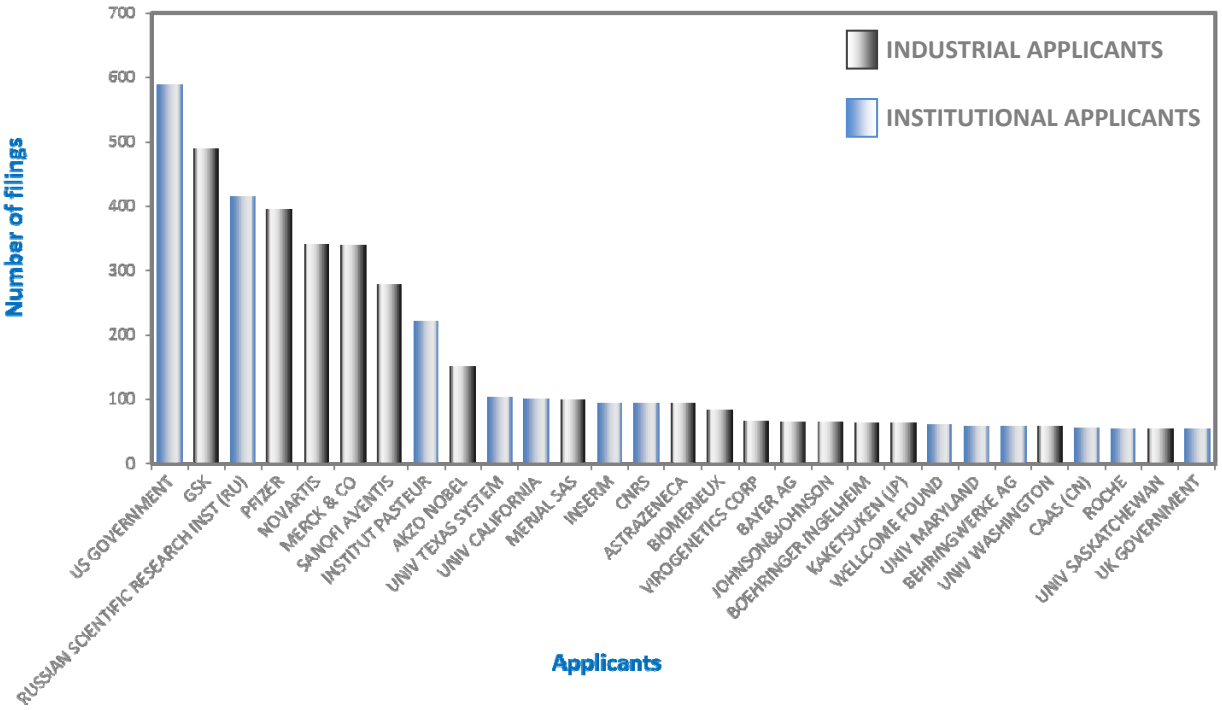


Figure 6 - List of main applicants (≥ 50 patent or patent applications)

The US Government laboratories and Russian Scientific Research Institutes dominate in terms of number of patent families. GSK, Novartis, Pfizer, Merck&Co and Sanofi-Aventis have a strong global position. It should be noted that this position may be explained by the mergers and acquisition strategy of these large pharmaceutical companies. To do these statistics, affiliates and subsidiaries were gathered under their parent company except in some cases. For example, Merial and Sanofi-Aventis were not grouped together because of the separation between animal and human health. These groupings were performed via a home-made database of mother companies and subsidiaries developed with Elsevier's business intelligence database[2], companies' websites, annual reports, business intelligence reviews and websites…

For more precision, the table below details this regrouping.

[2] http://www.elsevierbi.com/companies

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
US GOVERNMENT (US)	NIH; US DEPARTMENT OF AGRICULTURE; US ARMY; US DEPARTMENT OF VETERANS AFFAIRS; US DEPARTMENT OF HEALTH AND HUMAN SERVICES; US DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
GSK (UK)	AFFYMAX TECH NV; ALLEN AND HANBURYS LTD; BEECHAM GROUP LTD; BEECHAM LAB; BURROUGHS WELLCOME CO; CORIXA CORP; GLAXO GROUP LTD; GLAXO LAB LTD; GLAXO SMITHKLINE BIOLOGICALS SA; GLAXO WELLCOME INC; GLAXOSMITHKLINE BEECHAM BIOLOGICALS SA; ID BIOMEDICAL CORP; ID VACCINE;INTELLIVAX INC; PLIVA HRVATSKA D O O; RIBI IMMUNOCHEM RESEARCH INC; SMITHKLINE FRENCH CANADA LTD; SMITHKLINE RIT BE; SMITHKLINE BEECHAM ANIMAL HEALTH; SMITHKLINE BEECHAM CORP; SMITHKLINE BEECHAM BIOLOGICALS SA; SMITHKLINE BEECHAM PHARMA GMBH; SMITHKLINE BIOCHEMICALS SA; SMITHKLINE BIOLOGICALS SA; SMITHKLINE CORP; SMITHKLINE R I T
RUSSIAN SCIENTIFIC RESEARCH INST (RU)	FGU research centers (e.g. FGU VNIIZZh Federal'noe Gosudarstvennoe Uchrezhdenie "Federal'nyi Tsentr Okhrany Zdorov'ya Zhivotnykh", Russia)
PFIZER (US)	AGOURON PHARMA; ALPHARMA AS; AMERICAL CYANAMID CO; AMERICAN HOME CORP PROD; APOLLON INC; COLEY PHARM GMBH; COLEY PHARM GROUP INC; CYANAMID IBERICA SA; CYANAMID WEBSTERS PTY LIMITED; DIMMINACO AG; EMBREX INC; CARLO ERBA SPA; FORT DODGE AUSTRALIA PTY; FORT DODGE LAB INC; FORT DODGE VETERINARIA SA; GENETICS INSTITUTE INC; HAPTOGEN LTD; EURALAB LTD WYETH; PARKE DAVIS AND CO; PFIZER INC; PFIZER PRODUCTS INC; PFIZER VACCINES LLC; PHARMACIA AND UPJOHN CO LLC; PHARMACIA SPAIN; POWDERJECT RES LTD; POWDERJECT VACCINES INC; POWDERMED LTD; PRAXIS BIOLOGICS INC; SEARLE AND CO; THE UPJOHN COMPANY; WARNER LAMBERT CO; WYETH CORP; WYETH DRUGS CO LTD; WYETH FARMA S A; WYETH FORT DODGE LAB; WYETH HOLDING CORP; WYETH HOME PRODUCTS CORP; WYETH PHARMACEUTICALS
NOVARTIS (CH)	BIOCINE SCLAVO SPA; BIOCINE SPA; CETUS ONCOLOGY CORP; CHIRON BEHRING GMBH AND CO; CHIRON CORP; CIBA CORNING DIAGNOSTICS CORP; CIBA GEIGY AG; CIBA LTD; EVANS VACCINES; HEXAL PHARMA GENTECHNIK GMBH; IMUTRAN LTD; NEUTEC PHARMA LTD; NEUTEC PHARMA PLC; NOVARTIS AG; NOVARTIS ANIMAL HEALTH INC; NOVARTIS BIOTECHNOLOGY WUHAN; NOVARTIS ERFIND VERWALT GMBH; NOVARTIS PHARMA GMBH; NOVARTIS VACCINES AND DIAGNOSTICS INC; NOVARTIS VACCINES INST FOR GLOBAL HEALTH SRL; PATHOGENESIS CORP; SANDOZ AG; SANDOZ PHARMACEUTICALS CORP; SANDOZ SA; SCALVO SPA; SCLAVO BIOCINE SPA; VIAGENE INC
MERCK & CO	ANGELETTI P INST RICHERCHE BIO (IL); BANYU PHARMA CO LTD; INTERVET AUSTRALIA PTY LIMITED; INTERVET INC; MERCK AND CO INC; MERCK PATENT GMBH; MERCK SERONO BIODEVELOPMENT SA; MERCK SHARP AND DOHME CORP; ORGANON TEKNIKA BV; SCHERING CORP; SCHERING PLOUGH ANIMAL HEALTH CORP; SCHERING PLOUGH CORP; SCHERING PLOUGH VETERINARY CORP; SHARP AND DOHME INC; SHERING PLOUGH LTD; SIBIA NEUROSCIENCES INC

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
SANOFI AVENTIS (FR)	ACAMBIS INC; SANOFI PASTEUR SA; ACAMBIS RES LTD; AVENTIS PASTEUR INC; AVENTIS PHARMA DEUTSCHLAND GMBH; AVENTIS PHARMA SA; CHINOIN GYOGYSZER ES VEGYESZET; CONNAUGHT LAB INC; CONNAUGHT LAB LTD; CONNAUGHT LAB SWIFTWATER; HOECHST AG; HOECHST ROUSSEL VET GMBH; HOECHST UK LTD; MERIEUX ORAVAX; ORAVAX INC; AVENTIS PASTEUR; PASTEUR MERIEUX; PASTEUR MERIEUX CONNAUGHT; PASTEUR MERIEUX SERUM ET VACCINS SA; PASTEUR MERIEUX SERUM ET VACCINS SA; PASTEUR SANOFI; PEPTIDE THERAPEUTICS LTD; PHYLAXIA SANOFI OLTOANYAGTERME; RICHARDSON MERRELL INC; SANOFI ANIMAL HEALTH INC
INSTITUT PASTEUR (FR)	INSTITUT PASTEUR; INST PASTEUR D ALGERIE; INST PASTEUR DE LILLE; INST PASTEUR DE PARIS; INST PASTEUR DE TUNIS; INST PASTEUR OF SHANGHAI; PASTEUR INST OF BRUSSELS
AKZO NOBEL (NL)	AKZO N V; AKZO NOBEL; AKZO NOBEL COATINGS INT BV; ICI LTD; ICI TASMAN LTD
UNIV TEXAS SYSTEM (US)	BOARD OF REGENTS OF THE UNIVERSITY OF TEXAS SYSTEM; TEXAS HEALTH SCIENCE CENTER UNIVERSITY; UNIV TEXAS MEDICAL SCHOOL
UNIV CALIFORNIA (US)	UNIV CALIFORNIA; UNIV SOUTH CALIFORNIA
MERIAL SAS	MERIAL; MERIAL SELECT INC
INSERM (FR)	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE; INSERM; INST NAT SANT RECH MED; INSERM TRANSFERT SA
CNRS (FR)	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS)
ASTRAZENECA (UK)	ARROW THERAPEUTICS LTD; ASTRA AB; ASTRAZENECA AB; CAMBRIDGE ANTIBODY TECHNOLOGY LTD; MEDIMMMUNE VACCINES INC; MEDIMMUNE INC; SYMBICOM AB
BIOMERIEUX (FR)	BIOMERIEUX SA; INSTITUT MERIEUX; MERIEUX ORAVAX; RHONE MERIEUX
VIROGENETICS CORP	VIROGENETICS CORP
BAYER AG (DE)	BAYER AG; BAYER ANIMAL HEALTH GMBH; BAYER HEALTHCARE AG; BAYER PHARMACEUTICALS CORP; FARBENFABRIKEN BAYER AG; HANKUK BAYER CHEMICAL CO LTD; MILES LABORATORIES INC; MITSUI PHARMACEUTICALS; MOLECULAR DIAGNOSTICS INC; SCHERING AG; SCHERING PLOUGH ANIMAL HEALTH
JOHNSON&JOHNSON (US)	ALZA CORP; BERNA BIOTECH AG; CENTOCOR INC; CRUCELL HOLLAND BV; DEPUY MITEK INC; JANSSEN ALZHEIMER IMMUNOTHERAP; JOHNSON AND JOHNSON CONSUMER; ORTHO DIAGNOSTICS; ORTHO MCNEIL PHARM INC; ORTHO PHARMACEUTICAL CORPORATION; SBL VACCIN AB; SCHWEIZ SERUM AND IMPFINSTITUT; SCIOS INC; SCIOS NOVA INC

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
BOEHRINGER INGELHEIM (DE)	BOEHRINGER INGELHEIM CORP; BOEHRINGER INGELHEIM INTERNATIONAL GMBH; BOEHRINGER INGELHEIM NOBL LABORATORIES INC; BOEHRINGER INGELHEIM PHARMA; BOEHRINGER INGELHEIM VETMEDICA GMBH
KAKETSUKEN (JP)	CHEMO SERO THERAPEUTIC RESEARCH INST; JURIDICAL FOUNDATION CHEMO SERO THERAPEUTIC RESEARCH INST
WELLCOME FOUND (UK)	THE WELLCOME FOUNDATION LTD
UNIV MARYLAND (US)	UNIV MARYLAND; UNIV MARYLAND BALTIMORE; UNIV MARYLAND COLLEGE PARK; UNIV MARYLAND BIOTECHNOLOGY INST
BEHRINGWERKE (DE)	BEHRINGWERKE AG; BEHRINGWERKE AKTIENGESELLSCHAFT
UNIV WASHINGTON (US)	UNIV WASHINGTON
CAAS (CN)	CAAS; VETERINARY RES INST ; HARBIN VETERINARY RES INST CHINESE ; LANZHOU VETERINARY RES INST; SHANGHAI VETERINARY RES INST BIOTECHNOLOGY RESEARCH INSTITUTE CAAS
ROCHE (CH)	BOEHRINGER MANNHEIM; CHUGAI PHARMACEUTICAL; F HOFFMANN LA ROCHE; GENENTECH; IGEN INT ; MIRUS ; ROCHE DIAGNOSTICS; ROCHE VITAMINS; SYNTEX; TANOX; TANOX BIOSYSTEM
UNIV SASKATCHEWAN (CA)	UNIV SASKATCHEWAN
UK GOVERNMENT (UK)	UNITED KINGDOM GOVERNMENT; SECRETARY OF DEFENCE BRITANNIC; NATURAL ENVIRONMENTAL RESEARCH

Table 7 - Applicants and their affiliates (≥ 50 patent or patent applications)

For the 30 main applicants in term of filings, the graphs below detail the preferred office of first and second filings

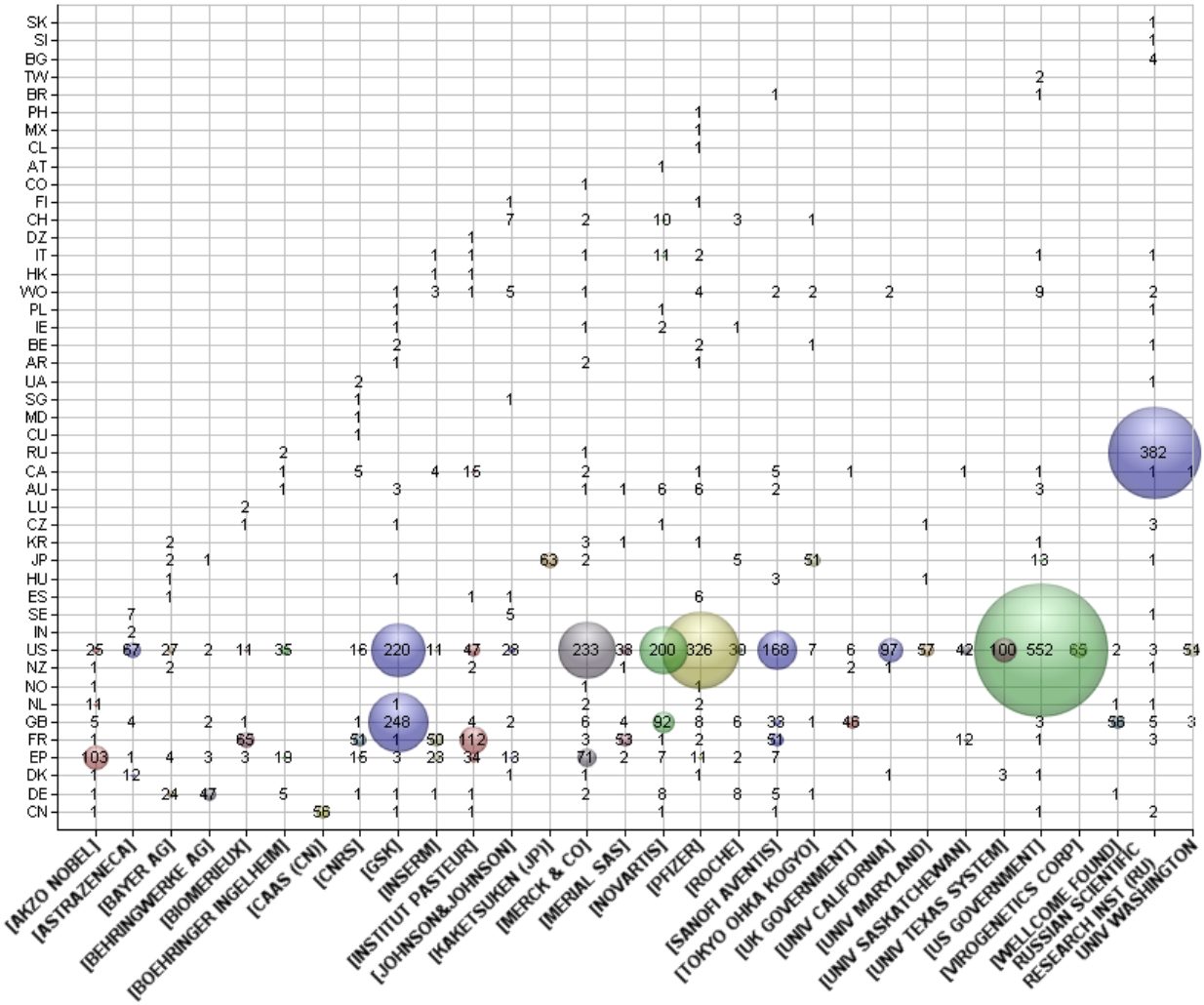


Figure 7 - Main applicants' preferred offices of first filings

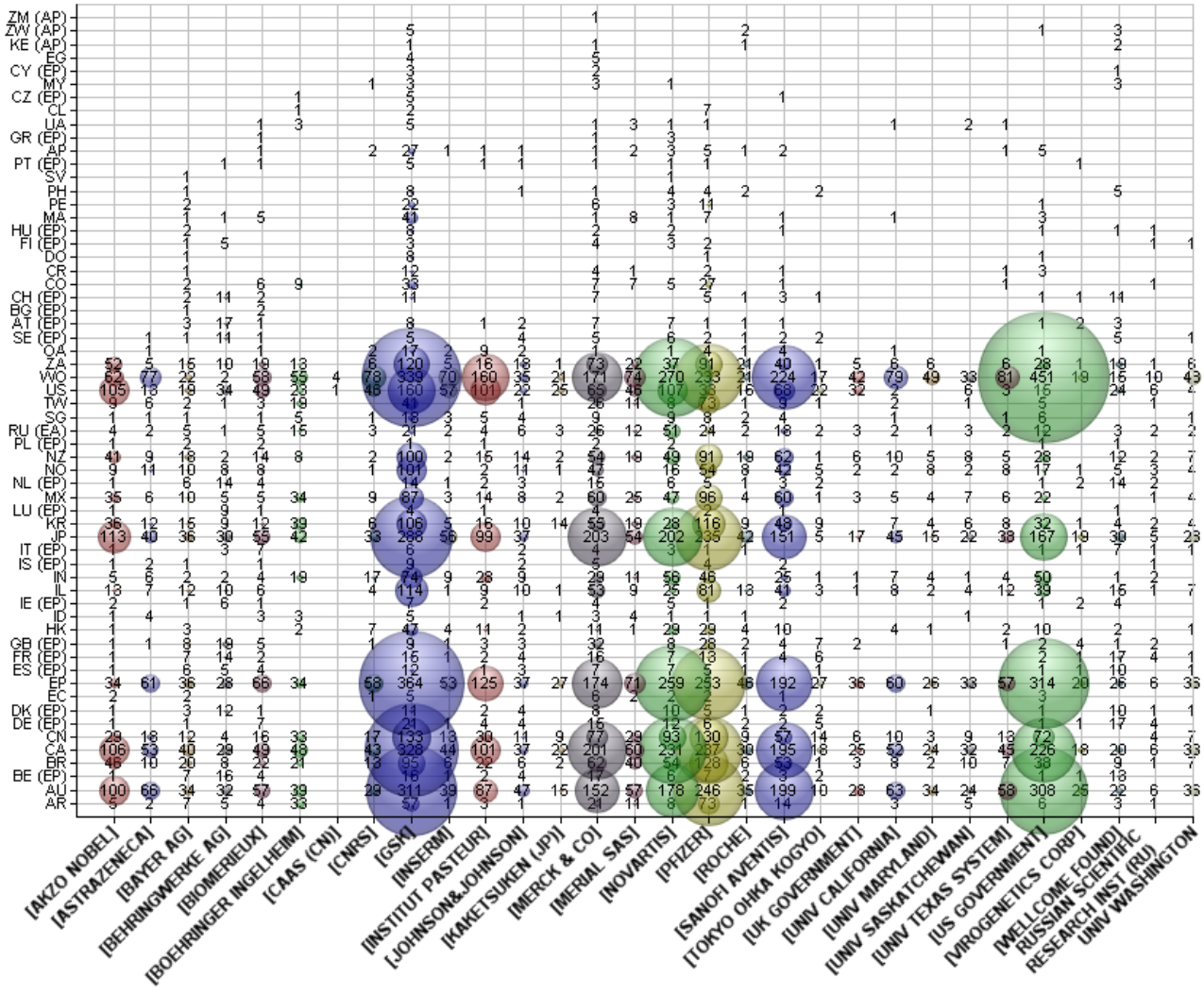


Figure 8 - Main applicants' preferred offices of second filings

The following graph details the evolution of the number of first filings by applicant since 1950. Such a graph allows the identification of pioneer or emerging applicants in terms of filings. Before, 1950, only 5 filings were done (one for Merck & Co (via SHARP&DOHME) in 1944, 3 for Pfizer in 1946 and 1 for Pfizer in 1949).

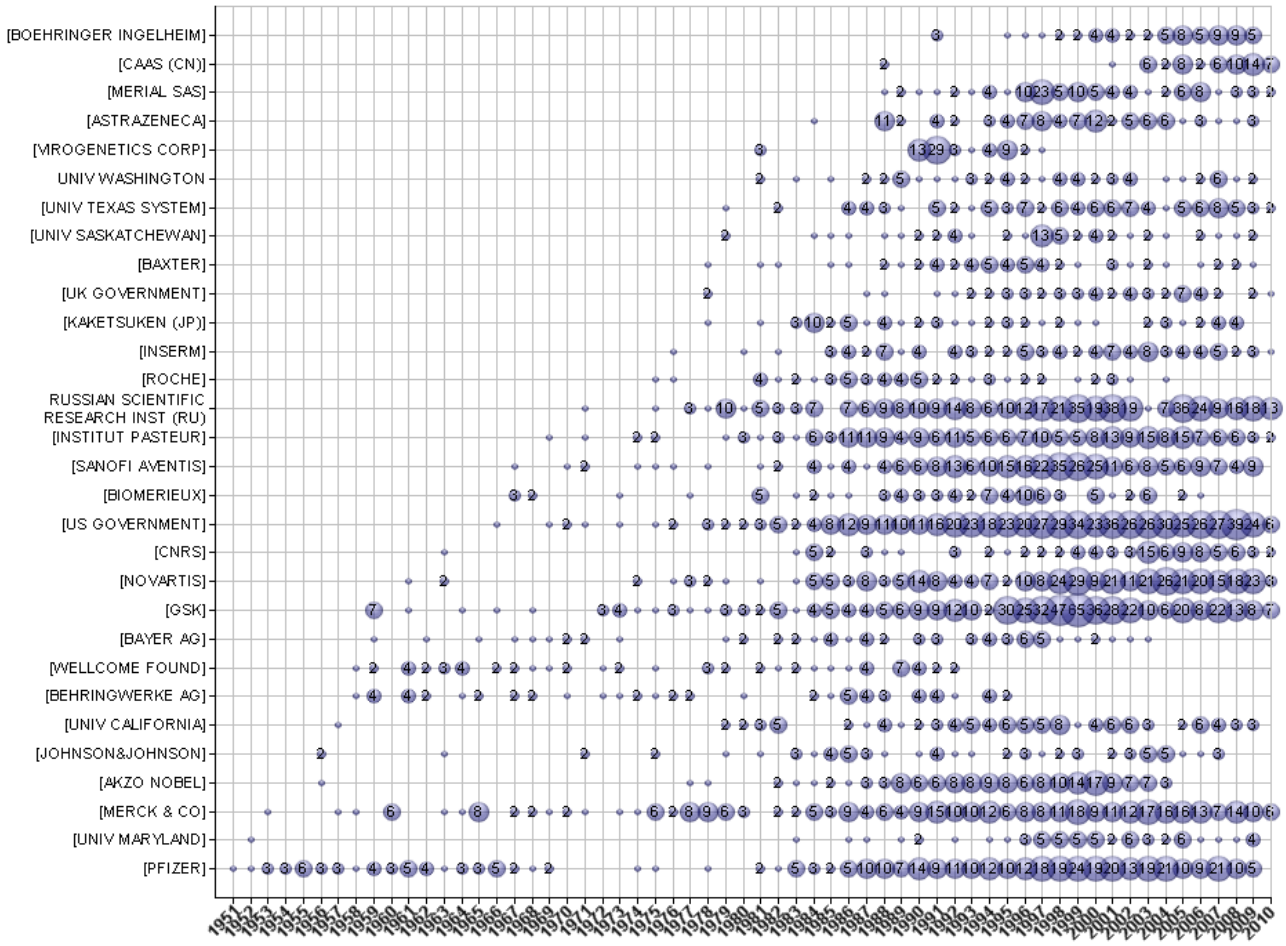


Figure 9 - Evolution of main applicants' filings by year of first filing

1.2.6. Brazilian focus

This section focuses on the 75 patent families having Brazil as office of first filing.

The figure below represents the evolution of these filings:

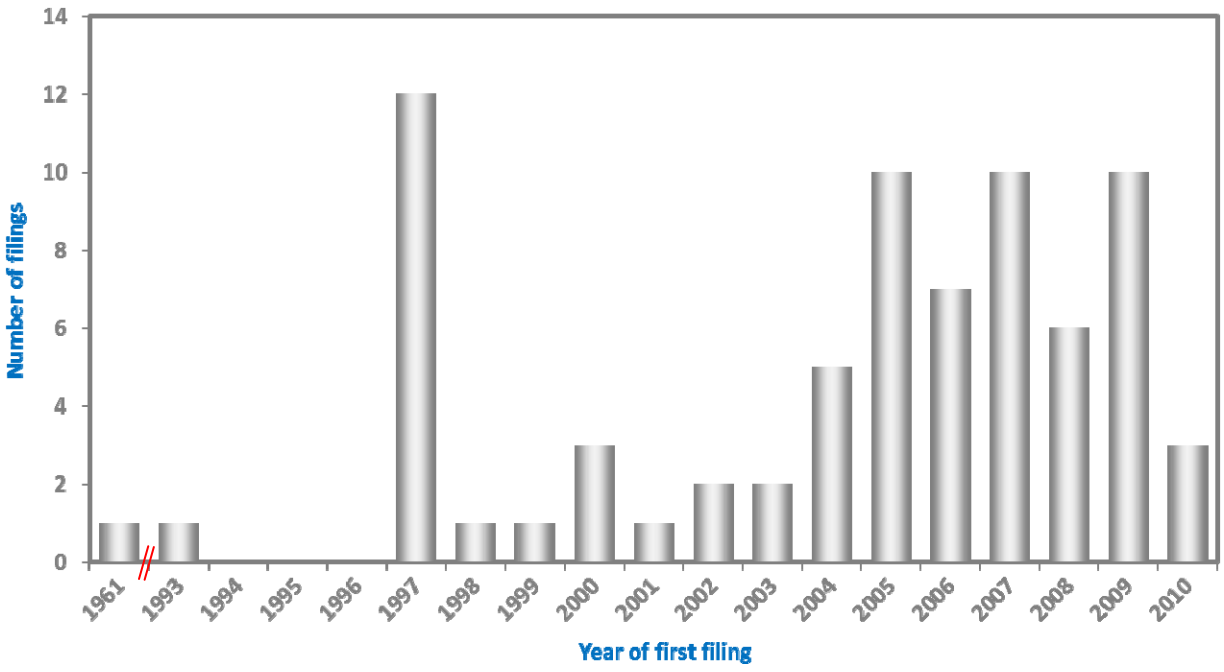


Figure 10 - Evolution of Brazilian first filings

Since 2005, each year Brazilian first filings have been between 5 and 10 applications.

The choice of offices of second filing is represented below:

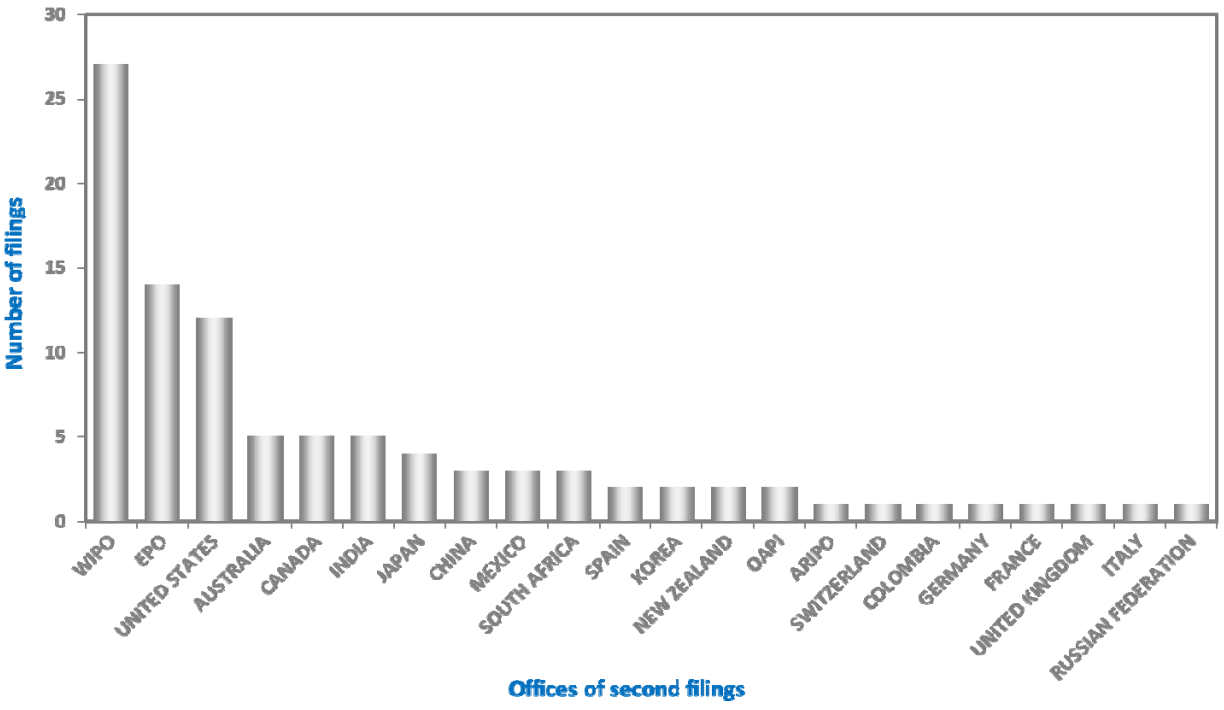


Figure 11 - Offices of second filings of Brazilian priority applications

In addition to the WIPO, the United States and the EPO were the main choices as Office of Second Filing.

The following graph shows the main applicants classified by the size of their patent portfolio.

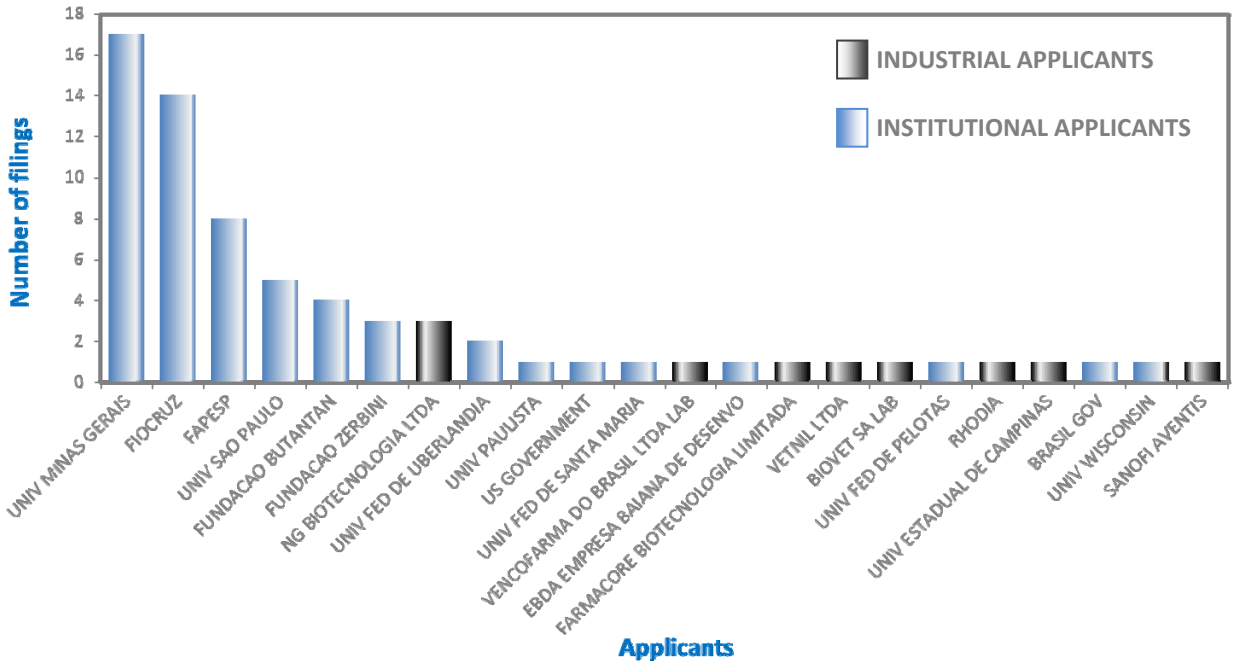


Figure 12 - List of main applicants selecting Brazil as office of first filing

Most of main applicants were Brazilian institutional applicants.

1.2.7. Indian focus

This section focuses on the 69 patent families having India as office of first filing. Contrary to the Brazilian patent office, Indian patent office only published electronically granted patent and not patent applications which therefore underestimates the number of filings.

The figure below represents the evolution in filing. This figure shows that the number of patents is increasing since the beginning of the 2000s. The decreasing phenomena since 2007 might be explained by the grant lag of the Indian patent office which is about 3-4 years.

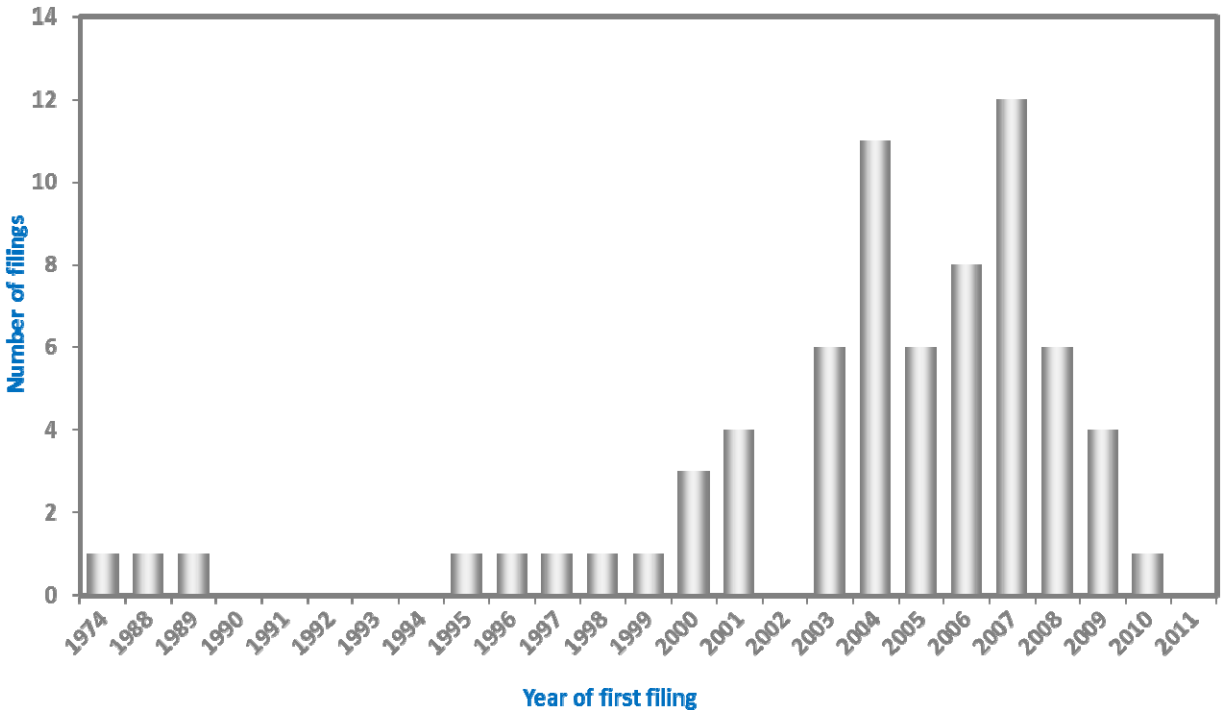


Figure 13 - Evolution of Indian first filings

The choice of Office of Second Filing is represented below:

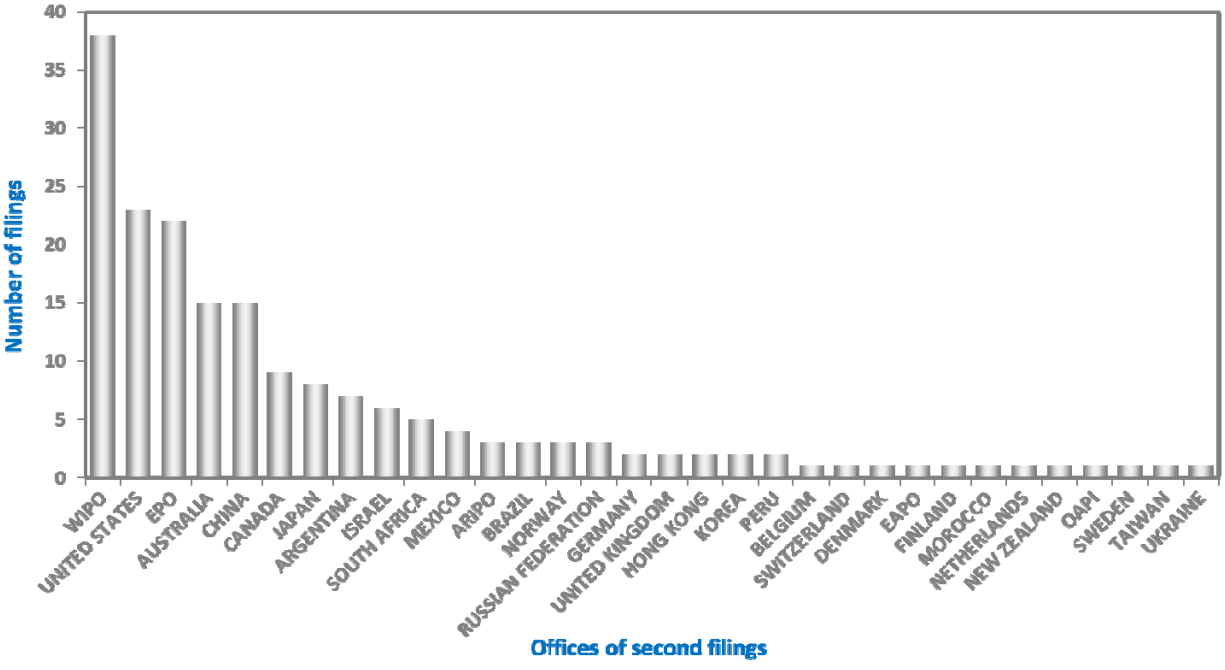


Figure 14 - Offices of second filings of Indian priority applications

In addition to the WIPO, the United States, the EPO, Australia and China were the main choices as office of second filing.

The following graph shows the main applicants classified by the size of their patent portfolio.

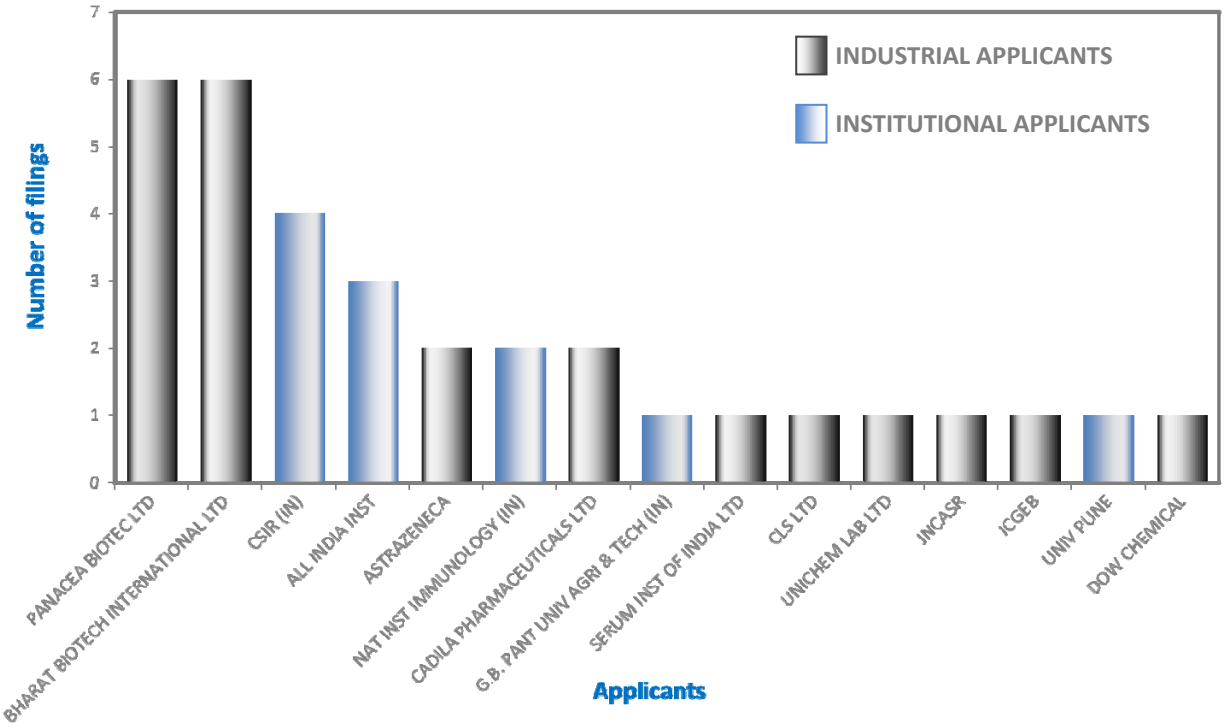


Figure 15 - List of main applicants selecting India as office of first filing

Except some important Indian Research Institutes (CSIR, ALL INDIA), main applicants are Indian biotech companies.

1.2.8. Chinese focus

This section focuses on the 1133 patent families having China as office of first filing.

The figure below represents the evolution in filing. This figure shows that, as of 2003, massive filings stemmed from China reaching in 2010 almost 180 patent applications.

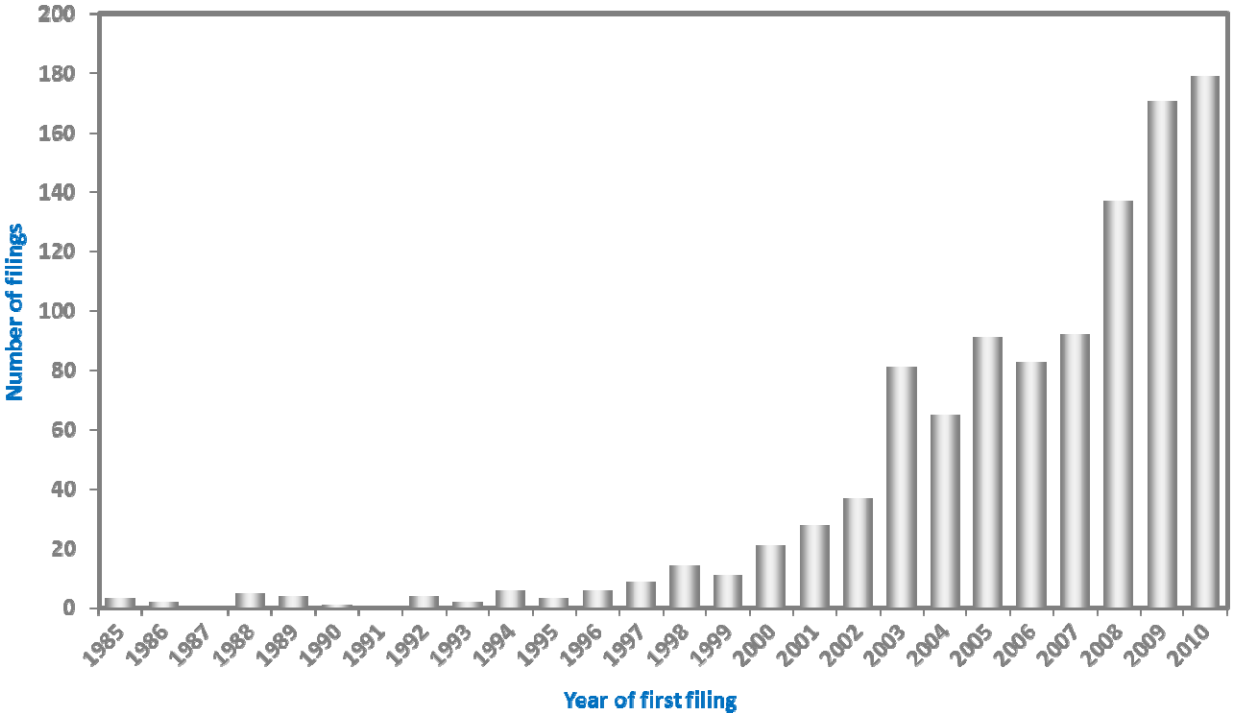


Figure 16 - Evolution of Chinese first filings

The choice of Office of Second Filing is represented below:

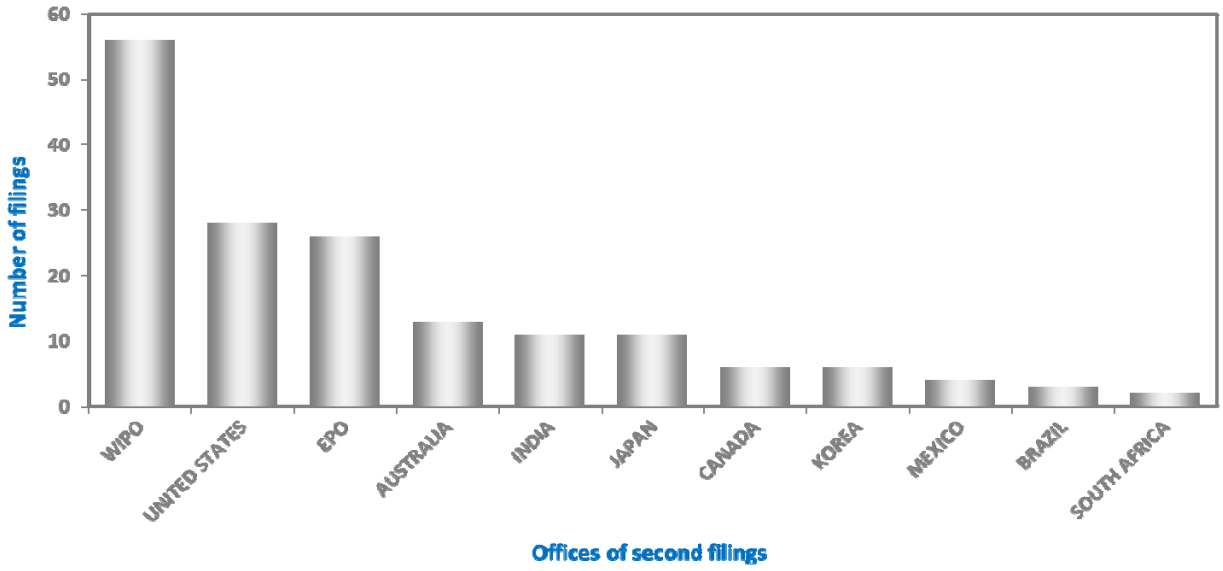


Figure 17 - Offices of second filings of Chinese priority applications

It is important to note here that very few second filings stemmed from Chinese applicants. When extended, the United States and EPO dominated as offices of second filings for Chinese patent applications. Note that other countries such as India, Japan and Australia were also chosen as offices of second filings.

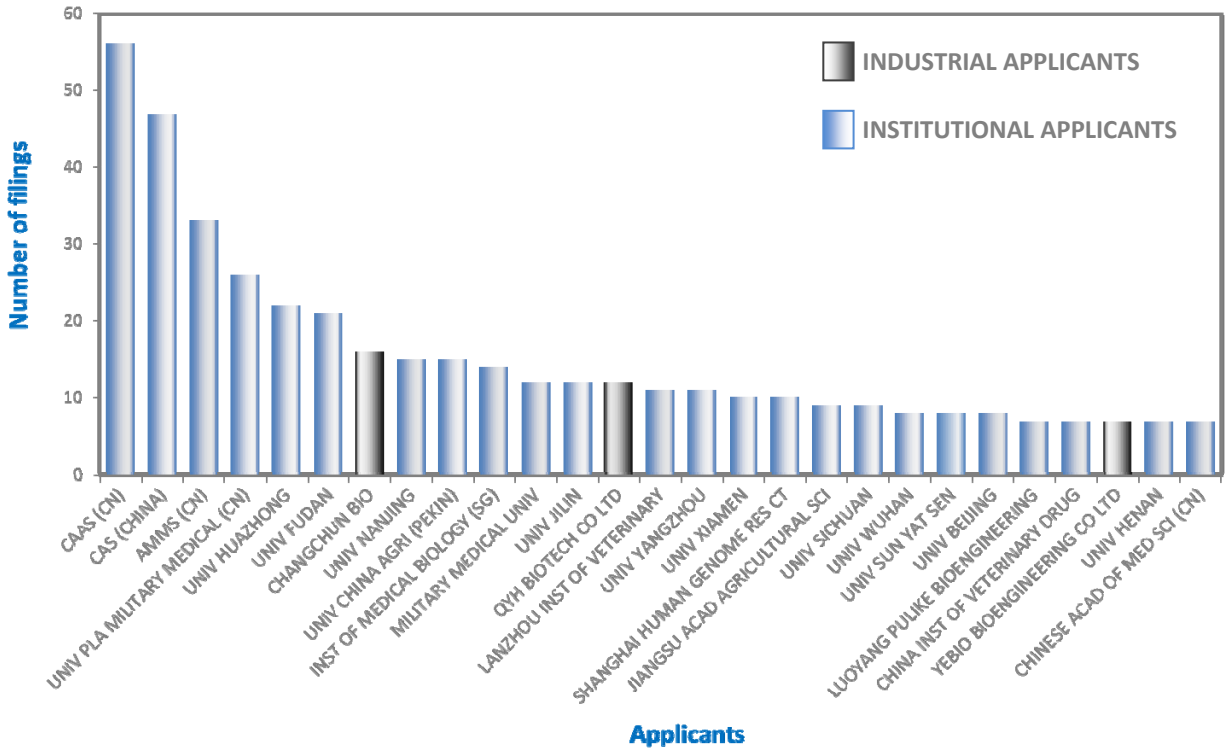


Figure 18 - List of main applicants selecting China as office of first filing

Most of main applicants were Chinese institutional applicants from the Chinese Academy of Sciences or from Chinese Universities. The few industrial applicants were Chinese Biotech companies.

China shows a different behaviour regarding patent applications in the field of vaccines compared to Brazil and India that have a more similar tendency.

2. Active ingredients of human pneumococcal conjugate vaccines

2.1. Search methodology

2.1.1. Introduction

This section describes the search methodology developed to retrieve patents and patent applications claiming active constituents of human conjugate vaccines against *Streptococcus pneumoniae*. The narrative of this search history shows how the search was performed. It describes specific tools, databases, and challenges encountered and methods of circumventing. The search consisted generally of the use of combinations of keyword and classification searches, the intellectual review of search results for refining the queries and excluding irrelevant documents, and a final benchmarking of the search strategy through inclusion of documents cited in relevant documents. This section also discusses the limits of the use of patent classification codes (IPC, ECLA…) when looking for patents and patent applications dealing with active constituents of human conjugate vaccines against *Streptococcus pneumoniae*.

2.1.2. Methodology and databases

A background study was first performed by looking at some literature on pneumococcal conjugate vaccines in order to collect keywords to build the patent queries and especially to help us determine the relevance of a patent family compared to another one, given that only patents describing "active constituents" had to be taken into account. Reviews such as Webster et al. BMC Public Health 2011, 11(Suppl 3):S26 were useful to make a list of keywords as well as general articles found on the Internet about the disease and its related vaccines[3]. A list of useful links can be found at the end of the section.

As a next step, a review of patent classification was carried out to identify patent classification codes related to pneumococcal antigens.

With the list of keywords and patent classification codes established such as described, queries were built and run into Patbase database (Minesoft ™).

[3] http://www.who.int/wer/2007/wer8212.pdf

http://en.wikipedia.org/wiki/Pneumococcal_conjugate_vaccine

2.1.3. Background study

2.1.3.1 Review of the literature

The bacterium responsible for Pneumonia was initially named *Pneumococcus* when it was discovered in 1881, to be then termed *Diplococcus pneumoniae* in 1920 http://en.wikipedia.org/wiki/Streptococcus_pneumoniae - cite_note-2and renamed as *Streptococcus pneumoniae* in 1974[4].

In addition to Pneumonia, *S. pneumoniae* causes many types of pneumococcal infections such as acute sinusitis, otitis media, meningitis (one of the most common causes of bacterial meningitis in adults), bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess.

A conjugate, or conjugated vaccine, is a type of vaccine that is created by joining an antigen to a protein molecule. It usually consists of (but is not limited to) a polysaccharide antigen combined with a carrier protein. The protein part of a conjugate vaccine acts as a carrier for the antigen, and serves to magnify the immunological response to it.

Pneumococcal conjugate vaccines (PCV) are used to protect infants and young children. There are currently three PCV vaccines available on the global market: Prevnar (called Prevenar in some countries), Synflorix and Prevnar 13.

Prevnar (heptavalent vaccine) contains the cell membrane sugars of seven serotypes of pneumococcus, conjugated with Diphtheria proteins. It was manufactured by Wyeth (now Pfizer). The key patent family related to Prevnar is represented by US 5,360,897. It was approved by the U.S. Food and Drug Administration in February 2000[5].

Synflorix (decavalent vaccine) is produced by GlaxoSmithKline (GSK) contains ten serotypes of pneumococcus (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F) which are conjugated to a carrier protein. It was approved by the European Medicines Agency in January 2009 and received market approval of European Commission in March 2009. Synflorix is covered by the key patent family of EP2277535[6].

Prevnar 13 (triskaivalent vaccine), produced by Pfizer, contains thirteen serotypes of pneumococcus (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) which are conjugated to a carrier protein. Prevnar 13 was approved by the U.S. Food and Drug Administration in February 2010.

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[4] See, e.g.: http://www.who.int/wer/2007/wer8212.pdf

http://en.wikipedia.org/wiki/Pneumococcal_conjugate_vaccine

[5] http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm137057.htm

[6] http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10039.htm

List of patent studies

http://www.who.int/vaccine_research/documents/IVR_IPR_Tokyo_Session2_McDiarmid_presentation.pdf

From this background study, a list of keywords was established.

Keywords related to *Pneumococcus*: *pneumococcus*, *pneumococci*, pneumococcal, *Streptococcus pneumoniae, S. pneumonia(e), Diplococcus pneumonia(e), D. pneumonia(e)*

Keywords related to vaccines: Vaccin(es), vaccination, vaccinating, antigen(s), antigenic, immunogen(s), immunogenic, immunise, immunisation, immunising, immunize, immune response

Keywords related to conjugate: conjugate(d), glycoconjugate(s), as well as the words fused, fusion, linked, coupled, bound, associat(ed), attach(ed), merg(ed), chimer(s), chimeric; close to the words protein(s), peptide(s), peptidic, carrier(s) (and all related keywords)

Keywords related to commercialized human pneumococcal conjugate vaccines: Prev(e)nar, Synflorix

2.1.3.2 Review of relevant classification codes

By screening the international, European, American and Japanese patent classifications, the codes corresponding to medicinal preparations containing antigens or antibodies of Streptococcus were collected. The following codes were thereby identified:

International Patent Classification (IPC):

A61K39/09

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/09 Streptococcus

A61K39/385

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

US Patent Classification (USPC):

424/237.1

[0] 424 Drug, bio-affecting and body treating compositions
[1] 424/184.1 Antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-mediated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.). Subject matter involving an antigen, an epitope, or another immunospecific immunoeffector, such as an immunospecific vaccine, an immunospecific stimulator of cell-mediated immunity, an immunospecific tolerogen, or an immunospecific immunosuppressor.

[2] 424/234.1 Bacterium or component thereof or substance produced by said bacterium (e.g., Legionella, Borrelia, Anaplasma, Shigella, etc.). Subject matter involving a bacterium, a component of a bacterium, or a substance produced by a bacterium.
[3] 424/236.1 Toxin or toxoid, except endotoxin (e.g., exotoxin, enterotoxin, etc.). Subject matter involving a bacterial toxin or toxoid, except an endotoxin.
[4] 424/237.1 Staphylococcus or Streptococcus. Subject matter wherein the toxin or toxoid originates from a bacterium of the genus Staphylococcus or from a bacterium of the genus Streptococcus.

424/193.1

[0] 424 Drug, bio-affecting and body treating compositions
[1] 424/184.1 Antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-mediated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.)
[2] 424/193.1 Conjugate or complex. Subject matter involving a conjugate or a complex.
(1) Note. A conjugate is taken to mean a coupling of one substance to another via covalent means, either directly via a covalent bond or indirectly via a chemical linking group.
(2) Note. A complex is taken to mean a coupling of one substance to another via noncovalent means (e.g., via adsorption).
(3) Note. The conjugates and complexes provided for in this subclass and indented subclasses are often of the hapten-carrier type. A hapten is a substance that can bind an antibody, but which cannot induce production of an antibody unless it is coupled to a carrier that is immunogenic. A hapten is usually, but not always, of low molecular weight. Common carriers, for vaccination purposes in humans, are tetanus toxoid and diphtheria toxoid.

European classification (ECLA):

A61K39/09, A61K39/09A

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/09 [N: Lactobacillales, e.g. Aerococcus, Enterococcus, Lactobacillus, Lactococcus], Streptococcus
[3] A61K39/09A [N: Streptococcus]

A61K39/385

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

Japanese File-Index (Japan FI):

A61K39/09

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/09 Streptococcus

A61K39/385
[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

2.1.4. Search strategy

The patent search started by evaluating the number of patents and patent applications dealing with *Streptococcus pneumoniae*. Therefore, patent queries using truncations (mentioned by a * in the queries) of keywords related to *Streptococcus pneumoniae* were built. As the core of the invention is described in the title, abstract and claims of the patent family members, the queries were carried out in these fields (e.g. TAC in Patbase).

1.1.1.1. Keyword-based queries

QUERY 1/ TAC=(pneumonia* OR pneumoco*)

This query led to 7162 INPADOC families as search results. Most of the patent families did not refer to *Streptococcus pneumoniae* but to *Mycoplasma pneumonia(e)*, *Klebsiella pneumonia(e), Chlamydia (ou chlamydophylla) pneumonia(e)*… The perimeter of search was thereby narrowed by specifying the genus of the bacteria or at least the abbreviated terminology (e.g *S. pneumoniae*).

QUERY 2/ TAC=(((S OR strepto*) WF1 pneumonia*) OR pneumococ*)

"WF1" means "one word before"

This query led to 2429 INPADOC families as search results. The families were related to *Streptococcus pneumoniae* but not yet to vaccines because many patents claimed antibiotics, diagnostic tests, methods of culture… The next step was therefore to limit the results to patent families claiming vaccines.

QUERY 3/ (QUERY 2) AND TAC=(vaccin* OR antigen* OR immunogen* OR immunis* OR immuniz*)

This query led to 1058 INPADOC families as search results. At this stage, there was a mix of patent families claiming conjugate vaccines and other type of vaccines as well as diagnostic methods, or therapeutic antibodies. It was therefore necessary to introduce a limitation to conjugate vaccines.

QUERY 4/ (QUERY 3) AND TAC=(carrier* OR conjugat*)

This query resulted in a list of 661 INPADOC families as search results. However, the set of results showed too much noise,i.e.e a high fraction of irrelevant patents because the keyword "carrier" also retrieved patent families related only to the delivery of vaccines. At this stage, it was therefore decided to suppress it and to use it later, associated with other keywords.

QUERY 5/ (QUERY 3) AND TAC=(conjugat*)

This query provided 396 INPADOC families as search results. However, some patent families did not refer to conjugate vaccines but to vaccines conjugated with pharmaceutical carriers to improve their

delivery or to immunoconjugates (antibodies conjugated to chemical entities for a therapeutic use). Queries were therefore built to remove these patents (QUERY 6, QUERY 7).

QUERY 6/ (QUERY 5) AND TAC=(conjugat* W10 pharmaceutic*)

"W10" means "10 words around".

This query led to 55 INPADOC families as search results. A review of these patent families was performed in order to distinguish these claiming both a conjugate pneumococcal vaccine and vaccines conjugated with pharmaceutical carriers, and these claiming only vaccines conjugated with pharmaceutical carriers.

The patent families not within the scope of this study were stored in a folder in order to remove them afterwards.

QUERY 7/ (QUERY 5) AND TAC=immunoconjugat*

This query led to 15 INPADOC families as search results. All these patents did not refer to conjugate vaccines except one (US5785973) that used the term "immunoconjugate" to name a conjugate vaccine. When reviewing these patent, an « extended patent family » filed by IMMUNOMEDICS was identified as being outside the scope of the study. This "extended family" was referenced as "VLF30687837 » in Patbase. It gathered 95 patent families and 23 of them were brought by QUERY 5.

The patent families not entering in the scope of this study were stored in a folder in order to remove them afterwards.

At this stage, a review of the set of results brought by QUERY 5 but without the patent families identified as out of the scope of the study (and stored in the folder "patent families to be removed") was performed.

QUERY 8/ (QUERY 5) AND NOT RF= patent families to be removed 1

"RF" means "Recorded Folder"

This query led to 357 INPADOC families. The review of these patent families highlighted many patents claiming a formulation of conjugate vaccines against meningitis combining conjugate vaccines of several agents responsible for this disease (e.g. Nesseiria antigens, pneumococcal antigens, hib antigens…). 37 patents were therefore eliminated and stored in the folder "patent families to be removed" in order to remove them afterwards.

Among the other patent families brought by QUERY 8, many did not correspond to active constituents of pneumococcal conjugate vaccines but they described:

-Regimens of immunisation (e.g. US2008026002);

-Methods of administration and delivery systems (e.g. US2007009542; US2002094338; US2005070876; US2002010428; US2008066739; US2002038111);

-Administration of pneumococcal conjugate vaccines in the regimens of vaccination against other pathogens (e.g. US2009047353 - The method of claim 46, wherein the medicament is administered to a patient at substantially the same time as a pneumococcal conjugate vaccine);

- Description of vaccine formulations (e.g. US2002107265);

- Composition of multivalent vaccines in which additional antigens are added and among these potential additional antigens, pneumococcus is mentioned (e.g. US2007161088; US2006121059);

- Purification processes of antigens that could be used in the development of conjugate vaccines (e.g. US2008286838; CN102094053);

- Production of therapeutic antibodies (e.g. WO05070458; US2009191217; WO10094720);

- Methods of culture of microorganisms that could be used in the process of manufacturing pneumococcal conjugate vaccines (e.g. US2010290996);

- Detection methods such as evaluation of the efficacy of a pneumococcal conjugate vaccine (e.g. US2005260694; RU2027190, US4308026; US4185084; US2005208608);

- Adjuvants (US2005158329; US2009010964; US2004047882; US6262029);

- Vaccines against allergy based on pneumococcal conjugate vaccines (e.g. WO0074716);

- Methods using Pneumococcus polysaccharide conjugates for use against other infectious diseases (e.g. US2003099672; WO0062802);

- Methods that do not require conjugation to a carrier protein (e.g. US2009136547); immunomodulators (US2004156857; US5985264; WO11041691).

All the patent families corresponding to such inventions were eliminated and stored in the folder “patent families to be removed” in order to remove them afterwards.

At this stage, the folder “patent families to be removed” contained 248 patent families and it remained 148 patent families of QUERY 5 that dealt with active constituent of pneumococcal conjugate vaccines.

As QUERY 5 was analyzed and a first pool of relevant patent families was constituted, new queries were built to find out if other patent families not mentioning “conjugate” but answering to the description of “conjugate vaccines”, by using other keywords, could be identified. The first step consisted in combining the words describing a conjugation such as fused, fusion, linked, coupled, bound, associat(ed), attach(ed), merg(ed), chimer(s), chimeric (and all related keywords) with these describing the conjugated molecule such as protein(s), peptide(s), peptidic or carrier(s).

QUERY 9/ ((QUERY 3) AND TAC=((fuse~ OR link* OR coupl* OR chimer* OR associat* OR attach* OR merg* OR bound) W10 (protein* OR peptid* OR carrier*))) AND NOT (QUERY 5)

“~”: “fuse~” finds fuse, fused, fusing

This query led to 159 INPADOC families but after reviewing them, only 14 were relevant (WO10079464, WO09106085, US2010092504, US2002064533, US2006039922, WO03035106, WO08124646, WO11013097, US6165468, US2008095803, US4402939, WO08119358; US2006002941; WO11103588). Many of the patent families that were not retrieved dealt with adjuvants, pharmaceutically acceptable carriers, use of pneumococcal protein (or peptide) as carrier.

Most pneumococcal conjugate vaccines were based on glycoconjugates. Therefore, these keywords were tested to see if new patent families could be retrieved.

QUERY 10/ ((QUERY 3) AND TAC=glycoconjugate*) AND NOT ((QUERY 4) OR (QUERY 9))

This query led to 2 INPADOC families but only one was relevant (WO11027116).

As three pneumococcal conjugate vaccines are commercially available, it was interesting to see if the trade mark was used in the patent literature.

QUERY 11/ TAC=(prevnar OR synflorix) AND NOT ((QUERY 4) OR (QUERY 9))

This query led to 2 INPADOC families but any relevant one.

QUERY 12/ (TAC=((((D OR diplo*) WF1 pneumonia*)) AND conjuga*)) AND NOT ((QUERY 4) OR (QUERY 9))

This query led to 2 INPADOC families but only a relevant one.

1.1.1.2. Classification code based queries

Once the keyword based queries were all tested, queries based on patent classification codes were tested.

QUERY 13/ ((IC=A61K39/09 OR UC=424/237.1 OR EC=A61K39/09* OR JCI=A61K39/09) AND TAC=(pneumo* AND conjugat*) AND NOT ((QUERY 4) OR (QUERY 9))

"IC" means "international patent classification
"UC" means "US patent classification
"EC" means European classification
"JCI" means Japan File Index
This query led to 19 INPADOC families. After reviewing these families, only four were retrieved (PE13052007 ; NL300415; CO5241278; US5679768).

QUERY 14/ (((IC= A61K39/385) AND (QUERY 2)) AND NOT ((QUERY 4) OR (QUERY 9))

This query led to 22 INPADOC families. After reviewing these families, 4 were retrieved (FR2475900 ; KR20020000785 ; US2002032323; US2003162260 (entitled vaccine adjuvant but corresponding to a conjugate vaccine).

1.1.1.3. Queries with non-English keywords

After testing queries based on keywords and/or patent classification codes, queries were built with languages other than English (Latin and non-Latin).

QUERY 15/ (QUERY 2 AND TAC=(conjug* OR konjug*) AND NOT ((QUERY 4) OR (QUERY 9) OR (QUERY 13) OR (QUERY 14)))

This query led to 22 INPADOC families but only one claimed a vaccine (PE00602008). As with this query, no keywords specifically related to vaccine were used, most of the patent claimed treatments or detection methods based on conjugation.

QUERY 16/ [RU]: TAC=((стрептококк пневмонии) AND вакцина)

"**стрептококк пневмонии**" means "*Streptococcus pneumoniae*"
"**вакцина**" means "Vaccine"

QUERY 17/ [JP]: TAC=(ワクチン AND 肺炎連鎖球菌)

"**肺炎連鎖球菌**" means "*Streptococcus pneumoniae*"
"**ワクチン**" means "Vaccine"

QUERY 18/ [CN]: TAC=(肺炎链球菌 AND 疫苗)

"肺炎链球菌" means "*Streptococcus pneumoniae*"
"疫苗" means "Vaccine"

QUERY 19/ [KR]: TAC=(백신 AND 폐렴 연쇄 구균)

"폐렴 연쇄 구균" means "*Streptococcus pneumoniae*"
"백신" means "Vaccine"

By combining non Latin language terms (in Russian (RU), Japanese (JP), Chinese (CN) and Korean (KR)) and removing the previous ones ,i.e.

(QUERY 15 OR QUERY 16 OR QUERY 17 OR QUERY 18) AND NOT (QUERY 4 OR QUERY 9 OR QUERY 12 OR QUERY 13 OR QUERY 14)), 83 patent families were retrieved. After reviewing these families, many of them claimed vaccines but not conjugate vaccines (which is normal since no keyword related to conjugate was used to simplify the query) but this step allowed the recovery of 4 patent families not identified before (CN101024079 ; CN101130071; WO06065137; WO9839450).

These patents were not initially retrieved because of problem of machine translation that gave orthographic errors of translated keywords.

1.1.1.4. Consistency analysis of the patent pool

The citation analysis of the patent pool leads to a list of the most cited patents. These most cited patents were either already in our patent pool or outside. The patent families that were not included in the pool were checked and did not lead to the identification of further relevant patent families.

This confirms that the search strategy does not need further refinement with complementary keywords or IPC codes or else.

1.1.1.5. Refinement of the patent pool and final database

A total of 33 INPADOC patent families needed a review by technical experts in order to determine their relevancy.

A list of 33 potentially relevant INPADOC patent families were identified and reviewed in collaboration with the WIPO and WHO in order to validate or eliminate them from the final database. **The final database on human pneumococcal conjugate vaccines, created 3rd November 2011, contains 165 relevant INPADOC patent families** (22 INPADOC patent families were excluded through this second manual review)**.**

2.2. Statistical analysis

2.2.1. Number and evolution of patent filings and grants

Total number of patent families claiming active ingredients of human pneumococcal conjugate vaccines	165
Total different patents & patent applications	951
Average INPADOC Family Size	5.7 patents or applications/family
Granted patents	43%
PCT applications	68%

Table 8 - General statistics of patent filings and grants

The patent search resulted in 165 INPADOC families of patents and patent applications published until October 2011. These 165 patent families include 951 patents or published applications. Among these 165 patent families, 71 included one or more granted patents.

These 165 patent families contain three “Complex Patent Families“ (CPF):

- One claiming the US19910656773 priority (6 patent families out of 46 patent families of this CPF were included in this database) (filed by UNIV ALABAMA and/or UAB RESEARCH FOUNDATION)
- One claiming the GB19990006437 or the GB19990009077 priority (11 patent families out of 24 patent families of this CPF were included in this database) (filed by GSK)
- One claiming the GB20050026232 priority (11 patent families out of 44 patent families of this CPF were included in this database) (filed by GSK)

For more information on how families are built, please refer to WIPO standards references on Patent Family[7] or other references on the Internet [8]

Granted patents were identified by creating a query based on kind codes related to granted patents of all patenting authorities and applying it to the patent pool of active ingredients of human pneumococcal conjugate vaccines. Each patenting office has its own kind code system. For example, publications of the European Patent Office having a "B" kind code are granted patents, whereas publications having an "A1, A2, A3" kind code are applications. For the US Patent and Trademark Office, publications with an "A" kind code published before November 2000 and publications with kind code "B1, B2" are granted patent while publications with an "A1, A2" kind code published after November 2000 are applications.

Families having granted family members do not necessarily mean that protection has entered into force or that the patent is still valid. Granted patents may not be in force for several reasons including that the patent term expired, that fees have not been paid, or that it did not survive opposition or revocation procedures.

The figure below describes patenting activity over time and gives a view of patent grant rate in the field of active ingredients of human pneumococcal conjugate vaccines. The graph represents the number of patent families (Y axis) over the year of first filing (X axis). This year (priority year) was chosen rather than the publication year, as this is more indicative of patenting activities since they are less dependent on the varying publication policies and docket backlogs of patent offices. The count of families for each year of first filing is split into two fractions according to whether families included at least one granted patent or not.

The graph shows an increase in filings up to 1999, and then a second spike up to 2005.

The small fraction of grants in younger families reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO).

In the 1990s, more than 70% of patent families contained at least one granted patent while, after 2000, this rate did not go beyond 50%. The small fraction of grants in younger families (since 2005) reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO). For these families the examination of family members may still be pending or may not be requested yet.

For earlier years of filing, national publication policies and the evolution of national patent legislation have to be taken into account. For example, until November 2000, the US patent office only published granted US patents. Thereby, US applications that were not granted were in fact never published. For the coverage of national databases used in this study, please refer to corresponding

[7] http://www.wipo.int/standards/en/pdf/08-01-01.pdf

[8] http://www.intellogist.com/wiki/Patent_Families

appendix. In addition, because of the 18 months of publication delay after the date of patent filing, the data after 2009 are incomplete.

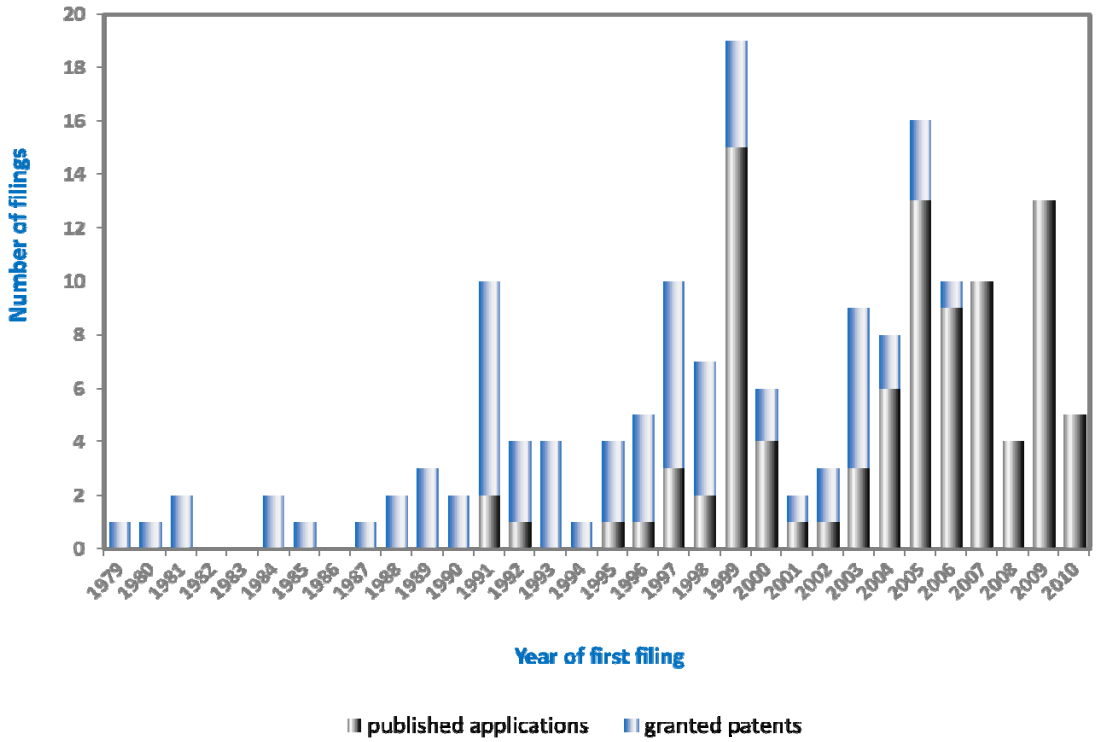

Figure 19 - Evolution of the number of granted and not granted patent families per year of first filing

A PCT application was filed for a large majority of patent families. In the figure below, it can be noted that peaks in 1991, 1999 and 2005 concerning patent families without PCT applications are only due to the “Complex Patent Families”.

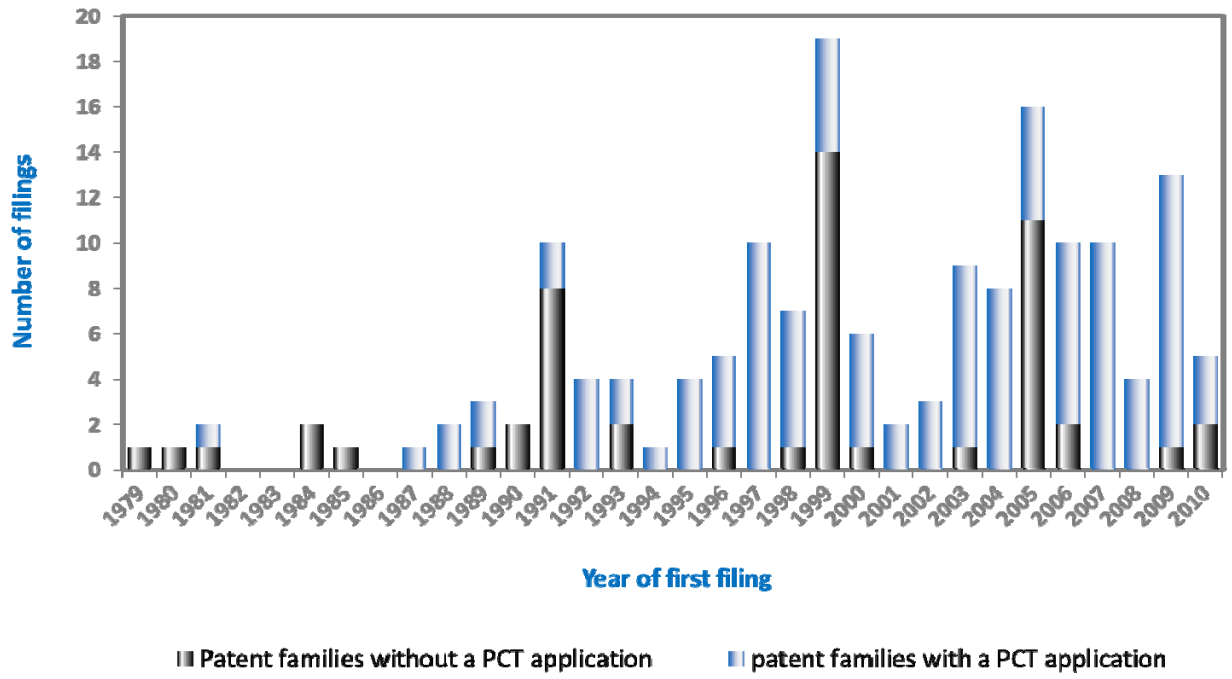

Figure 20 - Evolution of the number of patent families with and without PCT applications per year of first filing

The table below lists the office of origin of all PCT applications. This table was established by looking at the application number of a PCT filing that mentions the office of origin of the PCT (e.g. 2008WO-FR00687, this PCT application was filed via the French patent office).

Office of first filing	Number of PCT applications
UNITED STATES	50
EUROPEAN PATENT OFFICE (EPO)	22
INTERNATIONAL BUREAU (WIPO)	13
FRANCE	5
UNITED KINGDOM	5
ISRAEL	4
CANADA	3
DENMARK	3
KOREA	2
NETHERLANDS	2
AUSTRALIA	1
ITALY	1
JAPAN	1

Table 9 - Origin of PCT applications

PCT applications were mainly filed with national or regional offices and only few directly with the international bureau.

2.2.2. Location of first filings

An analysis of the place of filing of priority patents results in the following table. A map of these filings can be seen in appendix. The location of priority filings and their evolution may give an indication of the country of origin of applicants and the dynamic of innovation in these countries.

		79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	Total
PCT	WORLD																								2									2
AMERICA	UNITED STATES			2			2				1	1	2	9	4	4	1	4	2	7	5	3	2		1	6	2	2	6	3	2	11	1	83
	CANADA																										1							1
EUROPE	EUROPE																		1			1					1	1			1			5
	UNITED KINGDOM																				1	15	3	1		1	4	11	3	6			2	47
	FRANCE	1	1											1						1			1	1		1								7
	DENMARK																											1		1	1			3
	ITALY							1				2																						3
	GERMANY									1										1														2
	SWEDEN																		2															2
ASIA	CHINA																									1		1	1			1	2	6
	KOREA																			1												1		2
	JAPAN																				1													1
AUSTRALIA	AUSTRALIA										1																							1
Total		1	1	2	0	0	2	1	0	1	2	3	2	10	4	4	1	4	5	10	7	19	6	2	3	9	8	16	10	10	4	13	5	165

Table 10 - Evolution of first filings by offices

Early patent applications were filed in France but the United States and to a lesser extent the United Kingdom largely dominate as offices of first filing. The important number of priority filings in the red-circled number is due to the presence of "Complex Patent Families". Although a recent emergence of China can be seen through this analysis, it is not yet significant in terms of filings.

In order to have a better understanding of the country of origin and the innovation dynamic in these countries, it is more appropriate to take a look at the number of filings according to inventors' place of residence rather than the office of first filing.

To be able to make these statistics, the data related to Inventor's country (extracted from the address of the inventor), indexed in FamPat database (Questel™), was used. To do this, patent families of the database "Active Ingredients of human pneumococcal vaccines" were loaded into FamPat. This did not change the number of retrieved patent families although the definition of FamPat families is a little different from INPADOC families (FAMPAT families are built with patent applications having exactly the same priority whereas INPADOC families are built with patent applications having at least one priority patent application in common). Then, the number of filings naming at least one inventor coming from a country in particular was then counted.

It should be noted that totals of the two categories of the table are different because the inventors indicated in an individual patent application may have different countries of residence; each country was counted once, e.g. an application with two inventors residing in Belgium and one inventor residing in the United Kingdom would result in one count for each country.

		Number of filings in each patent authority	Number of filings according to inventors' place of residence
PCT	WORLD	2	/
AMERICA	UNITED STATES	83	67
	CANADA	1	11
	BRAZIL	/	1
EUROPE	EUROPE	5	/
	UNITED KINGDOM	47	9
	FRANCE	7	9
	DENMARK	3	4
	ITALY	3	20
	GERMANY	2	3
	SWEDEN	2	2
	BELGIUM	/	26
	ICELAND	/	1
	AUSTRIA	/	2
	NETHERLAND	/	7
EURASIA	BELARUS	/	1
	INDIA	/	2
ASIA	CHINA	6	7
	KOREA	2	3
	JAPAN	1	1
MIDDLE EAST	ISRAEL	/	1
AUSTRALIA	AUSTRALIA	1	2
Total		165	179

Table 11 - Comparison between place of filings and origin of the inventors

Based on these data, it was noted that Canadian innovation tends to be first protected through the US patent office and that that Italian, Dutch and Belgian tends to be first protected through the UK patent offices. Several reasons can co-exist to explain these differences:

- The interest in specific cases to use US provisional patents (even when the innovation do not stems from US inventors)
- The difference in location of patent officers and research team. For example, 26 applications filed by Belgian inventors but no filing registered at the Belgian patent office. This is explained by the fact that GSK vaccine research team is located in Belgium but files in the United Kingdom where are located the headquarters. On the same way, NOVARTIS/CHIRON research team is located in Italy but files in the United Kingdom.
- The interest of filing directly in English to lessen future translation fees

2.2.3. Average family size per office of first filing

These data were established by looking at the publication numbers of each family in order to extract the number of offices in which the applications were filed. However, for patent and patent applications of European countries filed via the European Procedure, a different counting was carried out because of specificities of European procedures. According to the designated and chosen offices, a new patent application number is attributed by these offices or not. For instance, German patent office will deliver a number (DE123456) after an extension via the European procedure while France will use the EP number (EP654321). When looking at the patent families via the patent & patent application numbers, it therefore created, improperly, a higher number of German extensions compared to French ones. Consequently, when a patent family contained a patent application filed via the EPO, the numbers issued by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family. In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

Office of first filing	Average family size	Standard deviation
AUSTRALIA (AU)	8.0	0.0
CANADA (CA)	1.0	0.0
CHINA (CN)	1.0	0.0
DENMARK (DK)	5.0	5.2
EPO (EP)	6.4	3.8
FRANCE (FR)	8.0	3.2
GERMANY (DE)	6.0	2.8
ITALY (IT)	4.3	1.5
JAPAN (JP)	11.0	0.0
KOREA (KR)	2.5	0.7
SWEDEN (SE)	4.5	4.9
UNITED KINGDOM (GB)	5.8	4.9
UNITED STATES (US)	5.8	3.9
WIPO (WO)	3.5	2.1

Table 12 - Average family size and standard deviation per office of first filing

It can be noted that Chinese patent families were never extended. The US and GB patent families are divided in two main groups: these that were never extended and these with a high number of extension (~12) which lead to an average family size of middle value but with a high standard deviation.

2.2.4. Location of second filings

An analysis of the location of second filings results in the following histogram. A map compiling these data can be found in the corresponding appendix. Countries chosen for the extension of priority filings are an indicator of the markets and/or the production sites. The choice of countries may also be guided by company's competitors and potential infringers, even if there is no market in these

corresponding territories. In Life Sciences, the choice can also be guided by usual locations of clinical trials (Poland, Hungary, Thailand, India…).

These data were established by looking at the patent numbers of each family without taking into account the number delivered by the office of first filing (see previous section for the explanation of the calculation).

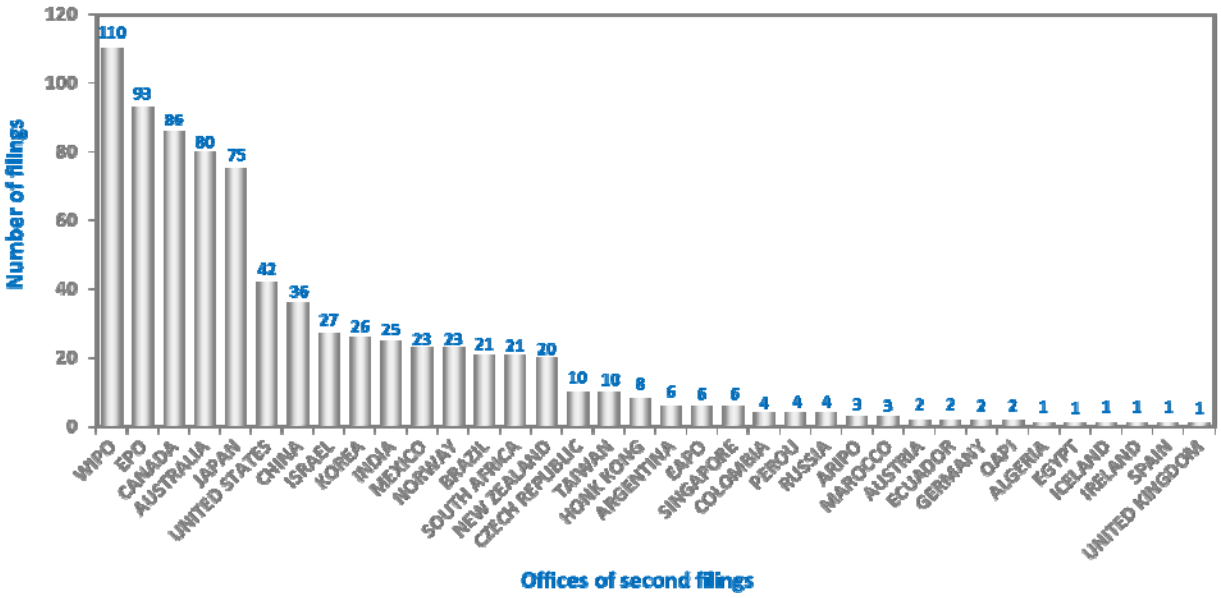

Figure 21 - Number of applications in the offices of second filings

Many second filings were performed via the PCT procedure (as seen in the previous section it represents 68% of the patent applications). The European patent office (EPO), Canada, Australia and Japan also dominate as offices of second filings. Beware that the importance of Australia must be understood in relation to the policy of the Australian patent office which automatically delivered an Australian patent number when the PCT mentions Australia even if no extension were filed in Australia during the national phase.

2.2.5. Breakdown of filings by IPC codes

The table below shows the most common relevant IPC codes present in the database.

IPC	Definition	Number of patent & patent applications
A61K39-09	Medicinal preparations containing antigens or antibodies, Bacterial antigens, Streptococcus	100
A61P31	Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics, Antibacterial agents	91
A61K39-385	Medicinal preparations containing antigens or antibodies, Haptens or antigens, bound to carriers	87
A61K47	Medicinal preparations characterised by the non-active ingredients used, e.g. carriers, inert additives [2	54
A61P37	Drugs for immunological or allergic disorders (e.g. immunomodulators)	53
C12N15	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification	45
C07K14-195	Peptides having more than 20 amino acids; from bacteriaGastrins; Somatostatins; Melanotropins; Derivatives thereof	43
A61K38	Medicinal preparations containing peptides	34
C07K14-315	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof, from bacteria · from Streptococcus (G), e.g. Enterococci	33
A61K39-085	Medicinal preparations containing antigens or antibodies (materials for immunoassay G01N 33/53)	25
C07K16	Immunoglobulins, e.g. monoclonal or polyclonal antibodies	25
C12P21	Preparation of peptides or proteins	25
Other C07K14	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof	25
G01N33	Investigating or analysing materials by specific methods not covered by groups G01N 1/00-G01N 31/00	24
Other A61K39	Medicinal preparations containing antigens or antibodies (except A61K39-09)	23
C07K17	Carrier-bound or immobilised peptides; Preparation thereof	19
C07K19	Hybrid peptides (hybrid immunoglobulins composed solely of immunoglobulins C07K 16/46)	18
A61K35-74	Medicinal preparations containing material or reaction products thereof with undetermined constitution, from bacteria	16

Table 13 - Number of patent families classified within relevant IPC codes

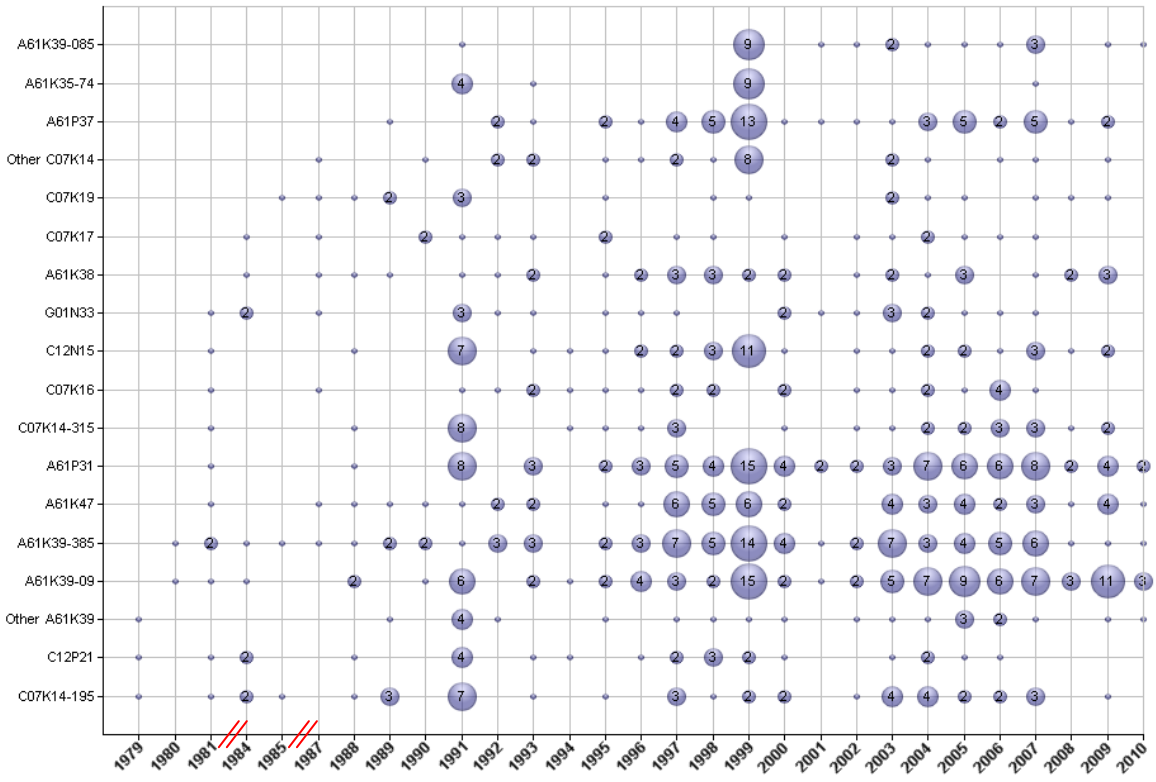

Figure 22 - Number of patent families classified within relevant IPC codes per year of first filing

No clear trend can be highlighted by the analysis of the evolution of IPC codes.

2.2.6. Analysis of applicants

Two types of applicants can be distinguished: institutional and industrial ones. The evolution of institutional vs. industrial priority filings (figure below) outlines the strong presence of industrial filings. Only few and old applications were jointly filed by an industrial and an institutional applicants.

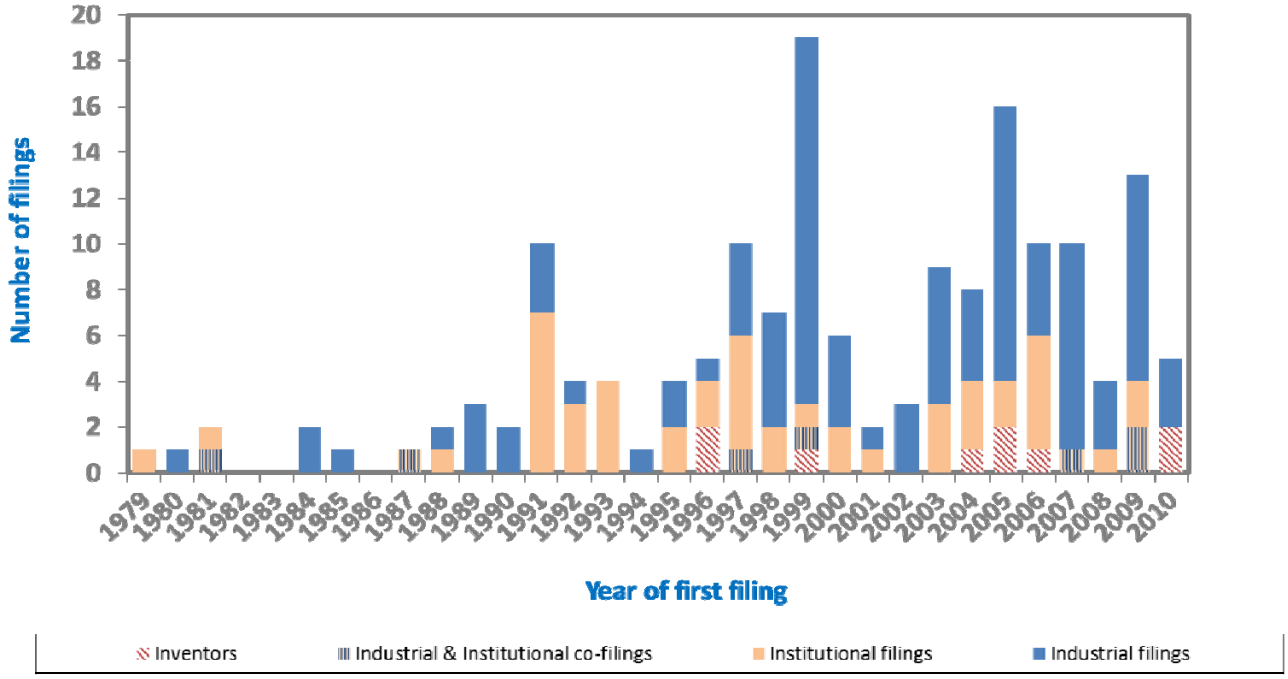

Figure 23 - Number of Institutional/Industrial/Individual priority filings per year of first filing

The following graph shows the main applicants classified by the size of their patent portfolio. Co-filings are counted for each co-owner. For instance, a patent application co-filed between US Government and GSK is counted once for US Government and once for GSK.

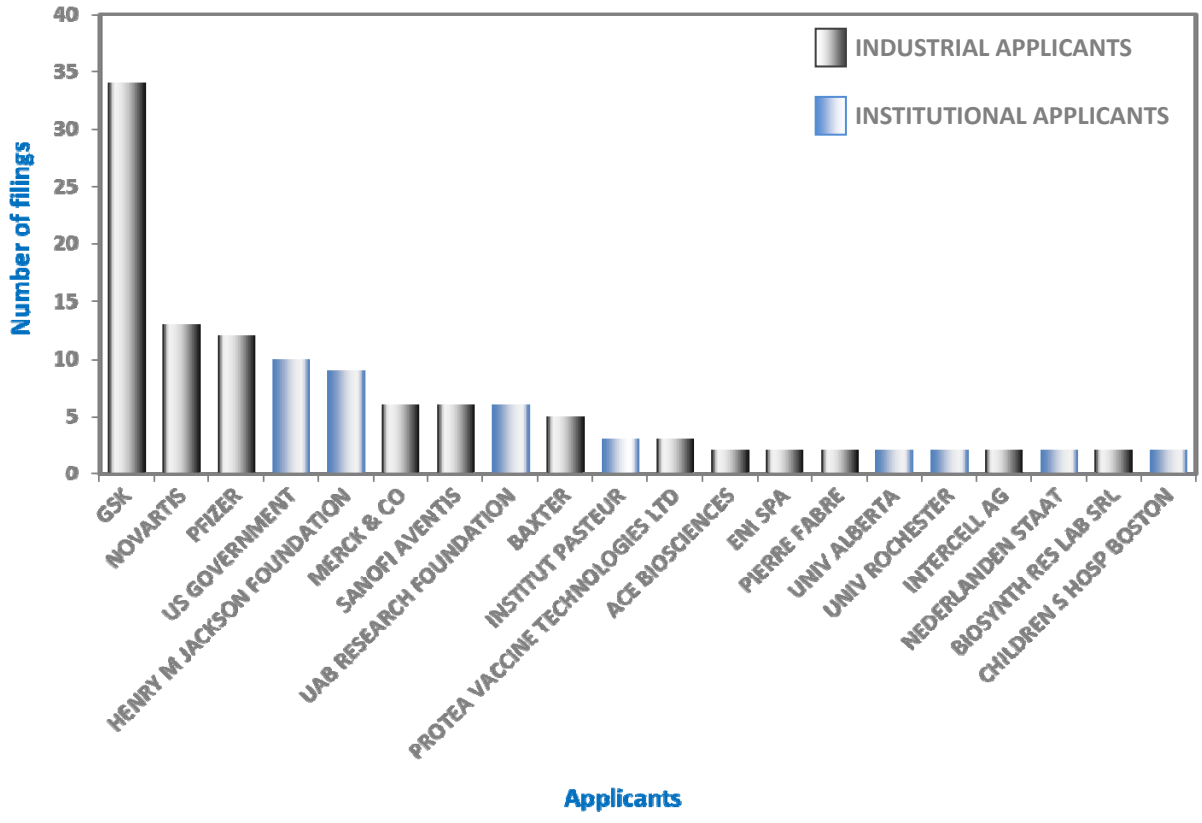

Figure 24 - List of main applicants (≥ 2 patent or patent applications)

The large pharmaceutical company, GSK, dominates in terms of number of patent families. It should however be noted that GSK has three "Complex Patent Families" that increases artificially the number of families due to the filings of Continuation in Part and Divisional but claiming the same Priority. When not taking these "Complex Patent Families" into account, GSK, Novartis, Pfizer and to a lesser extent Merck&Co, Sanofi Aventis and Baxter have a similar profile.

Please note that affiliates/subsidiaries were gathered under their parent company. These groupings were performed via a home-made database of mother companies and subsidiaries developed with Elsevier's business intelligence database[9], companies' websites, annual reports, business intelligence reviews and websites… For more precision, the table below details this regrouping.

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
GSK (GB)	GLAXOSMITHKLINE BIOLOGICALS (BE); SMITHKLINE BEECHAM BIOLOGICALS (BE)
NOVARTIS (CH)	CHIRON (US), SCLAVO (IT), NOVARTIS VACCINES AND DIAGNOSTICS
PFIZER (US)	AMERICAN CYANAMID (US), COLEY PHARMA GROUP (DE), POWDERJECT VACCINES (US), PRAXIS BIOLOGICALS INC (US), WYETH (US)
US GOVERNEMENT	US DEPARTMENT OF HEALTH AND SERVICES, US ARMY
HENRY M JACKSON FOUNDATION (US)	The Henry M. Jackson Foundation for the Advancement of Military Medicine
MERCK & CO (US)	MERCK & CO (US); IRBM P ANGELETTI (IT)
SANOFI-AVENTIS (FR)	AVENTIS PASTEUR (FR); CONNAUGHT LABORATORIES (CA); PASTEUR MERIEUX SERUMS & VACCINS (FR); SANOFI PASTEUR (FR)
UAB RESEARCH FOUNDATION (US)	UAB RESEARCH FOUNDATION (=TTO of The University of Alabama at Birmingham)
BAXTER (US)	BAXTER BIOTECH; BAXTER HEALTHCARE; NORTH AMERICAN VACCINE; BAXTER INTERNATIONAL INC
INSTITUT PASTEUR (FR)	INSTITUT PASTEUR
PROTEA VACCINE TECHNOLOGIES (IL)	Purchased in 2008 by NasVax (IL)
ACE BIOSCIENCES (DK)	ACE BIOSCIENCES
INTERCELL AG (DE)	INTERCELL USA INC, INTERCELL AG
ENI SPA (IT)	ENIRICERCHE SPA
NETHERLANDS STAAT (NL)	NETHERLANDS STAAT
ALBERTA RESEARCH COUNCIL (US)	ALBERTA RESEARCH COUNCIL (since 2010 Alberta Innovates - Technology Futures)
UNIV ROCHESTER (US)	UNIVERISTY OF ROCHESTER
BIOSYNTH RES LAB SRL (IT)	BIOSYNTH RESEARCH LABORATORIES SRL
CHILDREN'S HOSP BOSTON (US)	CHILDREN'S HOSPITAL BOSTON
PIERRE FABRE (FR)	PIERRE FABRE MEDICAMENT; PIERRE FABRE SA

Table 14 - Applicants and their affiliates (≥2 patent or patent applications)

[9] http://www.elsevierbi.com/companies

For each applicant, the graphs below detail the preferred office of first and second filings.

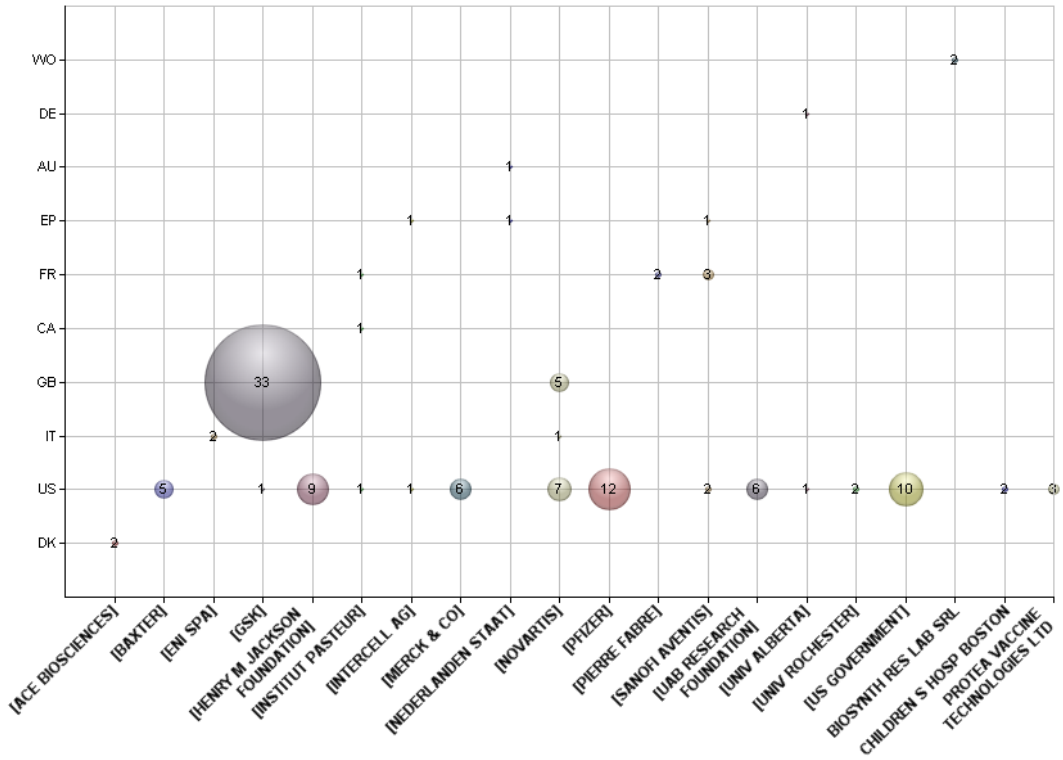

Figure 25 - Main applicants' preferred offices of first filings

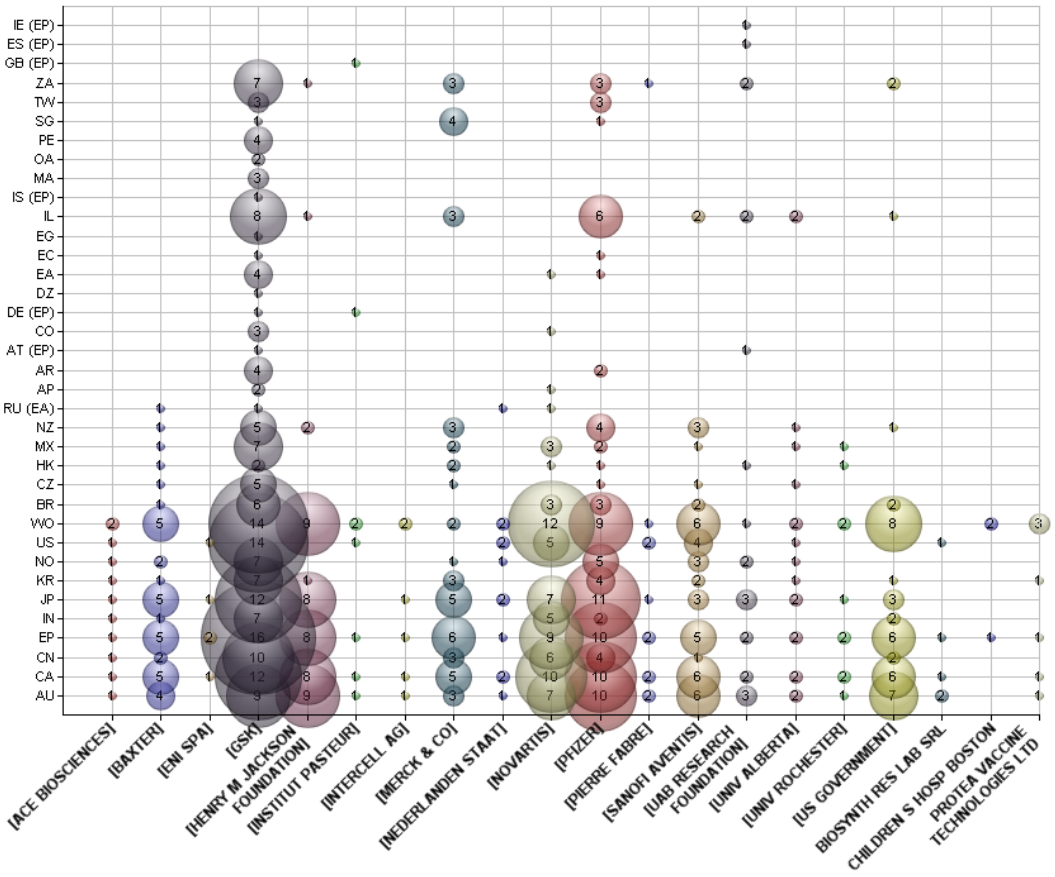

Figure 26 - Main applicants' preferred offices of second filings

The following graph details the evolution of first filings by applicant. The year corresponds to the first priority year of the patent family. Such a graph allows the identification of pioneer or emerging applicants in terms of filings.

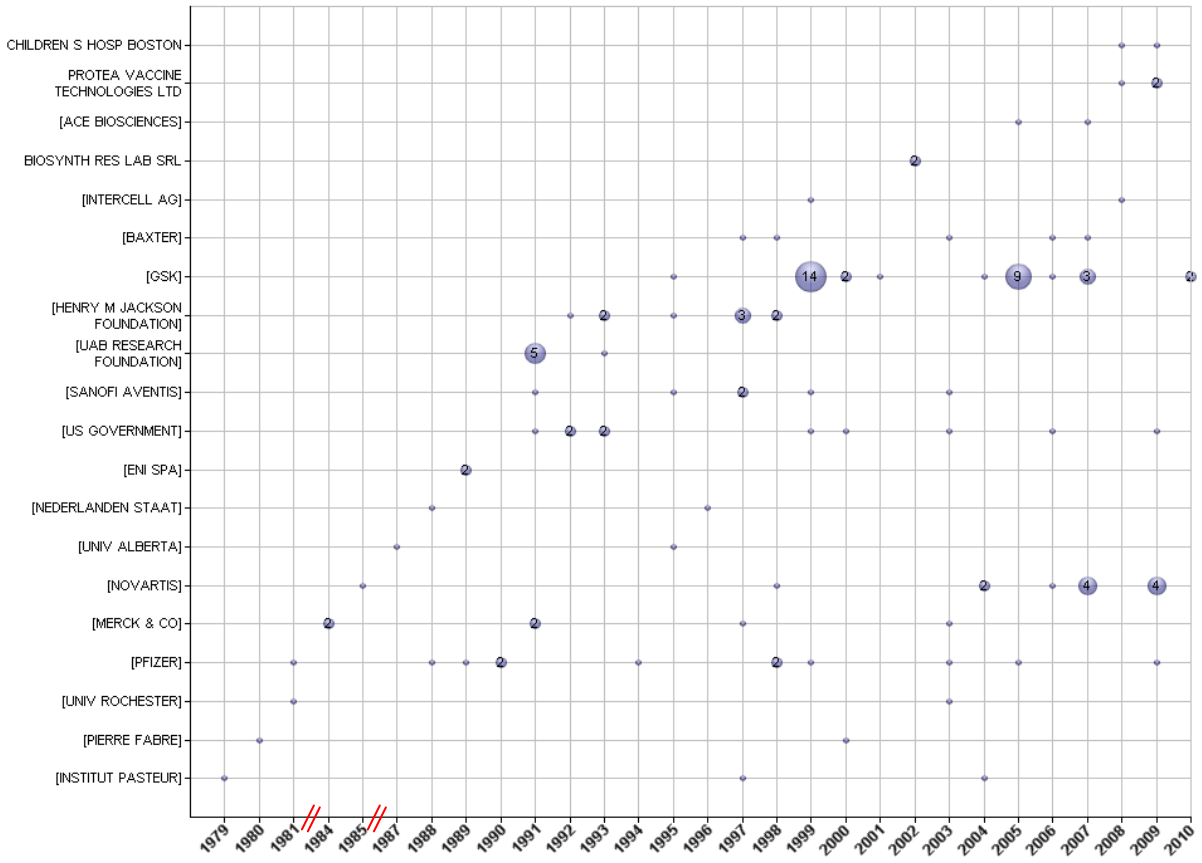

Figure 27 - Evolution of main applicants' filings (by year of first filing)

Pasteur Institute was the first research centre to file patent application about pneumococcal conjugate vaccines. Among the most active applicants, it can be noted that the Henry M. Jackson foundation and the UAB research foundation only filed patent applications before 2000 while GSK and Novartis filed the majority of their patent applications after 2000. Pfizer, the US government laboratories and to a lesser extent Merck & Co and Baxter have regularly filed patent applications since their first filing. Among the emerging applicants, the company Protea Vaccine Technologies has to be considered.

Among the first three applicants, only Novartis is not marketing pneumococcal conjugate vaccines yet but this might be explained by the fact that this company was very active in this field only recently.

The following table details the average family size by applicant. Please note that, because of the particular numbering of patent applications filed during the national phase of the European procedure (see section 2.2.3. for the detailed explanation), when a patent family contained a patent application filed via the EPO, the numbers delivered by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family.

In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

These data show that institutional applicants tend to file smaller families compared to industrial applicants. The 3 “Complex Patent Families” tend to lower the average family size (with a higher standard deviation).

Applicants	Average family size	Standard deviation
GSK	5.7	5.5
NOVARTIS	6.5	3.5
PFIZER	8.8	5.1
US GOVERNMENT	5.1	3.2
HENRY M JACKSON FOUNDATION	6.2	1.6
MERCK & CO	8.7	4.8
SANOFI AVENTIS	8.5	3.2
UAB RESEARCH FOUNDATION	4.5	3.9
BAXTER	8.2	2.6
INSTITUT PASTEUR	3.7	1.5
PROTEA VACCINE TECHNOLOGIES LTD	3.3	2.3
ACE BIOSCIENCES	6.5	6.4
ENI SPA	3.5	0.7
PIERRE FABRE	6.5	0.7
UNIV ALBERTA	10.0	2.8
UNIV ROCHESTER	6.0	2.8
INTERCELL AG	4.0	2.8
NETHERLANDSEN STAAT	7.0	1.4
BIOSYNTH RES LAB SRL	3.5	2.1
CHILDREN S HOSP BOSTON	2.5	0.7

Table 15 - Average family size per applicant

2.2.7. Analysis of inventors

The table below lists the various inventors with their associated applicants. Please note that ”Complex Patent Families” filed by GSK tend to increase artificially the number of inventor’s named on these corresponding filings.

Inventor	Number of filings	Assignee	Number of filings
Poolman Jan	25	**GSK**	24
		N/A	1
Biemans Ralph Leon	15	**GSK**	14
		N/A	1
Deschamps Marguerite	14	**GSK**	14
Capiau Carine	12	**GSK**	12
Desmons Pierre Michel	12	**GSK**	12
Prieels Jean Paul	12	**GSK**	12
Hermand Philippe Vincent	10	**GSK**	9
		N/A	1
Laferriere Craig Antony	9	**GSK**	9
Van Mechelen Marcelle	8	**GSK**	7
		N/A	1
Briles David	7	UAB RESEARCH FOUNDATION	6
		UNIV ALABAMA	1
Garcon Nathalie Marie	7	GSK	6
		N/A	1
Yother Janet	7	UAB RESEARCH FOUNDATION	6
		UNIV ALABAMA	1
Lees Andrew	6	HENRY M JACKSON FOUNDATION	6
		US GOVERNMENT	1
		BIOSYNEXUS INC	1
Mond James	6	HENRY M JACKSON FOUNDATION	6
		US GOVERNMENT	2
		BIOSYNEXUS INC	1
		UNIFORMED SERVICES UNIVERSITY HEALTH SCIENCES	1
Michon Francis	5	BAXTER	5
Duvivier Pierre	4	GSK	4
Mcdaniel Larry	4	UAB RESEARCH FOUNDATION	4
Porro Massimo	4	BIOSYNTH RES LAB SRL	2
		NOVARTIS	1
		PFIZER	1
Tolman Richard	4	MERCK & CO	3
		INSTITUT PASTEUR	1
Bianchi Elisabetta	3	ENI SPA	2
		MERCK & CO	1

Inventor	Number of filings	Assignee	Number of filings
Costantino Paolo	3	NOVARTIS	3
Dagan Ron	3	PROTEA VACCINE TECHNOLOGIES LTD	3
Kniskern Peter	3	MERCK & CO	3
Lee Che Hung Robert	3	US GOVERNMENT	3
		FIOCRUZ	1
		UNIV HOWARD	1
Marburg Stephen	3	MERCK & CO	3
Mizrachi Nebenzahl Yaffa	3	PROTEA VACCINE TECHNOLOGIES LTD	3
Moreau Monique	3	SANOFI AVENTIS	3
Pessi Antonello	3	ENI SPA	2
		MERCK & CO	1
Snapper Clifford	3	HENRY M JACKSON FOUNDATION	3
Snapper Clifford	3	UNIFORMED SERVICES UNIVERSITY HEALTH SCIENCES	1
		US GOVERNMENT	1
Tal Michael	3	PROTEA VACCINE TECHNOLOGIES LTD	3
Andrew Peter William	2	NETHERLANDSEN STAAT	1
		UNIV LEICESTER	1
Arumugham Rasappa	2	PFIZER	2
Bay Sylvie	2	INSTITUT PASTEUR	2
		UNIV PARIS SUD XI	1
		CNRS	1
Berti Francesco	2	NOVARTIS	2
Burke Pamela	2	MERCK & CO	2
Corradin Giampietro	2	ENI SPA	2
Donati Claudio	2	NOVARTIS	2
Eby Ronald	2	PFIZER	2
		UNIV ROCHESTER	1
		PROXIS BIOLOG INC	1
Gavard Ollivier Francis	2	GSK	2
Gorringe Andrew Richard	2	SERUM INST OF INDIA LTD	1
		HEALTH PROTECTION AGENCY (GB)	1
		MICROBIOLOGICAL RES AUTHORITY (GB)	1
Gransi Guido	2	NOVARTIS	2

Inventor	Number of filings	Assignee	Number of filings
Hagopian Arpi	2	MERCK & CO	2
Hennessey John	2	MERCK & CO	2
Ip Charlotte	2	MERCK & CO	2
Kubek Dennis	2	MERCK & CO	2
Laing Peter	2	LIPOXEN LTD	1
		ADJUVANTIX LTD	1
Malcolm Andrew	2	UNIV ALBERTA	2
		CHEMBIOMED LTD	1
Malley Richard	2	CHILDREN S HOSP BOSTON	2
		GENOCEA BIOSCIENCES INC	1
Masignani Vega	2	NOVARTIS	2
Miller William	2	MERCK & CO	2
Mitchell Timothy	2	NETHERLANDSEN STAAT	1
		N/A	1
Pillai Subramonia	2	PFIZER	2
Portnoi Maxim	2	PROTEA VACCINE TECHNOLOGIES LTD	2
Prasad A Krishna	2	PFIZER	2
Robbins John	2	US GOVERNMENT	2
		INTERCELL AG	1
		TECHLAB INC	1
Ruggiero Paolo	2	NOVARTIS	2
Schneerson Rachel	2	US GOVERNMENT	2
		INTERCELL AG	1
		TECHLAB INC	1
Schrotz-King Petra	2	ACE BIOSCIENCES	2
Svenson Stefan	2	N/A	2
Uitz Catherine	2	BAXTER	2

Table 16 - List of main inventors (≥2 patent or patent applications)

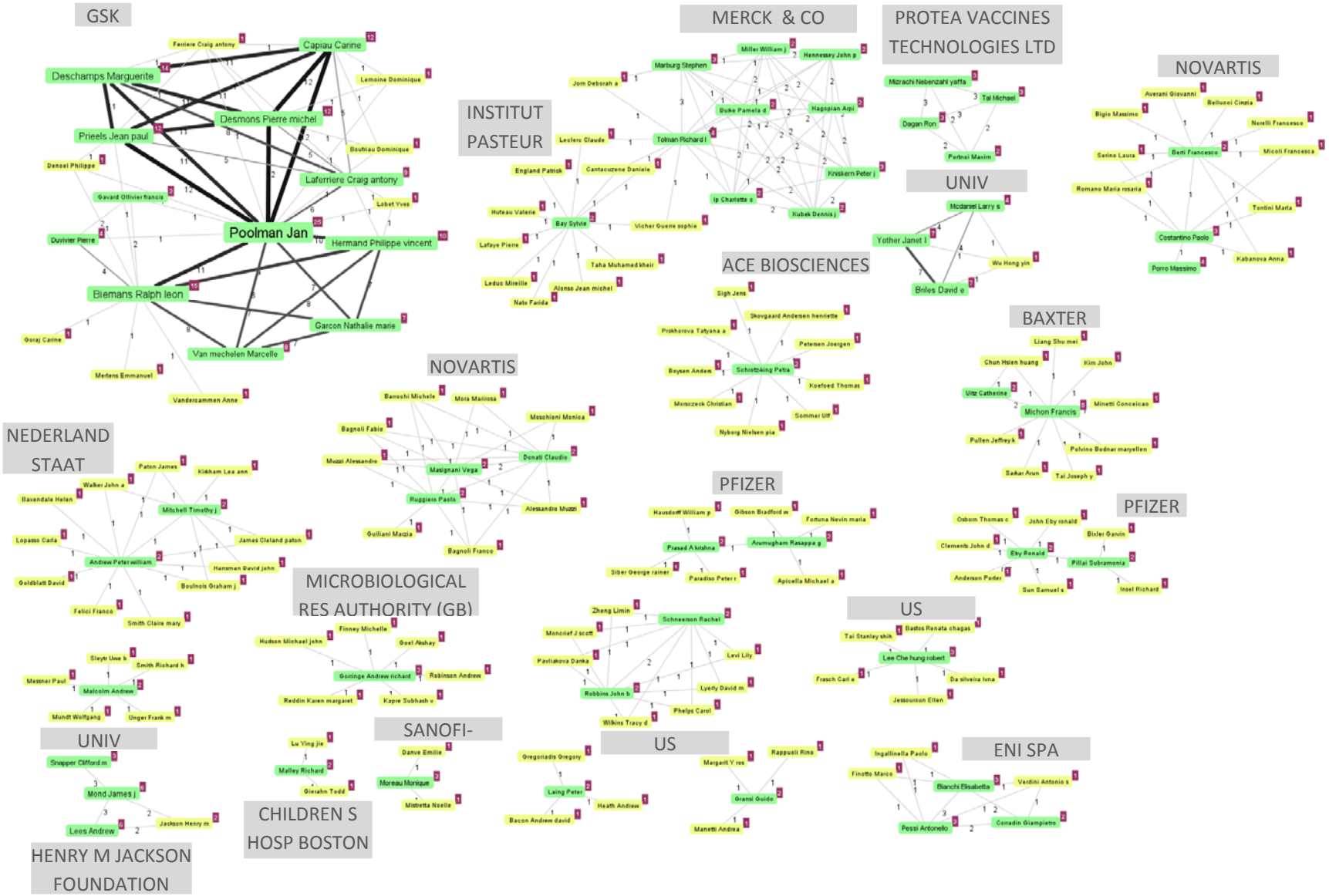

Figure 28 - Main research teams

2.2.8. Regional focuses: Brazil, India and China

This section focuses on patent families having Brazil, India or China as office of first filing. No patent family was created by first filing coming from India or Brazil. Only few were filed in China. Therefore, the table below lists all patent families stemming from China.

Priority number	Publication number	Title	Applicant
CN201010129404	CN101785857	Novel pneumococcal conjugate vaccine and preparation method thereof	
CN200910040659	CN101590224	High-efficiency 14-valent pneumococcal conjugate vaccine	CHANGCHUN CHANGSHENG LIFE SCIENCES
CN200610054832	CN101024079	Pneumo-streptococcal-polysaccharide adventitia jointed vaccine and preparing method	FUZHOU CHANGHUI BIOENGINEERING CO LTD
CN20031041407	CN1241937	Polyvalent pneumococcal polysaccharide combination vaccine	SHANGHAI JIAN YI TECH CO LTD
CN201010624063	CN102068690	Multi-price pneumococcus capsule polysaccharide union vaccine and preparation method	
CN200510027886	CN1899609	Pneumococcus polysaccharide protein coupling vaccine and its preparing method	UNIV FUDAN

Table 17 - List of patent families stemming from China

3. Active ingredients of human typhoid conjugate vaccines

3.1. Search methodology

3.1.1. Introduction

This section describes the search methodology developed to retrieve patents and patent applications claiming active constituents of human conjugate vaccines against typhoid. The narrative of this search history shows how the search was performed. It describes specific tools, databases, and challenges encountered and methods of circumventing. The search consisted generally of the use of combinations of keyword and classification searches, the intellectual review of search results for refining the queries and excluding irrelevant documents, and a final benchmarking of the search strategy through inclusion of documents cited in relevant documents. This section also discusses the limits of the use of patent classification codes (IPC, ECLA…) when looking for patents and patent applications dealing with active constituents of human conjugate vaccines against typhoid.

3.1.2. Methodology and databases

A background study was first performed by looking at some literature on typhoid conjugate vaccines in order to collect keywords to build the patent queries and especially to help us determine the relevance of a patent family compared to another one, given that only patent describing "active constituents" had to be taken into account. Articles such as *Audino Podda, et al., J Infect Dev Ctries, 2010; 4(6):404-411* were useful to make a list of keywords as well as general articles found on the Internet about the disease and its related vaccines[10].

As a next step, a review of patent classification was carried out to identify patent classification codes related to typhoid antigens.

With the list of keywords and patent classification codes established such as described, queries were built and run into FAMPAT database (Questel™). Therefore this document present the FAMPAT queries used to identify the relevant patent families of this focus. However, the final database, from where the statistical analyses were set-up, was created using INPADOC documents (Patbase export; Minesoft™).

[10] http://www.who.int/vaccine_research/diseases/diarrhoeal/en/index7.html
http://en.wikipedia.org/wiki/Typhoid_fever
http://en.wikipedia.org/wiki/Paratyphoid_fever

3.1.3. Background study

3.1.3.1 Review of the literature

Typhoid fever is a systemic infection caused by the bacterium *Salmonella enterica*, *serovar typhi* (*S. typhi*). This worldwide illness is transmitted by the ingestion of food or water contaminated by excreta from infected person or chronic carriers.

Enteric fevers also include paratyphoid fever caused by strains of three species of Salmonellae that are *Salmonella paratyphi* A, *S. paratyphi B* (or *S. schottmuelleri*) and *S. paratyphi* C (*S. hirschfeldii*). The paratyphoid bears similarities with typhoid fever, but its course is more benign.

Recent studies showed that around 22 million cases of typhoid fever occur each year. About 1% of the infected persons died from this illness with higher incidence in children and young adults between 5 and 19 years old.

As typhoid and paratyphoid do not affect animals, the transmission occurs only from human to human. In addition, it can only spread in contaminated environments where human excreta come into contact with water or food. Prevention therefore involves in priority sanitation and hygiene. However vaccines remain crucial for the limitation of these illnesses.

Apart from the heat-killed injectable whole-cell *S. typhi* vaccine used as far back as 1896 and still licensed today in several countries in spite of its high reactogenicity, two recent vaccines are currently recommended by the WHO for the prevention of typhoid. The injectable Vi polysaccharide vaccine (US5204098) was developed at the NIH in the 80's and licensed to Sanofi-Pasteur (Typhim ^{TM}, Sanofi-Pasteur; Typherix ^{TM}, GlaxoSmithKline; Typbar^{TM}, Bharat Biotech). The oral live attenuated Ty21a vaccine (US4632830) was developed at the "Swiss Serum and Vaccine Institute Berne" in the 80's and licensed to Berna Biotech now acquired by Dutch company Crucell (Vivotif TM, Crucell). Both demonstrated their efficacy in multiple randomized trials (between 50% to 80% protective) and are widely used worlwide. Several other live attenuated *S. typhi* vaccines are currently in development and seem to be even more immunogenic than Ty21a vaccine.

Due to the fact that classical used vaccines are poorly immunogenic in infant and cannot be used to vaccinate children less than 2 years of age, development of conjugate vaccines is a major necessity. Two typhoid conjugate vaccines are currently in development, one at the NIH using recombinant *Pseudomonas aeruginosa* exotoxin A as the protein carrier and the second at ALL India Institute of Medical Sciences in New Delhi using the OmpC protein from *S. typhi* as carrier.

A conjugate vaccine, or conjugated vaccine, is a type of vaccine that is created by joining an antigen to a protein molecule. It usually consists in (but is not limited to) a polysaccharide antigen combined with a carrier protein. The protein part of a conjugate vaccine acts as a carrier for the antigen, and serves to magnify the immunological response to it.

From this background study, a list of keywords was established.

<u>Keywords related to typhoid:</u> typhoid, paratyphoid, enteric fever, salmonella enterica enterica, salmonella typhi, s typhi, serovar typhi, salmonella paratyphi, s paratyphi, s schottmuelleri, s hirschfeldii

Keywords related to vaccines: vaccin(es), vaccination, vaccinating, antigen(s), antigenic, immunogen(s), immunogenic, immunise, immunisation, immunising, immunize, immune response (and all related keywords)

Keywords related to conjugate vaccines: conjugate(d), glycoconjugate(s), as well as the words fused, fusion, linked, coupled, bound, associat(ed), attach(ed), merg(ed), chimer(s), chimeric; close to the words protein(s), peptide(s), peptidic, carrier(s) (and all related keywords)

Keywords related to commercialized human typhoid conjugate vaccines: Vi polysaccharide vaccine, Typhim, Typherix, Typbar, Ty21a vaccine, Vivotif

3.1.3.2 Review of the relevant classification codes

By screening the international, European, American and Japanese patent classifications, the codes corresponding to medicinal preparations containing antigens or antibodies of *Salmonella typhi* or *Salmonella paratyphi* were collected. The following codes were thereby identified:

International Patent Classification (IPC):

A61K39/112

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/112 Salmonella; Shigella

A61K39/385

[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

US Patent Classification (USPC):

424/258.1

[0] 424 Drug, bio-affecting and body treating compositions
[1] 424/184.1 Antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-mediated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.). Subject matter involving an antigen, an epitope, or another immunospecific immunoeffector, such as an immunospecific vaccine, an immunospecific stimulator of cell-mediated immunity, an immunospecific tolerogen, or an immunospecific immunosuppressor.
[2] 424/234.1 Bacterium or component thereof or substance produced by said bacterium (e.g., Legionella, Borrelia, Anaplasma, Shigella, etc.). Subject matter involving a bacterium, a component of a bacterium, or a substance produced by a bacterium.
[3] 424/258.1 Salmonella (e.g., Salmonella typhimurium, etc.). Subject matter wherein the bacterium is of the genus Salmonella.

424/193.1

[0] 424 Drug, bio-affecting and body treating compositions

[1] 424/184.1 Antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-mediated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.)
[2] 424/193.1 Conjugate or complex. Subject matter involving a conjugate or a complex.
(1) Note. A conjugate is taken to mean a coupling of one substance to another via covalent means, either directly via a covalent bond or indirectly via a chemical linking group.
(2) Note. A complex is taken to mean a coupling of one substance to another via noncovalent means (e.g., via adsorption).
(3) Note. The conjugates and complexes provided for in this subclass and indented subclasses are often of the hapten-carrier type. A hapten is a substance that can bind an antibody, but which cannot induce production of an antibody unless it is coupled to a carrier that is immunogenic. A hapten is usually, but not always, of low molecular weight. Common carriers, for vaccination purposes in humans, are tetanus toxoid and diphtheria toxoid.

European classification (ECLA):

A61K39/02T, A61K39/02T3
[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/02T [N: Enterobacteriales, e.g. Enterobacter, Yersinia]
[3] A61K39/02T3 [N: Salmonella]
A61K39/385
[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

Japan File-Index (Japan FI):

A61K39/112
[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/02 Bacterial antigens
[2] A61K39/112 Salmonella; Shigella
A61K39/385
[0] A61K39/00 Medicinal preparations containing antigens or antibodies
[1] A61K39/385 Haptens or antigens, bound to carriers

3.1.4. Search strategy

The patent search started by evaluating the patents and patent applications retrieved by the classification codes based query. In a second time, the results of patent searches using keywords combination were evaluated. Therefore, patent queries using truncations (mentioned by a + in the queries) of keywords related to *Salmonella typhi*, *paratyphi*, vaccines and conjugates were built. As the core of the invention is described in the title, abstract and claims of the patent family members, the queries were carried out in these fields (e.g. BI/CL in Questel).

4.1.3.1 Classification codes based queries

QUERY 1: a first combination of classification codes led to 877 FAMPAT patent families.

((A61K-039/112)/IC) OU ((424258100)/PCLO) OU ((A61K-039/02T OU A61K-039/02T3)/ECLA) OU ((A61K39/112)/FI)

"IC" means "international patent classification
"PCLO" means "US patent classification
"ECLA" means European classification
"FI" means Japan File Index
For the rest of the document, please refer to the appendix.

877 results

→ The results are not specific to *Salmonella typhi* (e.g. *Shigella, Salmonella typhimurium* …), not specific to conjugate vaccines (e.g. diagnostic, adjuvant …) and not specific to human.

QUERY 2: a second combination of classifications codes led to 82 FAMPAT patent families.

(((A61K-039/112)/IC) OU ((424258100)/PCLO) OU ((A61K-039/02T OU A61K-039/02T3)/ECLA) OU ((A61K39/112)/FI)) ET (((A61K-039/385)/IC) OU ((424193100)/PCLO) OU ((A61K-039/385)/ECLA) OU ((A61K39/385)/FI))

82 results

→ The results, though more specific to conjugate vaccines (noise still exists), are not specific to *Salmonella typhi* (e.g. *Shigella*, *Salmonella typhimurium* …), and not specific to human.

Sample of irrelevant patent families

WO2010033275: Orally administerable vaccine for *Yersinia* pestis

CN101628114: Broad spectrum anti-tumor composite vaccine

WO2010026239: Composition comprising chitosan for ocular administration of vaccine(s) to avians

US2008267998: Combinations of gene deletions for live attenuated *Shigella* vaccine strains

EP2164521: Glycoconjugates and use thereof as vaccine against *Shigella flexneri* serotype 3A and X

Keyword-based queries

QUERY 3: mix of the three families of keywords

(((typhoid+ OU paratyphoid+ OU (enteric fever+) OU (salmonel+ enterica enterica) OU (salmonel+ 3AV typhi+) OU (s 3AV typhi+) OU (serovar typhi+) OU (salmonel+ 3AV paratyphi+) OU (s 3AV paratyphi+) OU (s 3AV schottmuelleri) OU (s 3AV hirschfeldii)) **ET** (vaccin+ OU immunogen+ OU antigen+ OU immunis+ OU immuniz+) **ET** (carrier+ OU +conjugat+))/BI/CLMS)

« BI » means that the reserach is carried out in the titles and abstracts of FAMPAT families
«CLMS» means that the reserach is carried out in the claims of FAMPAT families
For the rest of the document, please refer to the appendix.

498 results

→ A quick analysis of this set of data shows up that the words “typhimurium” or “typhi murium” did not bring relevant patent families and that these patent families were in number. *Salmonella typhimurium* causes gastroenteritis in humans and other mammals and is not involved in typhoid or paratyphoid fevers. The patent families brought by the word typhimurium were then analyzed to confirm this idea.

QUERY 4: check of the patent families containing the key word “typhimurium”

(((typhoid+ OU paratyphoid+ OU (enteric fever+) OU (salmonel+ enterica enterica) OU (salmonel+ 3AV typhi+) OU (s 3AV typhi+) OU (serovar typhi+) OU (salmonel+ 3AV paratyphi+) OU (s 3AV paratyphi+) OU (s 3AV schottmuelleri) OU (s 3AV hirschfeldii)) ET (vaccin+ OU immunogen+ OU antigen+ OU immunis+ OU immuniz+) ET (carrier+ OU +conjugat+))/BI/CLMS) **ET (typhimurium OU (typhi murium))/BI/CLMS**

274 results

→ Most of the documents did not enter in the scope of the study. They claimed vaccines against pathologies caused by *Salmonella typhimurium* or other technologies using *Salmonella typhimurium* antigens. However, 11 FAMPAT (Questel) patent families that seem relevant and 9 potentially relevant were saved manually using their publication numbers. All these patent families were reviewed in collaboration with the WIPO and WHO in a second time in order to validate or eliminate them from the final database.

Example of relevant patent family

WO2005110471: Preparation of salmonella broad-spectrum vaccines

Example of potentially relevant patent family

WO8809669: Avirulent microbes and uses therefor: Salmonella typhi

EP1539978: Method of isolating biologically active fraction containing clinically acceptable native S-lipopolysaccharides obtained from bacteria producing endotoxic lipopolysaccharides

QUERY 5: “relevant patents” check

(((typhoid+ OU paratyphoid+ OU (enteric fever+) OU (salmonel+ enterica enterica) OU (salmonel+ 3AV typhi+) OU (s 3AV typhi+) OU (serovar typhi+) OU (salmonel+ 3AV paratyphi+) OU (s 3AV paratyphi+) OU (s 3AV schottmuelleri) OU (s 3AV hirschfeldii)) ET (vaccin+ OU immunogen+ OU antigen+ OU immunis+ OU immuniz+) ET (carrier+ OU +conjugat+))/BI/CLMS) **SAUF (typhimurium OU (typhi murium))/BI/CLMS**

224 results

→ After reviewing the dataset, only 31 relevant FAMPAT patent families and 26 potentially relevant FAMPAT patent families were saved using their publication numbers. All these patent families were reviewed in collaboration with the WIPO and WHO in a second time in order to validate or eliminate them from the final database. Other patent families claimed a variety of technologies mentioning the keywords used in the query but that did not correspond to active constituents of typhoid conjugate vaccines:

- Detection methods (e.g. IN02598MU2008, CN102053153, KR20100101288, CA2084083)

- Description of vaccine formulations (e.g. WO2011014418)

- Methods of administration and delivery systems (e.g. WO2008116165, WO2007113665, AUPR602401)

- Adjuvants (e.g. DE102006007433, WO2006079989, WO2005107798)

- Non-conjugated typhoid vaccines (e.g. US2004213806, US2003031683, US2003068328, SE9901961)

- Production of therapeutic antibodies (e.g. WO9735884, DK63187, EP1833510)

→ In order to enlarge the query and check new patent families that could enter in the scope of the study, we decided to simplify the query writing "typhi+ OU paratyphi+" instead of "(s 3AV typhi+) OU (serovar typhi+) …"

QUERY 6: typhi+, paratyphi+

(((typhoid+ OU paratyphoid+ OU (enteric fever+) OU (salmonel+ enterica enterica) OU **(typhi+)** OU **(paratyphi+)** OU (s 3AV schottmuelleri) OU (s 3AV hirschfeldii)) ET (vaccin+ OU immunogen+ OU antigen+ OU immunis+ OU immuniz+) ET (carrier+ OU +conjugat+))/BI/CLMS)

8 families were retrieved after removing the 498 FAMPAT patent families already reviewed

→ No relevant patent families were identified

→Another investigation was conducted, adding new keywords to the field of keywords related to conjugate vaccines such as protein, peptide, polysaccharide and chimeric. Despite we already know that most of these patent families do no enter in the scope of the study, a quick manual review seemed necessary to eventually identify some relevant patent families.

QUERY 7: protein, peptide, polysaccharide, chimeric

(((typhoid+ OU paratyphoid+ OU (enteric fever+) OU (salmonel+ enterica enterica) OU (typhi+) OU (paratyphi+) OU (s 3AV schottmuelleri) OU (s 3AV hirschfeldii)) ET (vaccin+ OU immunogen+ OU antigen+ OU immunis+ OU immuniz+) **ET (prote+ OU pepti+ OU polysaccharid+ OU chimeric)**)/BI/CLMS)

391 families were retrieved after removing the 506 FAMPAT patent families already reviewed

→ 3 new relevant patent families within these 391 results were identified using these larger keywords. These patent families were reviewed in collaboration with the WIPO and WHO in a second time in order to validate or eliminate them from the final database.

WO200815480: Composition and method for modulating an immune response
IN02650DE2005: A vaccine
IN02648DE2005: A vaccine

Queries with non-English keywords

Non Latin language terms (Chinese, Japanese, Korean and Russian): for non-Latin languages, we only associated keywords related to typhoid and vaccines.

Paratyphi: 副伤寒 (Chinese), パラチフスA菌 (Japanese), 파라 티푸스 A 균 (Korean), паратифа (Russian)

Typhi: 伤寒 (Chinese), チフス菌 (Japanese), 티푸스 균 (Korean), брюшной тиф (Russian)

Typhoid: 伤寒症 (Chinese), 腸チフス (Japanese), 장티푸스 (Korean), брюшной тиф (Russian)

Paratyphoid: 副伤寒 (Chinese), パラチフス (Japanese), 파라 티푸스 (Korean), паратиф (Russian)

Enteric fever: 肠热症 (Chinese), 腸チフス (Japanese), 장티푸스 (Korean), брюшной тиф (Russian)

Vaccine: 疫苗 (Chinese), ワクチン (Japanese), 백신 (Korean), вакцина (Russian)

QUERY 9: non Latin language terms

((副伤寒 OU パラチフスA菌 OU 파라 티푸스 A 균 OU паратифа OU 伤寒 OU チフス菌 OU 티푸스 균 OU брюшной тиф OU 伤寒症 OU 腸チフス OU 장티푸스 OU брюшной тиф OU 副伤寒 OU パラチフス OU 파라 티푸스 OU паратиф OU 肠热症 OU 腸チフス OU 장티푸스 OU брюшной тиф) ET (疫苗 OU ワクチン OU 백신 OU вакцина))/BI/CLMS

By combining other Latin language terms and non-Latin language terms and removing the patent families already checked, 67 new patent families were identified.

After reviewing these families, no new relevant patent families were retrieved.

Consistency analysis of the patent pool

The citation analysis of the patent pool led us to a list of the most cited patents. These most cited patents were either already in our patent pool or outside. The patent families that were not included in the pool were checked and did not lead to the identification of further relevant patent families.

This confirms that the search strategy does not need further complementary refinement with complementary keywords or IPC codes, or else.

Refinement of the patent pool and final database

A total of 80 INPADOC patent families needed a review by technical experts in order to determine their relevancy.

These 80 relevant or potentially relevant FAMPAT patent families (corresponding to 73 INPADOC patent families) were reviewed in collaboration with the WIPO and WHO in order to validate or eliminate them from the final database. **The final database on human typhoid conjugate vaccines, created 5th October 2011, contained 36 relevant INPADOC patent families** (37 INPADOC patent families were excluded after this second manual review)**.** These 36 relevant INPADOC patent families correspond to 44 FAMPAT patent families.

3.2. Statistical analysis

3.2.1. Number and evolution of patent filings and grants

Total number of patent families claiming active ingredients of human typhoid conjugate vaccines	36
Total different patents & patent applications	158
Average INPADOC Family Size	4.4 patents or applications/family
Granted patents	30.5%
PCT applications	66.7%

Table 18 - General statistics of patent filings and grants

The patent search resulted in 36 families of patents and patent applications published until October 2011. These 36 patent families include 158 patents or published applications. Among these 36 patent families, 11 included one or more granted patents. These patent families did not contain any "Complex Patent Families".

Granted patents were identified by creating a query based on kind codes related to granted patents of all patenting authorities and applying it to the patent pool of active ingredients of human pneumococcal conjugate vaccines. Each patenting office has its own kind code system. For example, publications of the European Patent Office having a "B" kind code are granted patents, whereas publications having an "A1, A2, A3" kind code are applications. For the US Patent and Trademark Office, publications with an "A" kind code published before November 2000 and publications with kind code "B1, B2" are granted patent while publications with an "A1, A2" kind code published after November 2000 are applications.

Families having granted family members do not necessarily mean that protection has entered into force at all or the patent is still valid. Granted patents may not be in force for several reasons including that the patent term expired, that fees have not been paid, or that it did not survive opposition or revocation procedures.

The figure below describes patenting activity over time and gives a view of patent grant rate in the field of active ingredients of human typhoid conjugate vaccines. The graph represents the number of patent families (Y axis) over the year of first filing (X axis). This year (priority year) was chosen rather than the publication year, as this is more indicative of patenting activities since they are less dependent on the varying publication policies and docket backlogs of patent offices. The count of families for each year of first filing is split into two fractions according to whether families included at least one granted patent or not.

The graph shows rather continuous filings all over the period with two small peaks of filings in 2005 and 2007. The small fraction of grants in younger families (since 2005) reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO).

For earlier years of filing, national publication policies and the evolution of national patent legislation have to be taken into account. For example, until November 2000, the US patent office published only granted US patents. Thereby, US applications that were not granted were in fact never published. For the coverage of national databases used in this study, please refer to corresponding appendix. In addition, because of the 18 months of publication delay after the date of patent filing, the data after 2009 are incomplete.

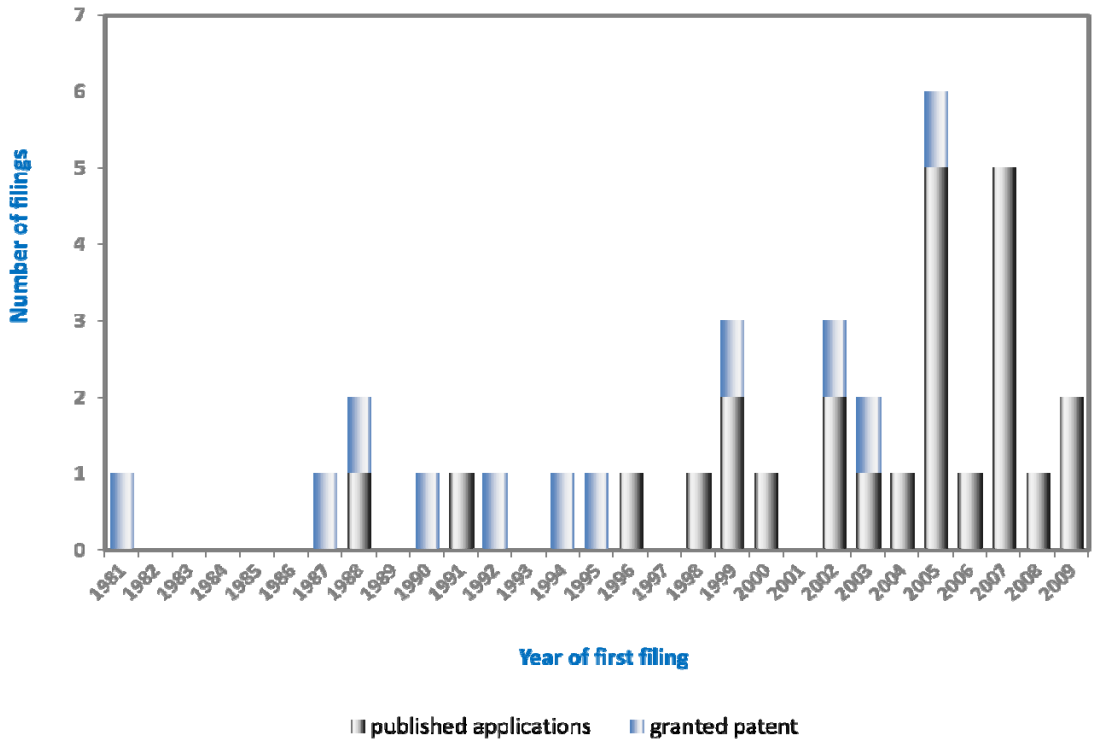

Figure 29 - Evolution of the number of granted and not granted patent families per year of first filing

A PCT application was filed for a large majority of patent families. Only 8 families did not contain a PCT application.

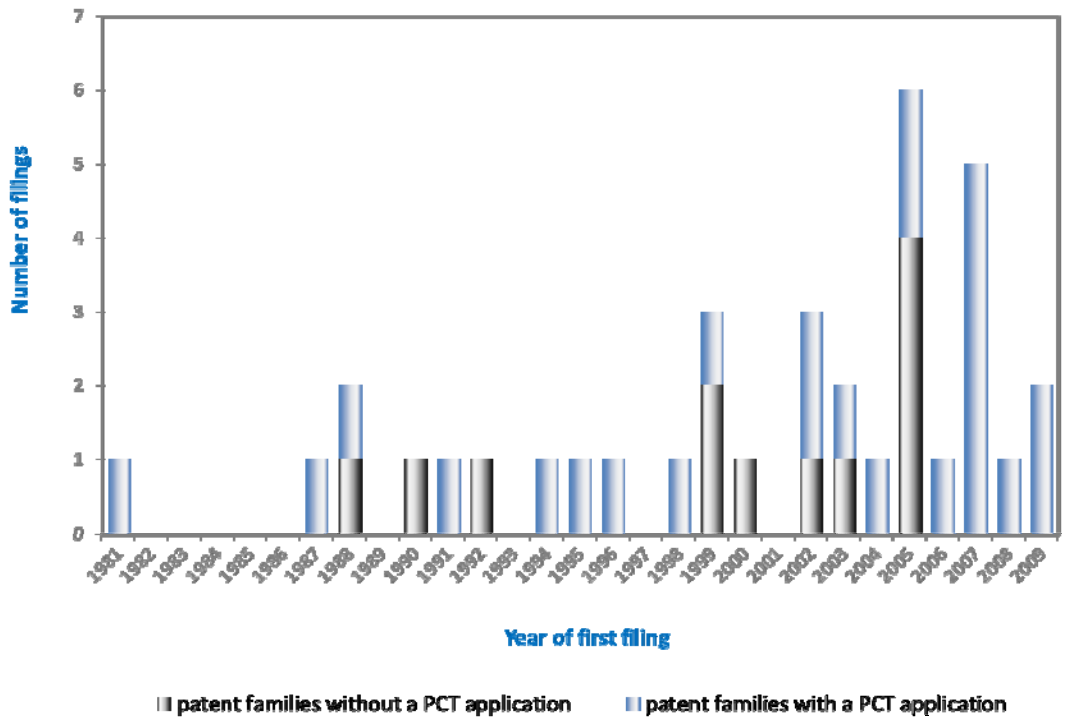

Figure 30 - Evolution of the number of patent families with and without PCT applications per year of first filing

The table below lists the office of origin of all PCT applications. This table was established by looking at the application number of a PCT filing that mentions the office of origin of the PCT (e.g. 2008WO-FR00687, this PCT application was filed via the French patent office).

Office of first filing	Number of PCT applications
UNITED STATES	11
EUROPEAN PATENT OFFICE (EPO)	6
INDIA	5
CANADA	1
CUBA	1
FRANCE	1
INTERNATIONAL BUREAU (WIPO)	1
UNITED KINGDOM	1

Table 19 - Origin of PCT applications

PCT applications were mostly filed with national or regional offices and only few directly with the international bureau.

3.2.2. Location of first filings

An analysis of the place of filing of priority patents results in the following table. A map of these filings can be seen in appendix. The location of priority filings and their evolution may give an indication of the country of origin of applicants and the dynamic of innovation in these countries.

First patent applications were filed in the United States that still dominate this sector as office of first filing. It can also be noted some recent filings stemming from the United Kingdom and India.

		81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	Total
	WORLD																1		1				1								3
AMERICA	UNITED STATES	1						1	2		1				1	1					1			1	1	2	1		1	1	15
	CUBA																						1								1
EUROPE	EUROPE																			1											1
	UNITED KINGDOM																			2								4		1	7
	FRANCE											1																			1
ASIA	INDIA																									4		1			5
	CHINA																						1								1
	KOREA																							1							1
	SINGAPORE												1																		1
Total		1	0	0	0	0	0	1	2	0	1	1	1	0	1	1	1	0	1	3	1	0	3	2	1	6	1	5	1	2	36

Table 20 - Evolution of first filings by offices

In order to have a better understanding of the country of origin and the innovation dynamic in these countries, it is more appropriate to take a look at the number of filings according to inventors' place of residence rather than the office of first filing.
To be able to make these statistics, the data related to Inventor's country (extracted from the address of the inventor), indexed in FamPat database (Questel^{TM}), was used. To do this, patent families of the database "Active Ingredients of human pneumococcal vaccines" were loaded into FamPat. This did not change the number of retrieved patent families although the definition of FamPat families is a little different from INPADOC families (FAMPAT families are built with patent applications having exactly the same priority whereas INPADOC families are built with patent applications having at least one priority patent application in common). Then, the number of filings naming at least one inventor coming from a country in particular was then counted.
It should be noted that totals of the two categories of the table are different because the inventors indicated in an individual patent application may have different countries of residence; each country was counted once, e.g. an application with two inventors residing in Belgium and one inventor residing in the United Kingdom would result in one count for each country.

Based on these data, it was noted that innovations stemming from Italian and Belgian inventors tend to be first protected through the UK patent office. Several reasons can co-exist to explain these differences:

- The difference in location of patent officers and research team (GSK vaccine research team is located in Belgium but files in the United Kingdom, NOVARTIS/CHIRON research team is located in Italy but files in the United Kingdom)
- The interest of filing directly in English to lessen future translation fees

		Number of filings in each patent authority	Number of filings according to inventors' place of residence
PCT	WORLD	3	-
AMERICA	UNITED STATES	15	14
	CUBA	1	1
	CANADA	-	2
	BRAZIL	-	1
EUROPE	EUROPE	1	-
	UNITED KINGDOM	7	3
	FRANCE	1	2
	SWITZERLAND	-	1
	ITALY	-	3
	GERMANY	-	1
	BELGIUM	-	5
	NETHERLAND	-	1
	SLOVAKIA	-	1
ASIA	INDIA	5	6
	CHINA	1	1
	KOREA	1	1
AFRICA	GHANA	-	1
AUSTRALIA	AUSTRALIA	-	1
Total		36	45

Table 21 - Comparison between place of filings and origin of the inventors

3.2.3. Average family size per office of first filing

These data were established by looking at the publication numbers of each family in order to extract the number of offices in which the applications were filed. However, for patent and patent applications of European countries filed via the European Procedure, a different counting was carried out because of specificities of European procedures. According to the designated and chosen offices, a new patent application number is attributed by these offices or not. For instance, German patent office will deliver a number (DE123456) after an extension via the European procedure while France will use the EP number (EP654321). When looking at the patent families via the patent & patent application numbers, it therefore created, improperly, a higher number of German extensions compared to French ones. Consequently, when a patent family contained a patent application filed via the EPO, the numbers issued by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family. In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

Office of first filing	Average family size	Standard deviation
CHINA (CN)	1	
CUBA (CU)	7	
EUROPEAN PATENT OFFICE (EPO)	8	
FRANCE (FR)	9	
UNITED KINGDOM (GB)	4	2.5
INDIA (IN)	2.2	1.6
KOREA (KR)	1	
SINGAPORE (SG)	2	
UNITED STATES (US)	5.4	3.7
INTERNATIONAL BUREAU (WIPO)	3.3	1.5

Table 22 - Average family and standard deviation size per office of first filing

US and UK patent families are divided in two main groups: those that were never extended and those with a high number of extensions (~10) which lead to a family size of medium value but with a high standard deviation.

3.2.4. Location of second filings

An analysis of the location of second filings results in the following histogram. A map compiling these data can be found in the corresponding appendix. Countries chosen for the extension of priority filings are an indicator of the markets and/or the production sites. The choice of countries may also be guided by company's competitors and potential infringers, even if there is no market in these corresponding territories. In Life Sciences, the choice can also be guided by usual locations of clinical trials (Poland, Hungary, Thailand, India…).

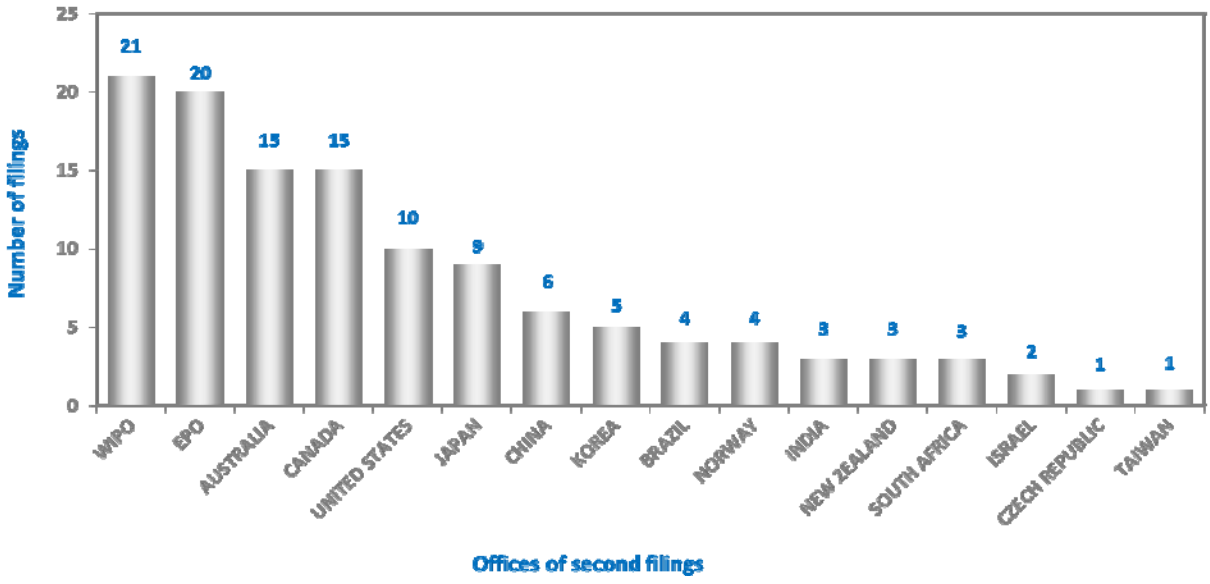

Figure 31 - Number of applications in the offices of second filings

Many second filings were performed via the PCT procedure (as seen in the previous section it represents 68% of the patent applications). The European patent office (EPO), Australia and Canada dominate as offices of second filings. Beware that the importance of Australia must be understood in relation to the policy of the Australian patent office which automatically delivered an Australian patent number when the PCT mentions Australia even if no extension were filed in Australia during the national phase.

3.2.5. Breakdown of filings by IPC codes

The figure below shows the most common relevant IPC codes present in the database.

IPC	Definition	Number of patent & patent applications
A61K39-385	Medicinal preparations containing antigens or antibodies, Haptens or antigens, bound to carriers	19
A61K39-112	Medicinal preparations containing antigens or antibodies, Bacterial antigens, Salmonella; Shigella	17
A61K47	Medicinal preparations characterised by the non-active ingredients used, e.g. carriers, inert additives [2]	12
A61P31	Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics, Antibacterial agents	12
C07K14-195	Peptides having more than 20 amino acids; from bacteriaGastrins; Somatostatins; Melanotropins; Derivatives thereof	7
C12N15	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification	7
A61P37	Drugs for immunological or allergic disorders (e.g. immunomodulators)	6
C07K17	Carrier-bound or immobilised peptides; Preparation thereof	6
Other A61K39	Medicinal preparations containing antigens or antibodies (except A61K39-09)	5
Other C07K14	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof	4
A61K35-74	Medicinal preparations containing material or reaction products thereof with undetermined constitution, from bacteria	3
C07K14-255	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof, from bacteria · Salmonella (G)	3
C07K16	Immunoglobulins, e.g. monoclonal or polyclonal antibodies	3
C07K19	Hybrid peptides (hybrid immunoglobulins composed solely of immunoglobulins C07K 16/46)	3
G01N33	Investigating or analysing materials by specific methods not covered by groups G01N 1/00-G01N 31/00	2
A61K39-385	Medicinal preparations containing antigens or antibodies, Haptens or antigens, bound to carriers	19

IPC	Definition	Number of patent & patent applications
A61K39-112	Medicinal preparations containing antigens or antibodies, Bacterial antigens, Salmonella; Shigella	17

Table 23 - Number of patent families classified within relevant IPC codes

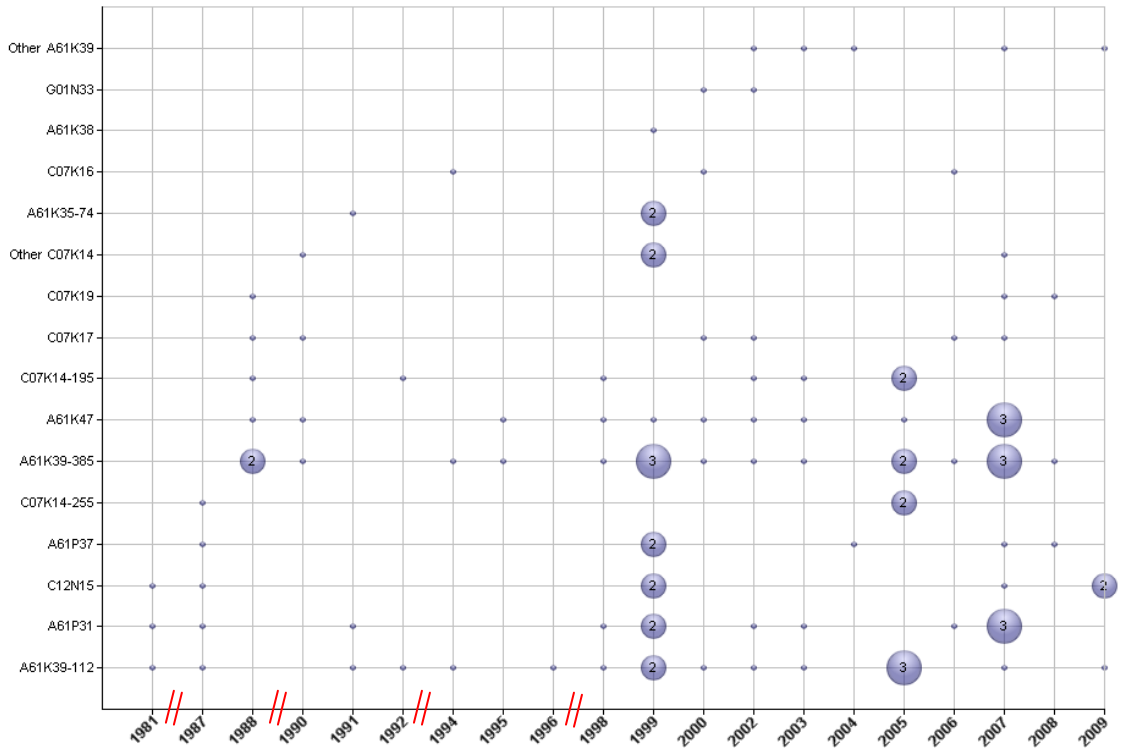

Figure 32 - Number of patent families classified within relevant IPC codes per year of first filing

No clear trend can be highlighted by the analysis of the evolution of IPC codes.

3.2.6. Analysis of applicants

Two types of applicants can be distinguished: institutional and industrial ones. The evolution of institutional vs. industrial priority filings (figure below) shows an equivalent sharing of the portfolio between this two types of applicants. Only few applications were jointly filed by an industrial and an institutional applicants.

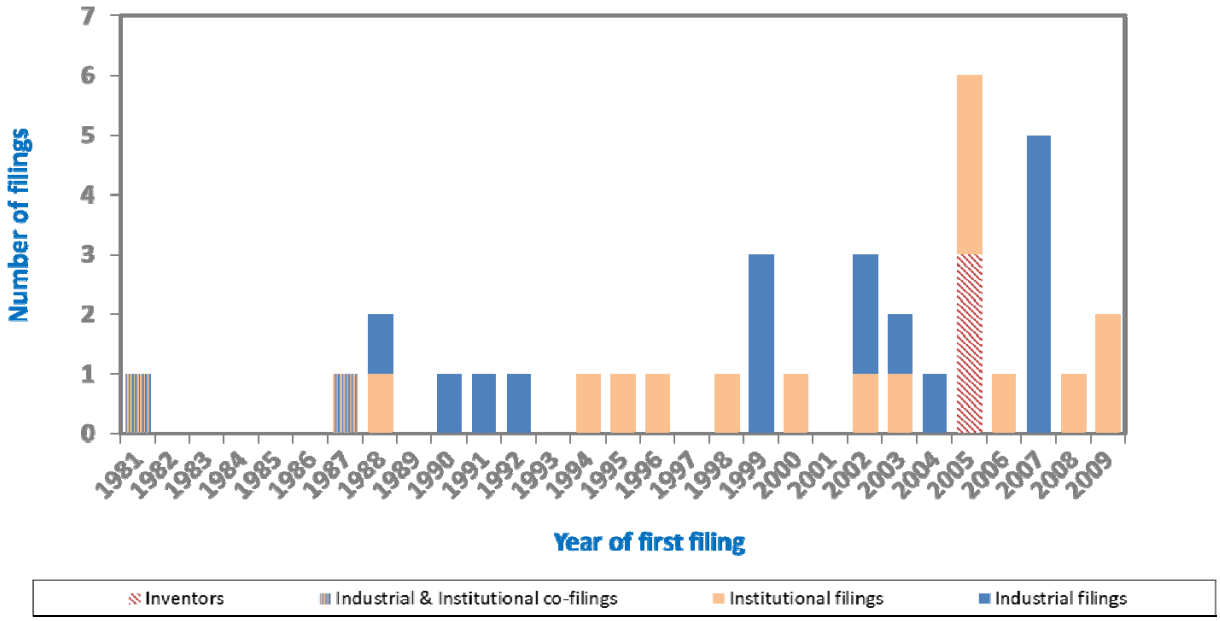

Figure 33 - Number of Institutional/Industrial/Individual priority filings per year of first filing

The following graph shows the main applicants classified by the size of their patent portfolio.

Co-filings are counted for each co-owner. For instance, a patent application co-filed between US Government and GSK is counted once for US Government and once for GSK.

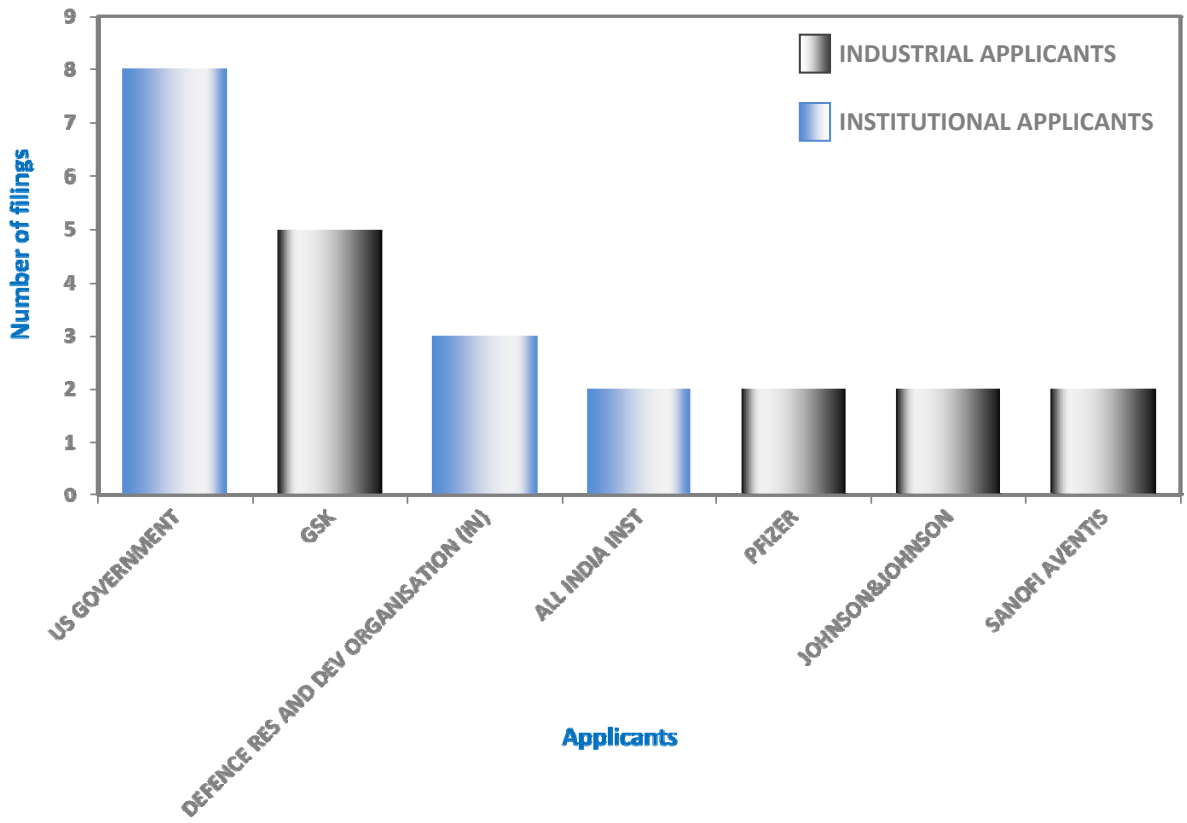

Figure 34 - List of main applicants (≥2 patent or patent applications)

The US Government laboratories and GSK dominate in terms of number of patent families, followed closely by Indian research institutes, Pfizer, Johnson&Johnson and Sanofi Aventis.

Please note that affiliates/subsidiaries were gathered under their parent company. These groupings were performed via a home-made database of mother companies and subsidiaries developed with Elsevier's business intelligence database[11], companies' websites, annual reports, business intelligence reviews and websites…

For more precision, the table below details this regrouping.

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
US GOVERNEMENT	US DEPARTMENT OF HEALTH AND SERVICES, US ARMY, NIH
GSK (GB)	GLAXOSMITHKLINE BIOLOGICALS (BE); SMITHKLINE BEECHAM BIOLOGICALS (BE)
DEFENCE RES AND DEV ORGANISATION (IN)	DEFENCE RESEARCH AND DEVELOPMENT ORGANISATION
ALL INDIA INST (IN)	ALL INDIA INSTITUTE OF MEDICAL SCIENCES
JOHNSON & JOHNSON (US)	SCHWEIZERISCHES SERUM- & IMPFINSTITUT BERN (CH)
PFIZER (US)	AMERICAN CYANAMID (US), PRAXIS BIOLOGICALS INC (US), WYETH (US)
SANOFI-AVENTIS (FR)	AVENTIS PASTEUR (FR); PASTEUR MERIEUX SERUMS & VACCINS (FR)

Table 24 - Applicants and their affiliates

For each applicant, the graphs below detail the preferred offices of first and second filings.

[11] http://www.elsevierbi.com/companies

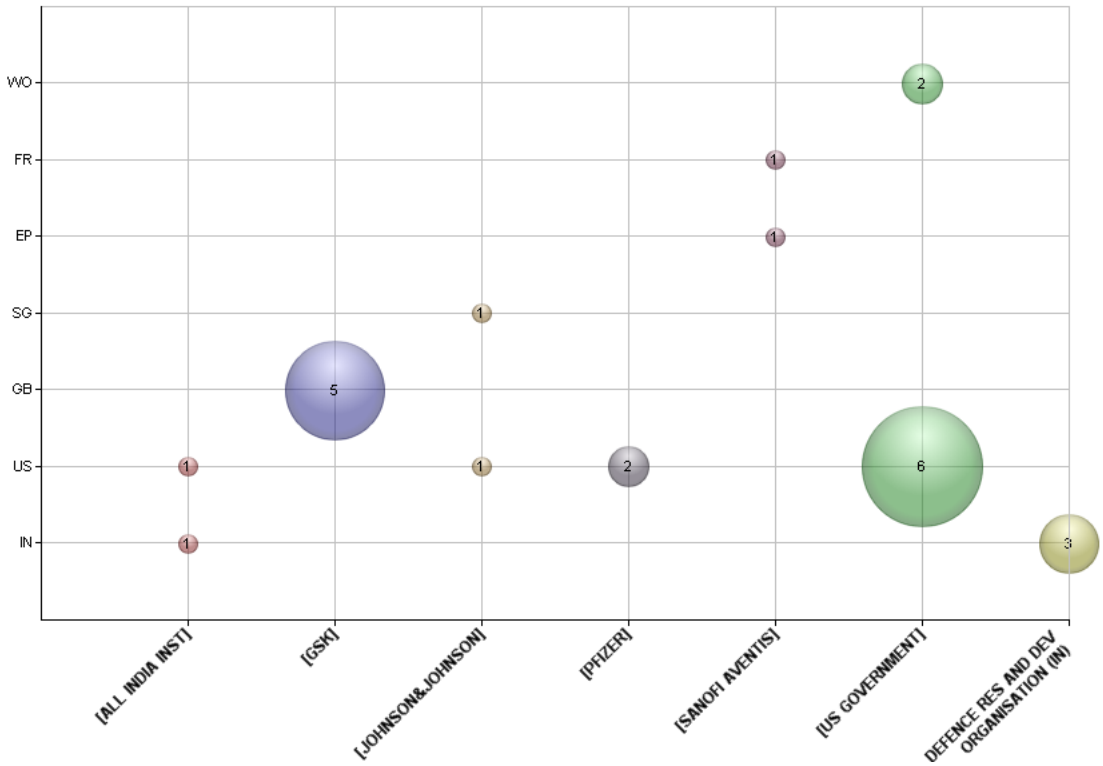

Figure 35 - Main applicants' preferred offices of first filings

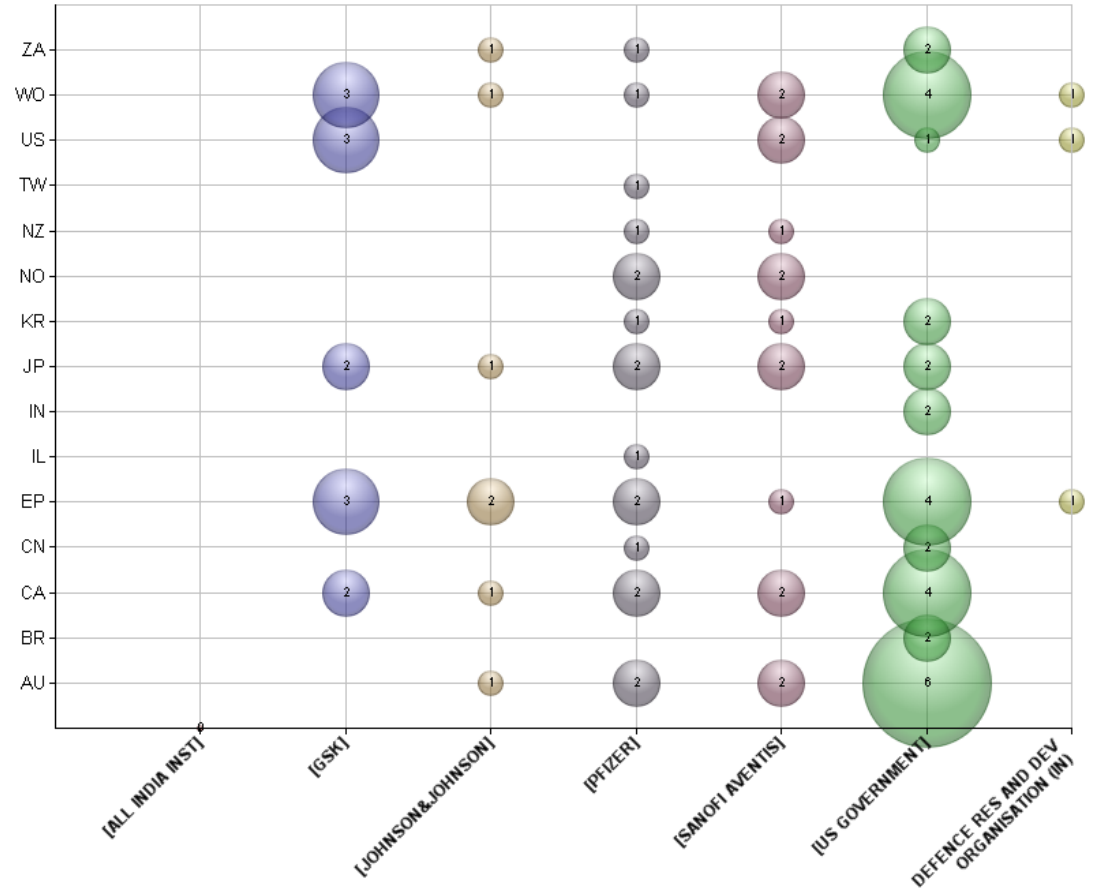

Figure 36 - Main applicants' preferred offices of second filings

The following graph details the evolution of office of first filing by applicant. The year corresponds to the first priority year of the patent family. Such a graph allows the identification of pioneer or emerging applicants in terms of filings.

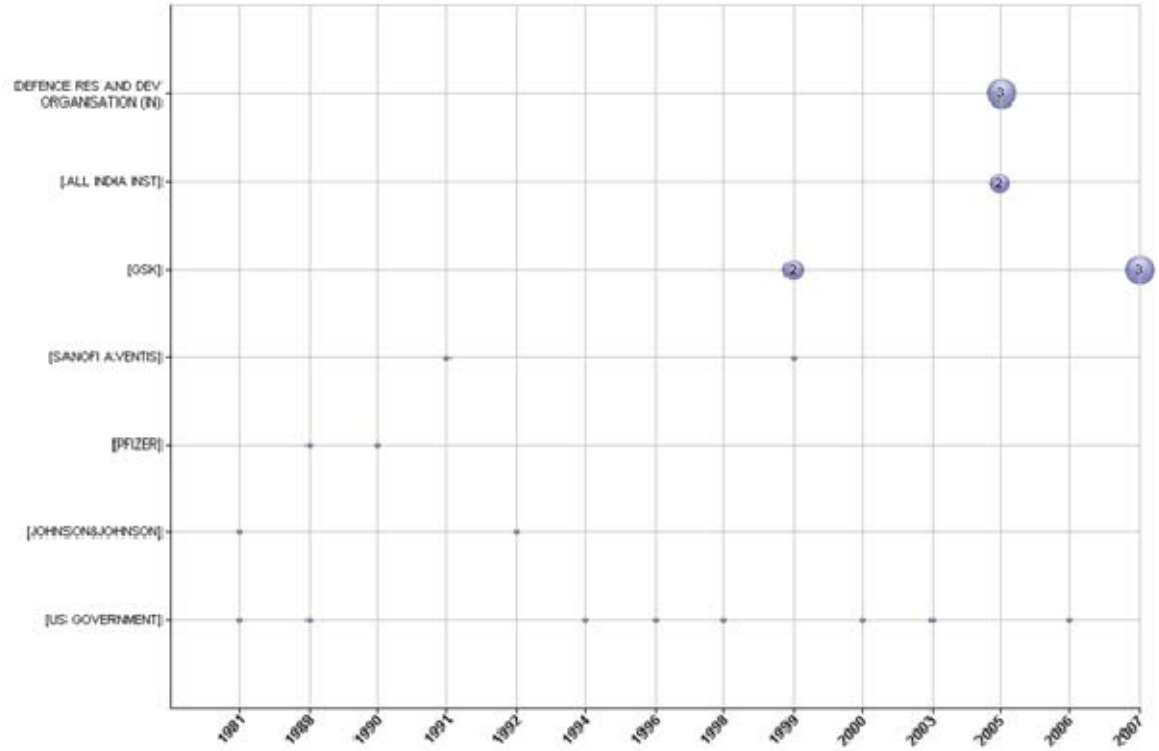

Figure 37 - Evolution of main applicants' filings (by year of first filing)

The US Government laboratories and Johnson&Johnson were the first applicants to file patent applications about typhoid conjugate vaccines but only the US Government laboratories kept filing over period.

Please note that, because of the particular numbering of patent applications filed during the national phase of the European procedure (see section 3.2.3. for the detailed explanation), when a patent family contained a patent application filed via the EPO, the numbers delivered by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family. In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent. Only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

Applicants	Average family size	Standard deviation
US GOVERNMENT	4.9	3.1
GSK	3.6	2.2
DEFENCE RES AND DEV ORGANISATION (IN)	2	1.7
ALL INDIA INST	1	
SANOFI AVENTIS	8.5	0.7
PFIZER	10	4.2
JOHNSON&JOHNSON	4.5	3.5

Table 25 - Average family size per applicant

These data show that industrial applicants filed rather large families.

3.2.7. Analysis of inventors

The table below lists the various inventors with their associated applicants.

Inventor	Number of filings	Assignee	Number of filings
Szu Shousun Chen	4	US GOVERNMENT	4
Biemans Ralph Leon	3	GSK	3
Duvivier Pierre	3	GSK	3
Capiau Carine	2	GSK	2
Deschamps Marguerite	2	GSK	2
Desmons Pierre Michel	2	GSK	2
Laferriere Craig Antony Joseph	2	GSK	2
Lee Che Hung	2	US GOVERNMENT	2
		FIOCRUZ	1
Moreau Monique	2	SANOFI AVENTIS	2
Poolman Jan	2	GSK	2
Porro Massimo	2	BIOSYNTH SRL	1
		PFIZER	1
Prieels Jean Paul	2	GSK	2
Robbins John	2	US GOVERNMENT	2
Schneerson Rachel	2	US GOVERNMENT	2

Table 26 - List of main inventors (≥2 patent or patent applications)

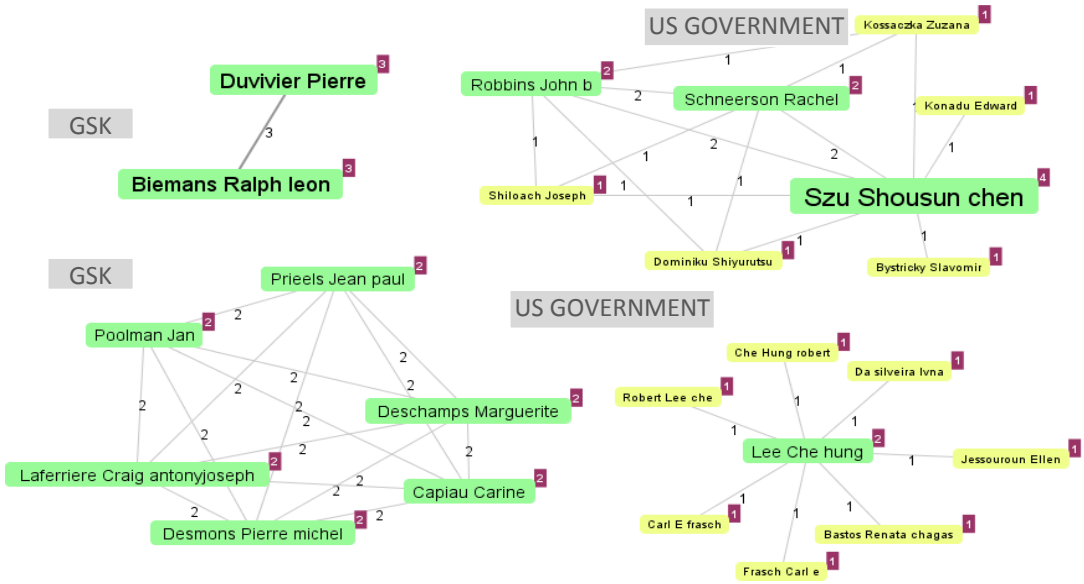

Figure 38 - Main research teams

3.2.8. Regional focuses: Brazil, India, China

This section focuses on patent families having Brazil, India or China as office of first filing. No patent families were created by first filing coming from Brazil. Only one was filed in China and two in India. The table below lists these few patent families stemming from China and India.

Priority number	Publication number	Title	Applicant
CN20021048876	CN1404873	Typhoid vaccine	LUZHU BIOLOGY TECHNOLOGY CO LTD
IN2007MU00786	EP2155244	Antigenic Polysaccharides and Process For Their Preparation	SERUM INST OF INDIA LTD
IN2005DE02648	EP1931389	Vaccine	DEFENCE RES AND DEV ORGANISATION (IN)
	IN02650DE2005	A Vaccine	DEFENCE RES AND DEV ORGANISATION (IN)
	IN02648DE2005	A Vaccine	DEFENCE RES AND DEV ORGANISATION (IN)
	IN02687DE2005	Cloning and expression of outer membrane protein C of Salmonella typhi ty 2 and conjugation of the purified insoluble protein to VI-K polysaccharide for use as a vaccine for tyophoid fever	ALL INDIA INST

Table 27 - List of patent families stemming from China and India

4. Active ingredient of human influenza vaccines

4.1. Search methodology

4.1.1. Introduction

This section describes the search methodology developed to retrieve patents and patent applications claiming active constituents of human vaccines against *influenza virus*. The narrative of this search history shows how the search was performed. It describes specific tools, databases, and challenges encountered and methods of circumventing. The search consisted generally of the use of combinations of keyword and classification searches, the intellectual review of search results for refining the queries and excluding irrelevant documents, and a final benchmarking of the search strategy through inclusion of documents cited in relevant documents. This section also discusses the limits of the use of patent classification codes (IPC, ECLA…) when looking for patents and patent applications dealing with active constituents of human vaccines against *influenza virus*.

4.1.2. Methodology and databases

A background study was first performed by looking at some literature on human influenza vaccines in order to collect keywords to build the patent queries and especially to help us determine the relevance of a patent family compared to another one, given that only patent describing "active constituents" had to be taken into account. Reviews including patent studies[12] were useful to make a list of keywords as well as general articles found on the Internet and patent families[13] about influenza virus and its related vaccines.

As a next step, a review of patent classification was carried out to identify patent classification codes related to human vaccines against influenza virus.

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[12] such as:
- "*A review of production technologies for influenza virus vaccines, and their suitability for deployment in developing countries for influenza pandemic preparedness*" conducted by the World Health Organization - Initiative for Vaccine Research,
- the "*Working Paper on Patent issues related to influenza viruses and their genes*", prepared by WIPO at the request of the World Health Organization,
- the "*WIPO Patent search report on pandemic influenza preparedness (PIP)-related patents and patent applications*", prepared by the International Bureau,

[13] http://www.who.int/influenza/vaccines/en/
http://en.wikipedia.org/wiki/Influenza
http://en.wikipedia.org/wiki/Orthomyxoviridae
http://www.patentlens.net/daisy/influenza/4132.html
http://www.boliven.com/boliven_landscapes/ip_report/Influenza_landscape

With the list of keywords and patent classification codes established such as described, queries were built and run into FAMPAT database (Questel™). Therefore this document presents the FAMPAT queries used to identify the relevant patent families of this focus. However, the final database, from where the statistical analyses were set-up, was created using INPADOC documents (Patbase export; Minesoft™).

4.1.3. Background study

4.1.3.1 Review of the literature

Influenza, commonly called as the flu, is an infectious disease caused by RNA viruses of the family *Orthomyxoviridae*, which affects mammals and birds: the influenza viruses. These viruses infect the airways of a subject and cause general respiratory symptoms, fever and extreme coldness, weakness and fatigue, body aches, headache and even nausea and vomiting. In humans, influenza may result in morbidity and mortality rates, especially in children and elderly persons.

Influenza viruses are divided in three subtypes: A, B - the two most common causes of influenza in man - and C. They are distinguishable by their antigenic determinants. Indeed, the influenza virions carry two major surface glycoprotein antigens, Hemagglutinin (HA) and Neuraminidase (NA). The HA and NA proteins are most susceptible to vary with 16 immune classes of HA (from H1 to H16) and 9 different NA classes (from N1 to N9). This provides the basis for the different influenza virus subtypes, like H9N2 or H5N1.

Influenza viruses have two essential immunological characteristics that represent a real challenge to vaccine makers. First, genetic variations called "antigenic drift" occur in the surface glycoproteins every few years, producing viruses that escape to resistance elicited by commercialized vaccines (seasonal influenza). Second, the "antigenic shift" concerns the fact that influenza viruses can exchange genetic material and merge resulting new strains different from both parental viruses (influenza pandemic). This new influenza strain emerges and starts easily spreading. One example of an influenza pandemic is the "Spanish flu" (H1N1) pandemic in 1918 with more than 20 million people killed worldwide. Another example is the case of the avian influenza that has crossed the species barrier from birds to mammals, including humans, such that the human population would be immunologically pathogenic to this new strain.

Nowadays, influenza has a critical importance for global public health. In this context, vaccination is the most effective solution for preventing infection and severe outbreaks caused by influenza viruses. Such a vaccine is composed with a whole but attenuated or killed virus or of a viral antigen such as the HA protein. The first efficient vaccine against influenza was developed in 1944 by Dr. Thomas Francis, Jr., with the funding of the American Army.

Several vaccine preparations are now commercially available: Begrivac, Flu shield, Fluad, Agrippal, Flumist, Fluogen, Fluvirin, Fluzone, Imovax, Istivac, Mutagrip, Sandovac, Tetagrip, Vaxigrip.

From this background study, a list of keywords was established:

<u>Keywords related to influenza virus:</u> influenza(l), influenzavirus, flu, (ortho)myxoviridae, virus, viral, viridae, virosome, strain(s), h(a)emagglutinin(s), HA protein(s)/gene(s)/sequence(s), neuraminidase(s), NA protein(s)/gene(s)/sequence(s), neuraminyl, H1N1, H2N2, H3N2, H5N1, virus-

like particle(s), VLP(s), attenuated, attenuation, attenuating+, inactivated, inactivation, inactivating, killed, live, (a)virulent.

Keywords related to vaccines: vaccin(es), vaccination, vaccinating, antigen(s), antigenic, immunogen(s), immunogenic, immunise, immunisation, immunising, immunize, immunization, immunizing, immune response, prevent, prevention, preventing, protect, protection, protecting.

4.1.3.2 Review of relevant classification codes

By screening the international, European, American and Japanese patent classifications, the codes corresponding to medicinal preparations containing antigens or antibodies of influenza virus were collected. The following codes were thereby identified:

International Patent Classification (IPC):

A61K 39/145

[0] A61K 39/00: Medicinal preparations containing antigens or antibodies
[1] A61K 39/145: Orthomyxoviridae, e.g. influenza virus

US Patent Classification (USPC):

424/209.100

[0] 424: Drug, bio-affecting and body treating compositions
[1] 424/184.1: antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-diated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.)
[2] 424/ 204.1: Virus or component thereof
[3] 424/ 209.1: Orthomyxoviridae (e.g., influenza virus, fowl plague virus, etc.)

424/210.100

[0] 424: Drug, bio-affecting and body treating compositions
[1] 424/184.1: antigen, epitope, or other immunospecific immunoeffector (e.g., immunospecific vaccine, immunospecific stimulator of cell-diated immunity, immunospecific tolerogen, immunospecific immunosuppressor, etc.)
[2] 424/ 204.1: Virus or component thereof
[3] 424/ 209.1: Orthomyxoviridae (e.g., influenza virus, fowl plague virus, etc.)
[4] 424/210.100: Subunit vaccine containing hemagglutinin or neuraminidase

European classification (ECLA):

A61K39/145

[0] A61K39: Medicinal preparations containing antigens or antibodies
[1] A61K39/12: Viral antigens

[2] A61K39/145: Orthomyxoviridae, e.g. influenza virus

C07K14/11

[0] C07K14: Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof
[1] C07K14/005 from viruses
[2] C07K14/08: RNA viruses
[3] C07K14/11: Orthomyxoviridae, e.g. influenza virus

Japan File-Index (Japan FI):

A61K39/145

[0] A61K39/00: Medicinal preparations containing antigens or antibodies
[1] A61K39/145: Orthomyxoviridae, e.g. influenza virus

4.1.4. Search strategy

4.1.3.3 Classification codes based queries

QUERY 1: Classification codes related to Orthomyxoviridae including influenza virus

((A61K-039/145)/IC) OU ((424209100)/PCLO) OU ((424210100)/PCLO) OU ((A61K-039/145)/ECLA) OU ((C07K-014/11)/ECLA) OU ((A61K39/145)/FI)

"IC" means "international patent classification
"PCLO" means "US patent classification
"ECLA" means European classification
"FI" means Japan File Index
For further details of command lines, please refer to the appendix.

This query led to 2397 FAMPAT families (published until November 2011). Under the IPC code A61K-039/145, the majority of patent families classified are related to influenza vaccines (e.g. US20080311153) including specific strains of the virus (e.g. RU2105063). However, the A61K-039/145 IPC code is not dedicated to humans and includes patent families claiming influenza vaccines for animals like horses (e.g. WO0160849), dogs (e.g. WO200897970), pigs (e.g. JP59039831) and birds (e.g. RU2009114430). Furthermore, patent families claim vaccines against the other genera of the family of *Orthomyxovirus* like *Isavirus* (e.g. WO200072878). Other patent families do not correspond to influenza vaccinal element (antigen, viral strain) but to the global process of production of such vaccines, as the use of liposomes (e.g. WO9749423) or adjuvants (e.g. WO2009151313), the replication of viruses in cell culture (e.g. US20030119183), their purification (e.g. WO200806780), the frozen stockpiling of vaccines (e.g. WO200817956)… Other patent families are about detection of influenza virus (e.g. WO2007134166) because the IPC code also includes patent families protecting materials for immunoassay (G01N33/53). Patent families referring to diagnostic (e.g. SU1463758), to antibody against influenza virus (e.g. WO200378600) and antiviral peptide are also classified under the A61K-039/145 IPC code. Furthermore, a lot of patent families did not refer to influenza virus but

to *Haemophilus influenza*(*e*) (e.g. EP2133359) or *Parainfluenza virus* (e.g. US2007134271) that are not virus of the *Orthomyxoviridae* family. Some patent families claim vaccines against bacteria as *Streptococcus equi* (e.g. EP0786518). Patent families belong to results although they seem to be unrelated to *Orthomyxovirus* and *influenza virus*, probably because the keyword "influenza" is mentioned in claims (e.g. WO200172281). In conclusion, the A61K-039/145 IPC code cannot be used to build a query mining influenza vaccines. The perimeter of search was thereby narrowed by eliminating patent families that do not deal with human influenza virus and completed by queries using keywords.

4.1.3.4 Keyword-based queries

QUERY 2: Name of the influenza virus, the infectious disease and the virus family (in title, abstract and claims).

(INFLUENZA+ OU FLU OU INFLUENZA_VIR+ OU ORTHO_MYXOVIR+ OU MYXOVIR+)/BI/CLMS

« BI » means that the research is carried out in the titles and abstracts of FAMPAT families.
« CLMS » means that the research is carried out in the claims of FAMPAT families.
« _ » replace a space, a – or no space at all (i.e. *ortho_mixoviridae* can retrieve the words *orthomixoviridae*, *ortho mixoviridae* or *ortho-mixoviridae*).
For further details of command lines, please refer to the appendix.

This query led to 20896 FAMPAT families. The results were related to influenza virus but not yet to vaccines (e.g. EP0007467) because many patents also claimed a treatment for influenza (e.g. ZA7905491), the detection of the virus (e.g. SU639941), a diagnostic test (e.g. SU1698288), a strain for modeling infection in mice (e.g. SU1735363), the replication of high growth virus strains in cell lines (e.g. US5824536) of their purification (e.g. EP0171086), an anti-influenza virus agent from plant extracts (e.g. JP2002145790)…

The influenza virus can also be quoted among a list of viruses in dependent claims (e.g. WO201056991) and one member of a family quotes the term "influenza" (e.g. WO200221614) or "flu" (e.g. US6378219) without link to the virus.

Furthermore, patent families claimed *Haemophilus influenzae* (e.g. WO200216440) or *Parainfluenza virus* (e.g. US6410023), that should be eliminated with a specific query.

The set of results was too noisy because of patent families not only related to *influenza* virus and/or vaccines. These irrelevant patent families had to be eliminated using specific queries.

QUERY 3: Defined subtypes of influenza virus (in title, abstract and claims).

((H1N# OU H2N# OU H3N# OU H4N# OU H5N# OU H6N# OU H7N# OU H8N# OU H9N# OU H10N#)/BI/CLMS) SAUF (H2NR OU H2NO OU H2NH)/BI/CLMS

« # » replaces strictly one character

This query led to 1903 FAMPAT families. Most of these patent families were retrieved with Query 2 (e.g. RU2416641). For H1N#, H1 is the first of known types of the protein Hemagglutinin, associated with one of the known types of the protein Neuraminidase (N#). The exclusion of "H2NR, H2NO and H2NH" was a way to suppress irrelevant patent families (e.g. WO2008093086).

However, some patent families did not refer to human influenza vaccines but to virus production (e.g. WO200745674), their detection (e.g. CN1858249)…

QUERY 4: Undefined subtypes of influenza virus (in title, abstract and claims).

((H#N# OU A_H#N# OU B_H#N# OU B_H#N#)/BI/CLMS PHR (+MYXOVIR+ OU +INFLUENZA+ OU FLU OU +VIRUS OU VIRAL OU +VIRIDAE OU SEROTYPE? OU STRAIN? OU ANTIGEN? OU SUBTYPE? OU H?EMAGGLUTININ? OU NEURAMINIDASE? OU +NEURAMINYL+ OU GL#COPROTEIN? OU PANDEMIC)/BI/CLMS) SAUF (HAND OU HANG OU HUNG OU HIND OU HINF OU HANK OU HONE OU HING OU HTND OU HSNI OU HENO OU HTNF OU HANP)/BI/CLMS

« ? » replaces one or more characters.

This query led to 1429 FAMPAT families. Most of these patent families were retrieved by the Queries 2 and 3 (e.g. RU2007127098). For H#N#, H# was one of the known types of the protein Hemagglutinin, associated with one the known types of the protein Neuraminidase (N#). The exclusion of "HAND, HANG, HUNG, HIND, HINF, HANK, HONE, HING, HTND, HSNI, HENO, HTNF and HANP" was a way to suppress irrelevant patent families, as those claiming the use of restriction enzymes such as HIND III (that is fetch through H#N# keyword, e.g. WO2006085016).

However, some patent families did not refer to human influenza vaccines as for the two precedent queries.

QUERY 5: Names of the other genera of virus of the *Orthomyxoviridae* (in title, abstract and claims).

(THOGOTO_VIRUS OU ISA_VIRUS)/BI/CLMS

This query led to 20 FAMPAT families. These results would be eliminated of the study, as the patent family covering a vaccine against *Isavirus* (e.g. WO200072878).

QUERY 6: Name of *Haemophilus influenza* (in title, abstract and claims).

((H?EMOPHILUS 1AV INFLUENZA?) OU (H?EMOPHILUS 1AV PARA_INFLUENZA?) OU (H AV INFLUENZAE))/BI/CLMS

"1AV" means "up to one word before the other".

This query led to 2044 FAMPAT families. *Haemophilus influenza*, formerly called Bacillus influenza, is a bacteria of the *Pasteurellaceae* family and was considered until 1933 as the cause of influenza. The results dealt with *Haemophilus influenza* (e.g. WO02060938), *Haemophilus influenzae* (e.g. US20110150889) and *Hemophilus influenza* (e.g. WO8912460). This query was used in order to eliminate these irrelevant results from the queries related to *influenza virus*.

QUERY 7: Name of *Parainfluenza virus* (in title, abstract and claims).

(PARA_INFLUENZA)/BI/CLMS

This query led to 1299 FAMPAT families. The *Parainfluenza virus* is a member of the *Paramyxovirus* family, and is different from the influenza virus. The review of these patent families highlighted many irrelevant results claiming for example recombinant parainfluenza virus vaccines (e.g. US6410023). This query was used in order to eliminate these results from the influenza queries. However, relevant patent families would also be eliminated with such a query because "para influenza" is a Spanish notion meaning "for influenza" (e.g. MX2011000459). But, these relevant results would be retrieved with complementary queries such as Spanish ones.

QUERY 8: Elimination of the other genera of virus of the *Orthomyxoviridae* family, *Haemophilus influenza* and *Parainfluenza virus*.

(QUERY 2 OR QUERY 3 OR QUERY 7) AND NOT (QUERY 5 OU QUERY 6 OU QUERY 7)

This query led to 19252 FAMPAT families.

At this stage, there was a mix of patent families quoting at least one of the keywords related to influenza virus and claiming vaccines and as well as diagnostic methods or therapeutic antibodies... It was therefore necessary to introduce a limitation to vaccines.

QUERY 9: Combination of the Query 8 and a query including synonymous of vaccines to get patent families related to influenza vaccines (in title, abstract and claims).

QUERY 8 ET (VACCIN+ OU IMMUNOGEN+ OU IMMUNIS+ OU IMMUNIZ+ OU ANTIGENIC)/BI/CLMS

This query led to 3802 FAMPAT families.

However, some patent families did not refer to influenza vaccines but to general vaccines, adjuvants, antiviral agents, inhibitors (e.g US20080181949)… and vaccines for animals (CA2535127). The next step was therefore to limit the results to human vaccines and a query was built to remove these irrelevant patent families.

QUERY 10: Elimination of patent families claiming animals (in title, abstract and claims).

QUERY 9 SAUF ((CHICKEN? OU FISH?? OU PIGEON? OU (NEWCASTLE DISEAS+) OU CATTLE OU AVIAN OU POULTRY OU (BURSAL DISEAS+) OU ANIMAL+ OU GOSLING OU GOOSE? OU CANINE OU CANID+ OU DOG? OU CAT? OU COW? OU FELINE OU EQUINE OU SWINE? OU PORCINE OU BIRD? OU EPIZOOTIC OU HOG? OU CALF OU BOVINE OU TURKEY? OU GOAT? OU SALMON? OU HORSE? OU SHEEP? OU DUCK? OU PIG? OU VETERINARY+ OU VET) SAUF (HUMAN? OU PATIENT? OU MAN OU WOMAN OU MEN OU WOMEN OU ADULT? OU MAMMAL? OU CHILD OU CHILDREN OU BABY OU BABIES OU INFANT? OU SUBJECT? OU PEOPLE))/BI/CLMS

This query led to 3097 FAMPAT families.

At this stage, patent families claiming a veterinary use of the invention (e.g. WO9406468, US5916879) were eliminated, except those that also covered a human use (e.g. WO2007082734). The last residual patent families related to animals would be cleaned by an intellectual screening.

However, some patent families did not refer to human influenza vaccines but to the virus production (e.g. WO200745674), their detection (e.g. CN1858249)…

The next step consisted therefore in limiting the results to patent families claiming the vaccines themselves and not the purification process, the cell culture of viruses… For this purpose, these irrelevant patent families were suppressed with queries of keywords not related to vaccines that were built for the study about vaccines in general (Part I).

All Queries from Query 11 to Query 23 were therefore used to suppress irrelevant patent families.

QUERY 11:

(((BIOREACTOR+ OU REACTOR+ OU INDUSTRIAL OU (LARGE SCALE) OU (MASS PRODUCTION))/TI) OU (((BIOREACTOR+ OU REACTOR+)/AB) ET ((METHOD OU PROCESS)/TI)))

QUERY 12:

(((MODEL?)/TI) SAUF (((SEQ ID)/TI/AB/CLMS) OU ((PREVENT+)/TI) OU ((ANTIGEN+ ET (IMMUNE RESPONSE))/TI/AB) OU ((VACCINE AGAINST)/TI/AB)))

QUERY 13:

(((GRAFT+ OU XENOGRAFT+ OU IMPLANT? OU TRANSPLANTATION+ OU IMMUNOSUPPRESSOR OU REJECTION OU (DOWN REGULATION))/TI/AB) SAUF (((((VACCIN+ AV COMPOSITION?) OU (IMMUNOGENIC AV COMPOSITION?)) ET INFECT+)/TI/AB/CLMS) OU (((SEQ ID)/TI/AB/CLMS) OU ((VACCIN+ AGAINST)/TI) OU ((VIR+ VACCIN+)/TI) OU (PROPHYLAC+/TI/AB) OU ((ELICIT+ PHR RESPONSE)/TI/AB/CLMS)) OU (ATTENUAT+ OU (IMMUNE AV RESPONSE))/TI))

QUERY 14:

(((DEVICE? OU NEEDLE+ OU MICRONEEDLE+ OU INJECT+ OU APPARATUS+ OU PEN OU SEMICONDUCTOR+ OU STENT+ OU CATHETER+ OU MAGNETIC OU AUTOMATIC)/TI) SAUF (((((VACCIN+ AV COMPOSITION?) OU (IMMUNOGENIC AV COMPOSITION?)) ET INFECT+)/TI/AB) OU ((((SEQ ID)/TI/AB/CLMS) ET VACCIN+/TI) OU ((VACCIN+ AGAINST)/TI) OU ((INJECTABLE VACCINE)/TI) OU ((VIR+ VACCIN+)/TI) OU (PROPHYLAC+/TI/AB)) OU (ATTENUAT+)/TI))

QUERY 15:

((A61P-035)/IC) ET ((TREAT+ OU THERAP+) SAUF (PROPHYL+ OU PREVENT+))/TI/AB/CLMS

QUERY 16:

(((CREAM? OU TABLET? OU AQUEOUS OU SOLVENT? OU GEL? OU POWDER+ OU OIL+ OU WATER OU EMULSI+ OU DRY OU DRIED)/TI) SAUF (((IMMUNIZ+ OU IMMUNIS+ OU ((ELICIT+ OU GENERAT+ OU INDUC+) 3AV IMMUN+))/TI/AB/CLMS) OU ((VACCIN+)/TI/AB) OU ((BACTERIN+)/TI/AB) OU (((ATTENUATED OU AVIRULENT) ET STRAIN+)/TI/AB/CLMS)))

QUERY 17:

(((CELL LINE?) OU CULTUR+ OU MATRI+)/TI) SAUF (((VACCIN+ OU IMMUNOGENIC OU ATTENUAT+ OU AVIRULENT OU INACTIVAT+)/TI) OU ((VACCIN+ ET (ATTENUAT+ OU IMMUNZ+ OU IMMUNIS+))/AB) OU ((VACCIN+ ET (IMMUNIZ+ OU IMMUNIS+ OU SEQ OU IMMUNOPROTEC+))/CLMS))

QUERY 18:

(CROHN OU ALZHEIMER OU (IMMUNE DISEASE?) OU (AUTOIMMUNE DISEASE) OU NEUROTOXICITY OU AMYLOID+ OU ARTHRITIS)/TI

QUERY 19:

(DELIVER+ SAUF (MENINGOCOCCAL OU PAPILLOMA OU TUBERCULOSIS OU ANTHRAX OU INFLUENZA+ OU FLU OU EPSTEIN OU ANGUILLARUM OU (HIV AV VACCINE)))/TI

QUERY 20:

ALLERG+/TI

QUERY 21:

((STABILIZER/TI) SAUF (((IMMUNOGENIC COMPOSITION+) OU (VACCIN+ PREPARATION) OU (VACCIN+ COMPOSITION+) OU (LIVE 2AV VACCIN+))/TI/AB/CLMS)) OU ((STABILI+ ET (FORMULATION OU CASSETTE OU CONFORMATION OU ANTIBOD+))/TI) OU (((STABILI+ ET PACKAGING)/TI/AB) SAUF (VACCIN+ COMPOSITION+)/TI) OU (((STABILI+)/TI) SAUF (VACCIN+ OU IMMUNOGENIC OU PREVENT+ OU PROTECT+ OU INACTIVAT+ OU ATTENUAT+)/TI/AB/CLMS)

QUERY 22:

(CANCER+ OU PROBIOTIC+)/TI

QUERY 23:

(((CANCER OU TUMO?R OU CARCINOM+) 2M (ANTIGEN+ OU PEPTID+)))/TI/AB/CLMS

QUERY 24:

QUERY 10 SAUF (QUERY 11 OU QUERY 12 OU QUERY 13 OU QUERY 14 OU QUERY 15 OU QUERY 16 OU QUERY 17 OU QUERY 18 OU QUERY 19 OU QUERY 20 OU QUERY 21 OU QUERY 22 OU QUERY 23)

This query led to 2324 FAMPAT families.

At this stage, irrelevant patent families were still present in the dataset. To eliminate them, the Query 25 was built with the suppression of recurrent terms (purif+, inhitor?...) related to results about *influenza virus* inhibitors, virus purification…

QUERY 25:

QUERY 24 SAUF ((PURIF+ OU +ASSAY+ OU ANTIBOD+ OU DETECT+ OU MENINGITIS OU ANKARA OU MALARIAL? OU ANTIVIRAL OU BACULO+ OU MURAMYL OU ANIMAL? OU COMPOUND? OU BACTER+ OU LIPOSOME? OU (+VIRUS+ SAUF (INFLUENZA+ OU FLU OU INFLUENZA_VIR+ OU ORTHO_MYXOVIR+ OU MYXOVIR+)) OU VECTOR+ OU DIAGNOST+ OU INHIBITOR? OU DERIVATIVE? OU EQUINE? OU IMMUNOGLOBULIN? OU IL_1 OU IL_2 OU MICRO_ORGANISM? OU +COCCUS OU +COCCAL)/TI) OU ((A61P-025+)/IC OU (A61P-035+)/IC)

This query led to 1379 FAMPAT families. An intellectual screening allowed checking the results of the Query 25 to decide if they had to be conserved in a list (e.g. RU2422517) or eliminated (KR20110072473). For this purpose, the title, abstract and claims of the 1379 results were manually analyzed. Such a detailed review allowed the identification of new keywords to validate the previous queries or build new ones, as well as the identification of irrelevant patent families to suppress them.

QUERY 26: Supplemental search concerning immune response

(INFLUENZA+ OU FLU OU INFLUENZA_VIR+ OU ORTHO_MYXOVIR+ OU MYXOVIR+)/BI/CLMS ET (IMMUN+ PHR RESPONSE?)/BI/CLMS

This query led to 2318 FAMPAT families. This query completed the relevant patent families of the Query 9 (keywords related to vaccines) with additional relevant results (e.g. WO2008054540). The new relevant results of this query were added in the list of selected patent families.

QUERY 27: Supplemental search concerning non-natural virus

(INFLUENZA+ OU FLU OU INFLUENZA_VIR+ OU ORTHO_MYXOVIR+ OU MYXOVIR+)/BI/CLMS PHR (ATTENUAT+ OU INACTIVAT+ OU KILLED OU LIVE OU VIRULENT OU AVIRULENT)/BI/CLMS

This query led to 1014 FAMPAT families. Most of them were already identified with previous queries (e.g. KR20080100632). The new relevant results of this query are added in the list of selected patent families.

QUERY 28: Supplemental search concerning virus-like particles

(INFLUENZA+ OU FLU OU INFLUENZA_VIR+ OU ORTHO_MYXOVIR+ OU MYXOVIR+)/BI/CLMS ET ((+LIKE PHR PARTICLE?) OU VLP?)/BI/CLMSoffice of first filings

This query led to 383 FAMPAT families.

The virus-like particles (VLPs) can induce an immune response since they include at least surface proteins displayed in a conformation similar enough to their native conformation. Moreover, these particles do not contain the complement of the genetic material required to the viral replication. Most of patent claiming VLPs were already identified with previous queries (e.g. WO2009105729) but new relevant patent families were identified (e.g. WO200200885) with this additional query. They were therefore added to the list of selected patent families.

QUERY 29: Supplemental search concerning virosomes

VIROSOME?/BI/CLMS

This query led to 215 FAMPAT families. Most of them were already identified with previous queries (e.g. WO2007107585). The new relevant results of this query were added to the list of selected patent families (e.g. US5879685, not included in the results of the Query 25).

Another investigation was conducted, adding new keywords related to the structure of influenza virus that was similar in composition for the viral particles of all influenza viruses. The virus structure is made of a viral envelope containing two main types of glycoproteins on the outside of the viral particles: Hemagglutinin (HA) and Neuraminidase (NA).

QUERY 30:

((H?EMAGGLUTININ? OU (HA AV (PROTEIN? OU GENE? OU SEQUENCE?)) OU (NA AV (PROTEIN? OU GENE? OU SEQUENCE?)) OU NEURAMINIDASE?) OU (ACETYL_NEURAMINYL+) OU (+NEURAMINYL+)) ET ((IMMUN+ PHR RESPONSE?) OU (PREVENT+ OU PROTECT+) OU (VACCIN+ OU IMMUNOGEN+ OU IMMUNIS+ OU IMMUNIZ+ OU ANTIGENIC))/BI/CLMS

This query led to 1355 FAMPAT families. The results mainly concerned the immune response elicited by the viral protein Hemagglutinin (HA) and Neuraminidase (NA). Most of them were already identified with previous queries (e.g. WO2010125202). An intellectual screening was the way to eliminate Neuraminidase not related to influenza virus (but to *Pasteurella multocida*, e.g. WO9816649). The new relevant results of this query were added to the list of selected patent families (e.g. CN1660421, not included in the results of the Query 25).

QUERY 31: Query in foreign language: French, Spanish, German, Russian, Japanese, Chinese and Korean.

French = “GRIPPE”means “influenza” and “VACCIN?” means “vaccine(s)”.

Spanish = “VACUNA(S)” means “vaccine(s)”.

German = “GRIPPE”means “influenza” and “IMPFSTOFF?” means “vaccine(s)”.

Russian = “ГРИПП”means “influenza” and “ВАКЦИНА” means “vaccine(s)”.

Japanese = “インフルエンザ”means “influenza” and “ワクチン” means “vaccine(s)”.

Chinese = “流行性感冒”means “influenza” and “疫苗” means “vaccine(s)”.

Korean = “인플루엔자”means “influenza” and “백신” means “vaccine(s)”.

(GRIPPE ET VACCIN?)/BI/CLMS OU (INFLUENZA ET VACUNA?)/BI/CLMS OU (GRIPPE ET IMPFSTOFF?)/BI/CLMS OU (ГРИПП ET ВАКЦИНА)/BI/CLMS OU (インフルエンザ ET ワクチン)/BI/CLMS OU (流行性感冒 ET 疫苗)/BI/CLMS OU (인플루엔자 ET 백신)/BI/CLMS

This query led to 1470 FAMPAT families. This query combined non English terms such as French (FR), Spanish (ES), German (DE), Russian (RU), Japanese (JP), Chinese (CN) and Korean (KR). Such a detailed study allowed the identification of further relevant patent families related to influenza vaccines, as well as patent families to be eliminated. Several relevant results (e.g. CL10702008) were thus added to the list of selected patent families.

These patents were not retrieved by former English queries because of mistakes in the automatic English machine translation.

4.1.3.5 Consistency analysis of the patent pool

The citation analysis of the patent pool led to a list of the most cited patents. The most cited patents were either already in our patent pool or outside. The patent families that were not included in the pool were checked and did not lead to the identification of further relevant patent families.

This confirms that the search strategy does not need further refinement with complementary keywords or IPC codes, or else.

4.1.3.6 Refinement of the patent pool and final database

A total of 79 INPADOC patent families needed a review by technical experts in order to determine their relevancy.

These 79 potentially relevant INPADOC patent families identified were reviewed in collaboration with the WIPO and WHO in order to validate (e.g. WO11014794) or eliminate (e.g. WO06045532) them from the final database. **The final database on human influenza vaccines, created 18th November 2011, contains 516 relevant INPADOC patent families** (45 INPADOC patent families were excluded through this second manual review)**.**

4.2. Statistical analysis

4.2.1. Number and evolution of patent filings and grants

Total number of patent families claiming active ingredients of human influenza vaccines	516
Total different patents & patent applications	2226
Average INPADOC Family Size	4.31 patents or applications/family
Granted patents	38.3%
PCT applications	53.7%

Table 28 - General statistics of patent filings and grants

The patent search resulted in 516 families of patents and patent applications published until November 2011. These 516 patent families include 2226 patents or published applications. Among these 516 patent families, 198 included one or more granted patents. These patent families contained two “Complex Patent Families“ (CPF):

- One claiming the U.S Provisional application 60/303,396 filed July 9, 2001 as first filing (6 patent families out of 56 patent families of this CPF were included in this database) (filed by BOGOCH ELENORE; BOGOCH SAMUEL)
- One claiming the GB20070007697 filed April 4, 2007 as first filing (2 patent families out of the 44 patent families of this CPF were included in this database) (filed by GLAXO SMITHKLINE BIOLOGICALS)

For more information on how families are built, please refer to WIPO standards references on Patent Family[14] or other references on the Internet [15]

Granted patents were identified by creating a query based on kind codes related to granted patents of all patenting authorities and applying it to the patent pool of active ingredients of human pneumococcal conjugate vaccines. Each patenting office has its own kind code system. For example, publications of the European Patent Office having a "B" kind code are granted patents, whereas publications having an "A1, A2, A3" kind code are applications. For the US Patent and Trademark Office, publications with an "A" kind code published before November 2000 and publications with kind code "B1, B2" are granted patent while publications with an "A1, A2" kind code published after November 2000 are applications.

Families having granted family members do not necessarily mean that protection has entered into force or that the patent is still valid. Granted patents may not be in force for several reasons including that the patent term expired, that fees have not been paid, or that it did not survive opposition or revocation procedures.

The figure below describes patenting activity over time and gives a view of patent grant rate in the field of active ingredients of human influenza vaccines. The graph represents the number of patent families (Y axis) over the year of first filing (X axis). This year (priority year) was chosen rather than the publication year, as this is more indicative of patenting activities since they are less dependent on the varying publication policies and docket backlogs of patent offices. The count of families for each year of first filing is split into two fractions according to whether families included at least one granted patent or not.

The graph shows a rather steady number of filings until 2002 (~10 filings a year) and a strong increase in the filings as of 2004 (to reach over 60 filings in 2009). A deeper analysis might confirm that this strong patenting activity was due to the bird flu pandemics that had been spreading throughout Asia since 2003, Europe in 2005, and the Middle East, as well as Africa, the following year. The high risk of transmission to humans pushed scientists to develop vaccines against new strains of influenza viruses.

The small fraction of grants in younger families reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO)..

[14] http://www.wipo.int/standards/en/pdf/08-01-01.pdf

[15] http://www.intellogist.com/wiki/Patent_Families

In the 1990s, more than 60% of patent families contained at least one granted patent while, since 2001, this rate has not exceeded 50%. The small fraction of grants in younger families (since 2005) reflects the pendency of patent issue, i.e. the time between the filing of an application and the grant of a patent which varies from a patent office to another and can last for several years (e.g. about 4 years for patents issued by EPO). For these families the examination of family members may still be pending or may not be requested yet.

For earlier years of filing, national publication policies and the evolution of national patent legislation have to be taken into account. For example, until November 2000, the US patent office published only granted US patents. Thereby, US applications that were not granted were in fact never published. For the coverage of national databases used in this study, please refer to corresponding appendix. In addition, because of the 18 months of publication delay after the date of patent filing, the data after 2009 are incomplete.

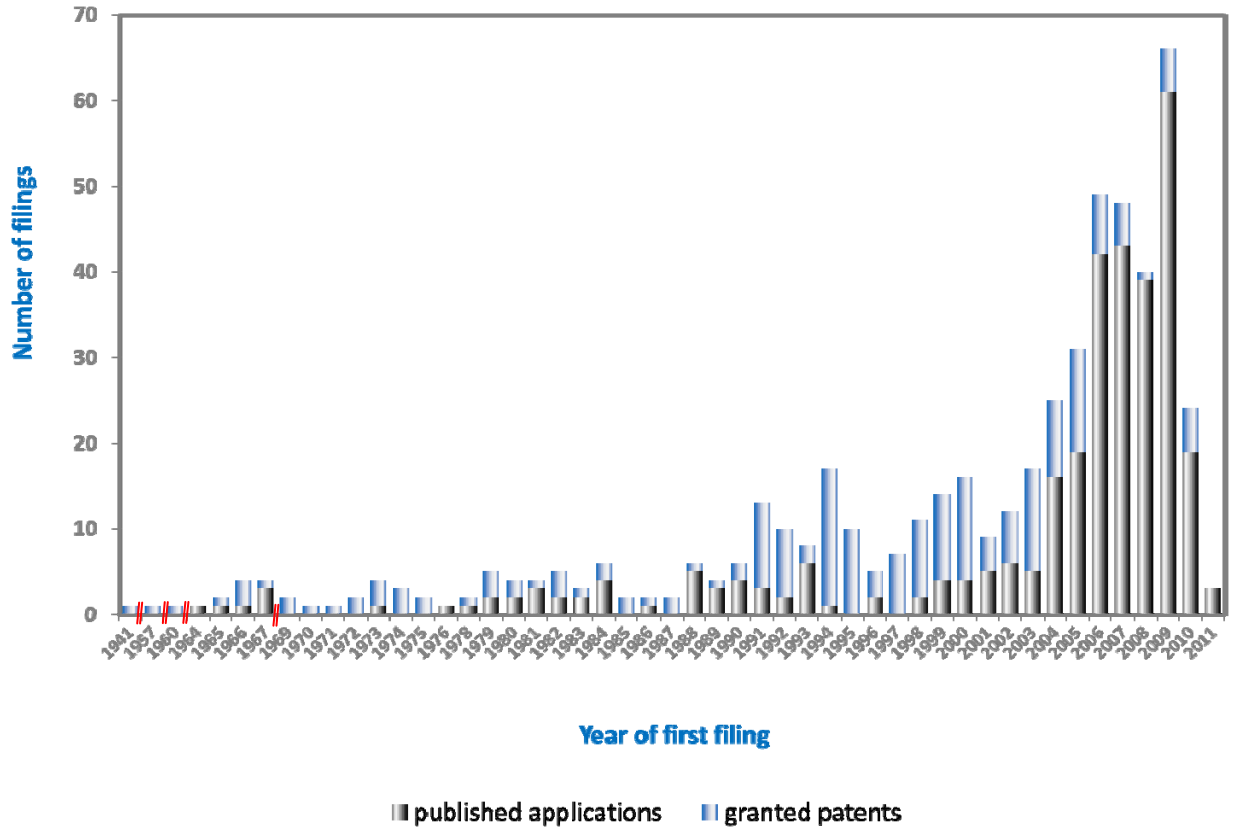


Figure 39 - Evolution of the number of patent families and without grants per year of first filing

Starting 1991, PCT applications were widely used to reach more than 70% of patent families.

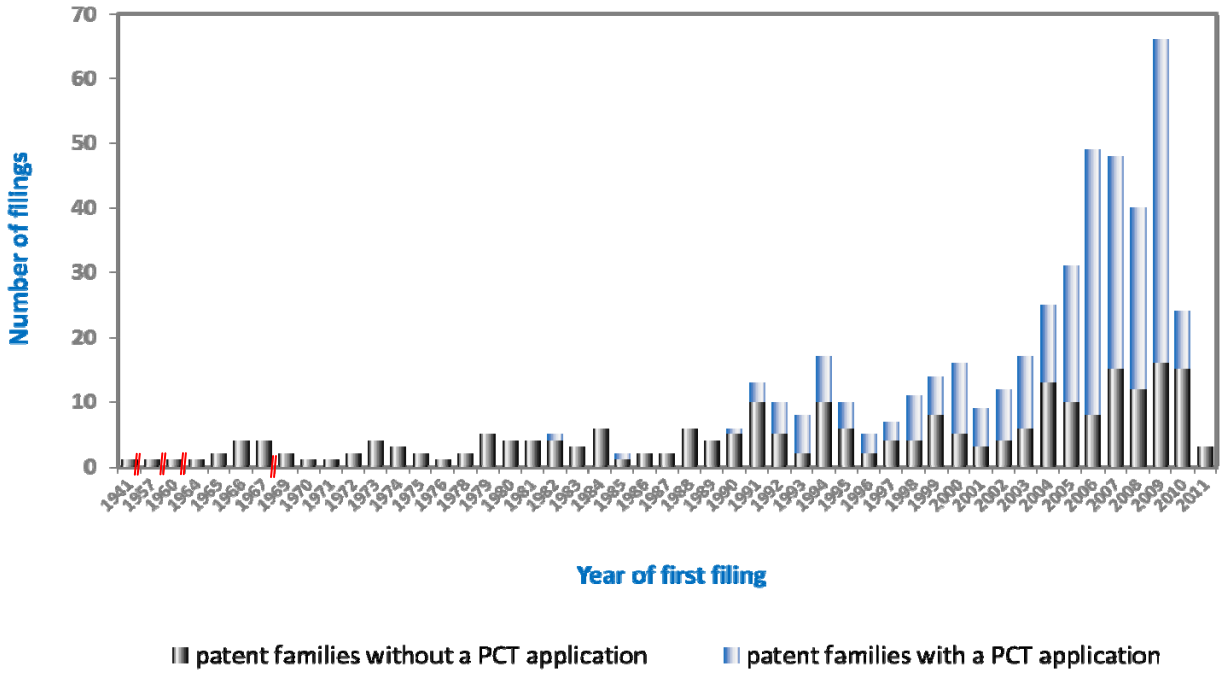


Figure 40 - Evolution of the number of patent families and without PCT applications per year of first filing

The table below lists the office of origin of all PCT applications. This table was established by looking at the application number of a PCT filing that mentions the office of origin of the PCT (e.g. 2008WO-FR00687, this PCT application was filed via the French patent office).

Office of first filing	Number of PCT applications
UNITED STATES	137
EUROPEAN PATENT OFFICE (EPO)	39
INTERNATIONAL BUREAU (WIPO)	20
UNITED KINGDOM	16
CANADA	11
JAPAN	10
AUSTRALIA	6
ISRAEL	6
KOREA	5
FINLAND	4
FRANCE	4
AUSTRIA	2
GERMANY	2
DENMARK	2
KAZAKHSTAN	2
NETHERLANDS	2
BELGIUM	1
CHINA	1

Office of first filing	Number of PCT applications
CUBA	1
SPAIN	1
INDIA	1
MEXICO	1
RUSSIA	1
SWEDEN	1
SINGAPORE	1

Table 29 - Origin of PCT applications

PCT applications were mainly filed with national or regional offices and only few directly with the international bureau.

4.2.2. Location of first filings

An analysis of the place of filing of priority patents results in the following table. A map of these filings can be seen in appendix. The location of priority filings and their evolution may give an indication of the country of origin of applicants and the dynamic of innovation in these countries.
The United States (that registered the first known patent application dealing with active ingredients of vaccines against human influenza) and Russia largely dominate as Office of first filing making this mapping the only “cold war”-like mapping analyzed through this study. The United Kingdom, Japan and recently China are playing runners up.

		41	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	TOTAL
PCT	WORLD																																				1					1												7
AMERICA	UNITED STATES	1						1	1	1		1			1	2	1			1	2			3	1	2			1			2	3	3	5	5	1	2	1	3	3	5	3	3	10	9	16	31	28	26	39	10		227
	CANADA																																				2																		2
	MEXICO																																																	1			1			2
	CUBA																																																	1						1
EUROPE	EUROPE																																		1				2		1	3	2	1		1		1	4		4			20
	UNITED KINGDOM		1						1					1		2					1					1		1						1	1	3				1	2	1	3	1		2	3	3	4	1	2			36
	FRANCE								1						1		1					2						1					1				1				1						1			1				11
	GERMANY																																				1		1	1			1		1									5
	IRELAND							1		1											1				1																														4
	FINLAND																																															2	1		1				4
	AUSTRIA																																							1	1			1									3
	HUNGARY																		1																									1											2
	ITALY																			1													1																						2
	DENMARK																																																		1	1				2
	SWITZERLAND																1																																						1
	BULGARIA																															1																							1
	SWEDEN																																	1																						1
	NETHERLANDS																																			1																				1
	SPAIN																																																							1
EURASIA	RUSSIAN FEDERATION								1												2	1	3	2	1	4		1		4	2	1	5	4		9	3		3	2	4	3		2	2	2	5	2	3		3	5		79
	KAZAKHSTAN																																																					2			2
ASIA	CHINA																																											1		1	3	7	2	3	1	9	6	8	3	44
	JAPAN																										1			1	1	1	3	1	1						2				1	2	2	3	3	1	3			26
	KOREA																	2																			2		1	1				2	1		1		2		2			14
	INDIA									1																																								1			1			3
	TAIWAN																																																				1			1
MIDDLE EAST	ISRAEL																						1							1	1	1		1						1														6
AFRICA	SOUTH AFRICA												1																																										1
AUSTRALIA	AUSTRALIA																																									2							1					3
Total		1	1	0	0	0	0	2	4	3	0	1	1	1	2	4	3	2	1	2	5	4	4	5	3	6	2	2	2	6	4	6	13	10	8	17	10	5	7	11	14	16	9	12	17	25	31	49	48	40	66	24	3	512

Table 30 - Evolution of first filings by offices

In order to have a better understanding of the country of origin and the innovation dynamic in these countries, it is more appropriate to take a look at the number of filings according to inventors' place of residence rather than the office of first filing.
To be able to make these statistics, the data related to Inventor's country (extracted from the address of the inventor), indexed in FamPat database (Questel^{TM}), was used. To do this, patent families of the database "Active Ingredients of human pneumococcal vaccines" were loaded into FamPat. This did not change the number of retrieved patent families although the definition of FamPat families is a little different from INPADOC families (FAMPAT families are built with patent applications having exactly the same priority whereas INPADOC families are built with patent applications having at least one priority patent application in common). Then, the number of filings naming at least one inventor coming from a country in particular was then counted.
It should be noted that totals of the two categories of the table are different because the inventors indicated in an individual patent application may have different countries of residence; each country was counted once, e.g. an application with two inventors residing in Belgium and one inventor residing in the United Kingdom would result in one count for each country.

It can thus be noted that innovation created by Canadian inventors tends to be first protected through the US patent office and that Italian, Dutch, German, Austrian and Belgium innovation tends to be first protected through UK or EP patent offices. Several reasons can co-exist to explain these differences:

- The interest in specific cases to use US provisional patents (even when the innovation do not stems from US inventors)
- The difference in location of patent officers and research team. For example, 19 applications filed by Belgian inventors but no filing registered at the Belgian patent office. This is explained by the fact that GSK vaccine research team is located in Belgium but files in the United Kingdom where are located the headquarters. On the same way, NOVARTIS/CHIRON research team is located in Italy but files in the United Kingdom.
- The interest of filing directly in English to lessen future translation fees

		Number of filings in each patent authority	Number of filings according to inventors' place of residence
PCT	WORLD	7	/
AMERICA	UNITED STATES	227	173
	CANADA	2	22
	MEXICO	2	3
	CUBA	1	1
EUROPE	EUROPE	20	/
	GERMANY	5	25
	UNITED KINGDOM	36	24
	BELGIUM	/	19
	AUSTRIA	3	16
	FRANCE	11	15
	NETHERLANDS	1	14
	ITALY	2	13
	SWITZERLAND	1	7
	SWEDEN	1	6
	FINLAND	4	4
	DENMARK	2	3
	SPAIN	1	2
	BULGARIA	1	1
	HUNGARY	2	1
	LATVIA	/	1
	SLOVAKIA	/	1
	ROMANIA	/	1
	IRELAND	4	/
EURASIA	RUSSIAN FEDERATION	79	66
	KAZAKHSTAN	2	2
	UKRAINE	/	1
ASIA	CHINA	44	42
	JAPAN	26	23
	KOREA	14	16
	INDIA	3	5
	SINGAPORE	/	4
	THAILAND	/	1
	TAIWAN	1	/
MIDDLE EAST	ISRAEL	6	11
AFRICA	SUDAN	/	1
	SOUTH AFRICA	1	/
OCEANIA	AUSTRALIA	3	12
	NEW ZEALAND	/	2
Total		512	538

Table 31 - Comparison between place of filings and origin of the inventors

4.2.3. Average family size per office of first filing

These data were established by looking at the publication numbers of each family in order to extract the number of offices in which the applications were filed. However, for patent and patent applications of European countries filed via the European Procedure, a different counting was carried out because of specificities of European procedures. According to the designated and chosen offices, a new patent application number is attributed by these offices or not. For instance, German patent office will deliver a number (DE123456) after an extension via the European procedure while France will use the EP number (EP654321). When looking at the patent families via the patent & patent application numbers, it therefore created, improperly, a higher number of German extensions compared to French ones. Consequently, when a patent family contained a patent application filed via the EPO, the numbers issued by the selected offices (during the national phases) were not recorded. These numbers were counted only if no EP filing was part of the family. In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

Office of first filing	Average family size	Standard deviation
AUSTRIA (AT)	7.3	2.1
AUSTRALIA (AU)	1.3	0.6
BULGARIA (BG)	1.0	
CANADA (CA)	2.0	1.4
SWITZERLAND (CH)	25.0	
CHINA (CN)	1.0	0.3
CUBA (CU)	13.0	
GERMANY (DE)	4.8	4.0
DENMARK (DK)	4.5	0.7
EUROPEAN PATENT OFFICE (EP)	7.0	4.5
SPAIN (ES)	2.0	
FINLAND (FI)	3.8	2.4
FRANCE (FR)	8.5	5.4
UNITED KINGDOM (GB)	7.9	5.6
HUNGARY (HU)	1.0	
IRELAND (IE)	1.0	
ISRAEL (IL)	2.8	3.1
INDIA (IN)	5.0	5.3
ITALY (IT)	1.0	
JAPAN (JP)	3.3	4.1
KOREA (KR)	1.5	0.9
KAZAKHSTAN (KZ)	2.0	
MEXICO (MX)	1.5	0.7
NETHERLANDS (NL)	10.0	
RUSSIA (RU)	1.2	1.3
SWEDEN (SE)	3.0	

Office of first filing	Average family size	Standard deviation
TAIWAN (TW)	2.0	
UNITED STATES (US)	5.4	4.4
INTERNATIONAL BUREAU (WO)	5.6	5.7
SOUTH AFRICA (ZA)	4.0	

Table 32 - Average family size and standard deviation per office of first filing

It can be noted that Russian, Chinese and Korean patent families were almost never extended while US, Japanese and European patent families are divided in two main groups: those that were never extended and those with a high number of extension (~12) which lead to an average family size of medium value but a high standard deviation.

4.2.4. Location of second filings

An analysis of the location of second filings results in the following histogram. A map compiling these data can be found in the corresponding appendix. Countries chosen for the extension of priority filings are an indicator of the markets and/or the production sites. The choice of countries may also be guided by company's competitors and potential infringers, even if there is no market in these corresponding territories. In Life Sciences, the choice can also be guided by usual locations of clinical trials (Poland, Hungary, Thailand, India…).

These data were established by looking at the patent numbers of each family without taking into account the number delivered by the office of first filing (see previous section for the explanation of the calculation).

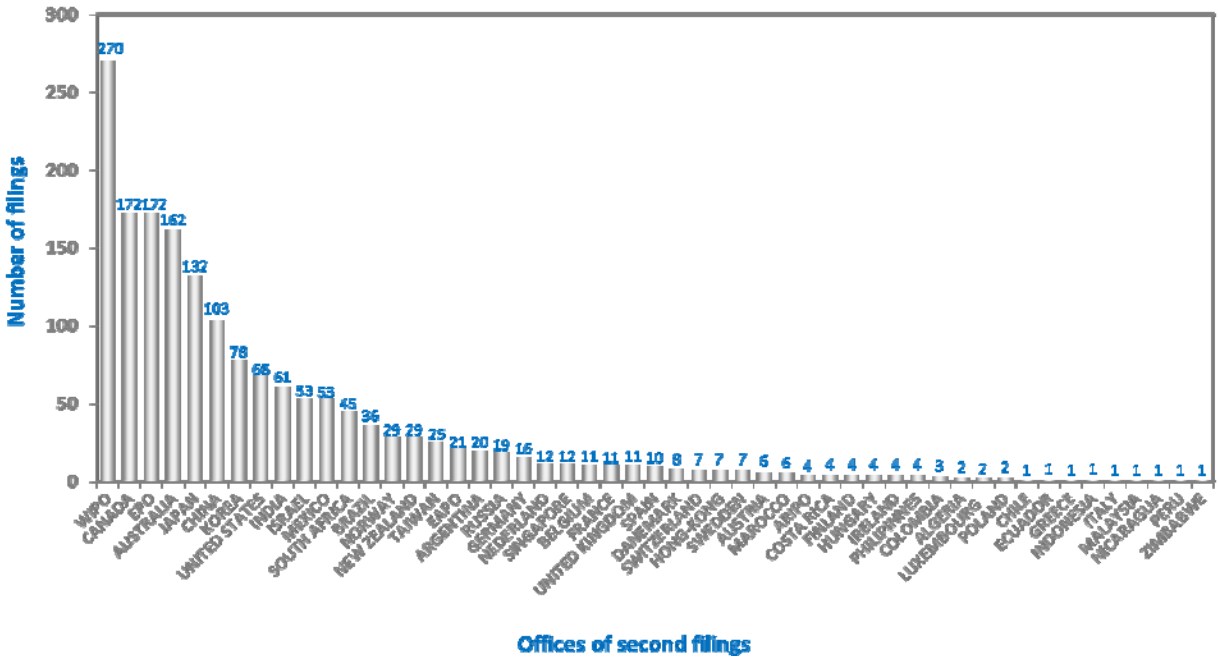


Figure 41 - Number of applications in the offices of second filings

Many second filings were performed via the PCT procedure (as seen in the previous section it represents 68% of the patent applications). Canada, the European patent office (EPO), Australia, Japan and China also dominate as offices of second filings. Beware that the importance of Australia must be understood in relation to the policy of the Australian patent office which automatically delivered an Australian patent number when the PCT mentions Australia even if no extension were filed in Australia during the national phase.

4.2.5. Breakdown of filings by IPC codes

The figure below shows the most common relevant IPC codes present in the database.

IPC	Definition	Number of patent & patent applications
A61K39-145	Medicinal preparations containing antigens or antibodies, Viral antigens, Orthomyxoviridae, e.g. influenza virus	385
A61P31-16	Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics, Antivirals, for RNA viruses, for influenza or rhinoviruses	233
C07K14-11	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof, from viruses, RNA viruses, Orthomyxoviridae, e.g. influenza virus	167
Other C12N15	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification	109
Other C12N7	Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (medicinal preparations containing viruses A61K 35/76; preparing medicinal viral antigen or antibody compositions, e.g. virus vaccines, A61K 39/00)	104
A61K39-12	Medicinal preparations containing antigens or antibodies, Viral antigens	87
A61P37	Drugs for immunological or allergic disorders (e.g. immunomodulators)	82
C07K14-005	Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof, from viruses	78
C12N7-4	Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (medicinal preparations containing viruses A61K 35/76; preparing medicinal viral antigen or antibody compositions, e.g. virus vaccines, A61K 39/00), Inactivation or attenuation; Producing viral sub-units	78
A61K39-39	Medicinal preparations containing antigens or antibodies, characterised by the immunostimulating additives, e.g. chemical adjuvants	77
C12N7-01	Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof (medicinal preparations containing viruses A61K 35/76; preparing medicinal viral antigen or antibody compositions, e.g. virus vaccines, A61K 39/00), Viruses, e.g. bacteriophages, modified by introduction of foreign genetic material (vectors C12N 15/00)	66

IPC	Definition	Number of patent & patent applications
A61K38	Medicinal preparations containing peptides	61
C12N15-44	Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification, Recombinant DNA-technology, DNA or RNA fragments; Modified forms thereof (DNA or RNA not used in recombinant technology C07H 21/00), Genes encoding microbial proteins, e.g. enterotoxins, Genes encoding viral proteins, Proteins from RNA viruses, e.g. flaviviruses, Orthomyxoviridae, e.g. influenza virus	60
C07H21	Compounds containing two or more mononucleotide units having separate phosphate or polyphosphate groups linked by saccharide radicals of nucleoside groups, e.g. nucleic acids	54
A61K48	Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy	51
A61K39-295	Medicinal preparations containing antigens or antibodies, Viral antigens, Polyvalent viral antigens (vaccinia virus or variola virus A61K 39/285); Mixtures of viral and bacterial antigens	39
C12N5-10	Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor (plant reproduction by tissue culture techniques A01H 4/00), Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells	34
C12Q1-70	Measuring or testing processes involving enzymes or micro-organisms (measuring or testing apparatus with condition measuring or sensing means, e.g. colony counters, C12M 1/34); Compositions therefor; Processes of preparing such compositions, involving virus or bacteriophage	31
Other A61K39	Medicinal preparations containing antigens or antibodies (except A61K39-145, A61K39-12, A61K39-39, A61K39-295, A61K39-395)	31
A61K35-76	Medicinal preparations containing material or reaction products thereof with undetermined constitution, Materials from micro-organisms, Viruses	27
C07K16-10	Immunoglobulins, e.g. monoclonal or polyclonal antibodies, against material from viruses, from RNA viruses	27
C07K19	Hybrid peptides (hybrid immunoglobulins composed solely of immunoglobulins C07K 16/46)	24
G01N33-569	Investigating or analysing materials by specific methods, Biological material, e.g. blood, urine, Chemical analysis of biological material, e.g. blood, urine; Testing involving biospecific ligand binding methods; Immunological testing, Immunoassay; Biospecific binding assay; Materials therefore, for micro-organisms, e.g. protozoa, bacteria, viruses	23
A61K39-395	Medicinal preparations containing antigens or antibodies, Antibodies (agglutinins A61K 38/36); Immunoglobulins; Immune serum, e.g. antilymphocytic serum	21

Table 33 - Number of patent families classified within relevant IPC codes

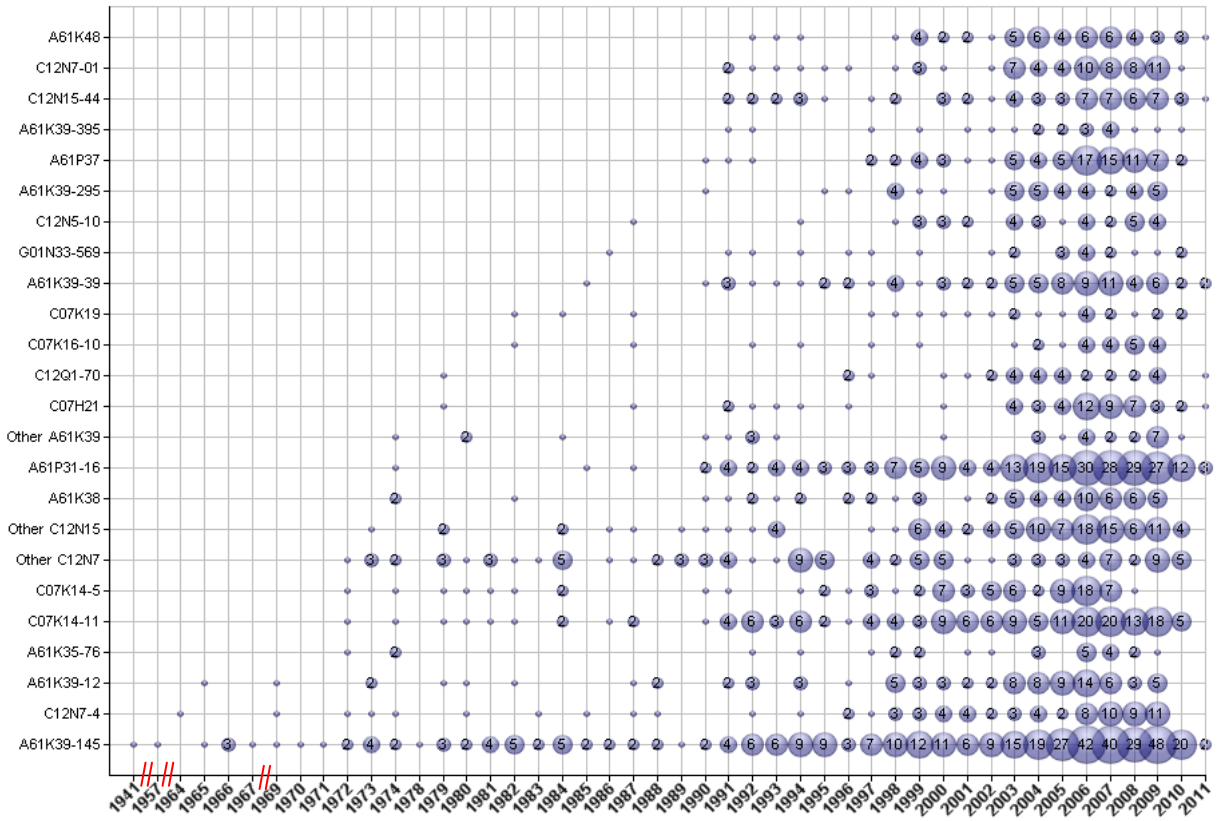


Figure 42 - Number of patent families classified within relevant IPC codes per year of first filing

No clear trend can be highlighted by the analysis of the evolution of IPC codes.

4.2.6. Analysis of applicants

Two types of applicants can be distinguished: institutional and industrial ones. The evolution of institutional vs. industrial priority filings (figure below) outlines the strong presence of institutional filings and the increasing number of industrial ones. Since 2003, It can be noted the emergence of co-filings between institutional and industrial applicants.

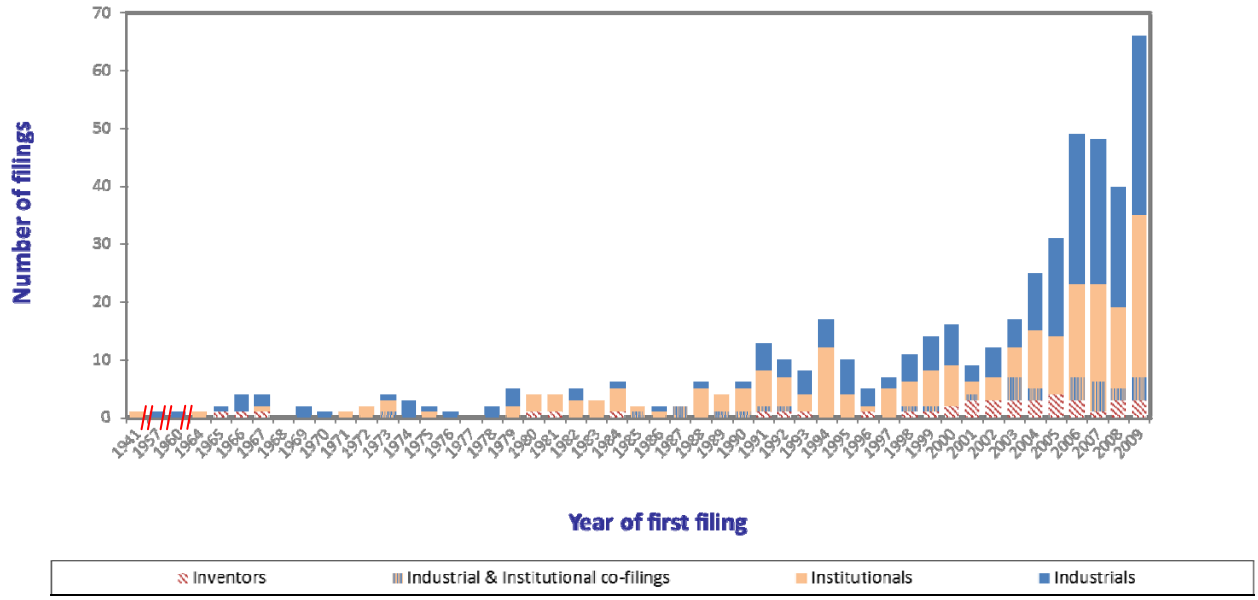


Figure 43 - Number of Institutional/Industrial/Individual priority filings per year of first filing

The following graph shows the main applicants classified by the size of their patent portfolio.

Co-filings are counted for each co-owner. For instance, a patent application co-filed between US Government and GSK is counted once for US Government and once for GSK.

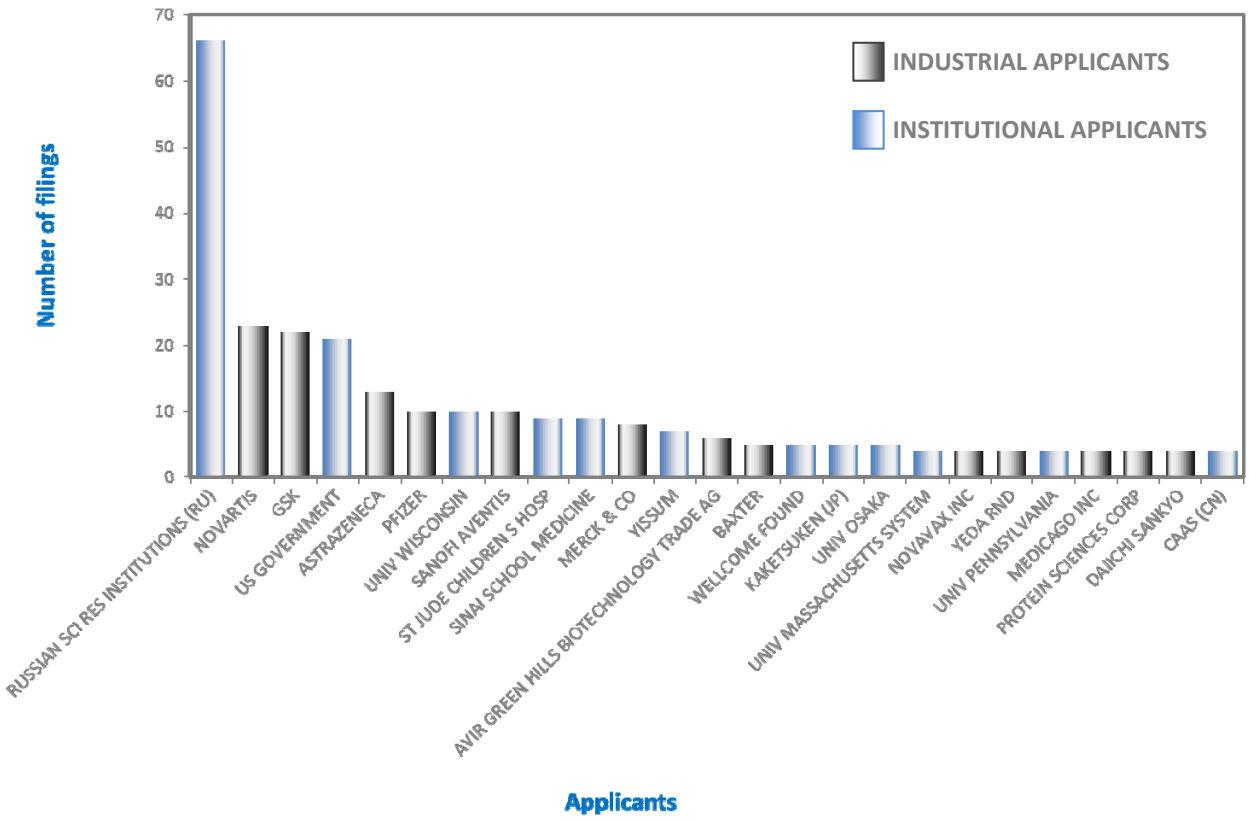


Figure 44 - List of main applicants (≥4 patent or patent applications)

The Russian scientific research institutions dominate in terms of number of filings outnumbering the US Government laboratories and the University of Wisconsin institutional filings. GSK, Novartis, Astrazeneca, Pfizer, Sanofi-Aventis and to a lesser extent Merck&Co hold a significant position.

Please note that affiliates/subsidiaries were gathered under their parent company. These groupings were performed via a home-made database of mother companies and subsidiaries developed with Elsevier's business intelligence database[16], companies' websites, annual reports, business intelligence reviews and websites…

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
RUSSIAN SCI RES INSTITUTIONS (RU)	SCIENTIFIC RESEARCH INSTITUTIONS (NII); GU NII EHKSPERIMENTAL NOJ MEDI; LE NIIEX MEDITSINY; NII GRIPPA RAMN; SANKT PETERBURGSKIJ NII VAKTSI; UCHREZHDENIE ROSSIJSKOJ AKADEMII MED NAUK NII; FEDERAL NOE GUP NPOB MED IMMUN; INST VIRUSOLOGII IM D I IVANOV; NAUCHNO ISSLEDOVATEL SKIJ INST EHKSPERIMENTAL
NOVARTIS (CH)	CHIRON; NOVARTIS; NOVARTIS VACCINES AND DIAGNOSTIC; SANDOZ
GSK (GB)	BEECHAM GROUP; GLAXO WELLCOME; GLAXOSMITHKLINE BIOLOGICALS; ID BIOMEDICAL; INTELLIVAX INT; RECHERCHE ET INDUSTRIE THERAPEUTIQUES (RIT); SMITHKLINE BEECHAM
US GOVERNMENT (US)	NIH; US DEPARTMENT OF AGRICULTURE; US ARMY; US DEPARTMENT OF VETERANS AFFAIRS; US DEPARTMENT OF HEALTH AND HUMAN SERVICES; US DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
ASTRAZENECA (GB)	AVIRON; MEDIMMUNE; MEDIMMUNE VACCINES (US)
PFIZER (US)	AMERICAN CYANAMID; POWDERJECT VACCINES; POWDERMED; AMERICAN HOME PRODUCTS; GD SEARLE & CO; WYETH
UNIV WISCONSIN (US)	WISCONSIN ALUMNI RESEARCH FOUNDATION
SANOFI AVENTIS (FR)	ACAMBIS INC; AVENTIS PASTEUR; CONNAUGHT LAB; PASTEUR MERIEUX; PASTEUR MERIEUX SERUMS VACC; SANOFI PASTEUR; SANOFI PASTEUR BIOLOGICS CO
ST JUDE CHILDREN S HOSP (US)	ST JUDE CHILDREN'S RESEARCH HOSPITAL
SINAI SCHOOL MEDICINE (US)	MOUNT SINAI SCHOOL OF MEDICINE
MERCK & CO (US)	INSTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ANGELETTI; BANYU PHARMACEUTICAL. MERCK AND CO; SCHERING PLOUGH
YISSUM (IL)	YISSUM RESEARCH DEVELOPMENT COMPANY (HEBREW UNIVERSITY OF JERUSALEM)
AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG (AT)	AVIR GREEN HILLS BIOTECHNOLOGY RES DEV TRADE AG
BAXTER (US)	BAXTER AG; BAXTER HEALTHCARE SA; BAXTER INT; BAXTER VACCINE AG; IMMUNO AG

[16] http://www.elsevierbi.com/companies

APPLICANTS (NATIONALITY)	ASSIGNEES (NATIONALITY IF DIFFERENT FROM APPLICANTS)
WELLCOME FOUND (GB)	WELLCOME FOUNDATION LTD
KAKETSUKEN (JP)	CHEMO SERO THERAPEUT RES INST
UNIV OSAKA (JP)	RESEARCH FOUNDATION FOR MICROBIAL DISEASES OF OSAKA UNIVERSITY
UNIV MASSACHUSETTS SYSTEM (US)	UNIVERSITY OF MASSACHUSETTS MEDICAL CENTER
NOVAVAX INC (US)	NOVAVAX INC
YEDA RND (IL)	YEDA RESEARCH AND DEVELOPMENT CO LTD
UNIV PENNSYLVANIA (US)	UNIV PENNSYLVANIA
MEDICAGO INC (US)	MEDICAGO INC
PROTEIN SCIENCES CORP (US)	PROTEIN SCIENCES CORP
DAIICHI SANKYO (JP)	DAIICHI SEIYAKU CO LTD; DAIICHI PHARMACEUTICAL CO LTD
CAAS (CN)	HARBIN VETERINARY RES INST

Table 34 - Applicants and their affiliates

For each applicant, the graphs below detail the preferred office of first and second filings.

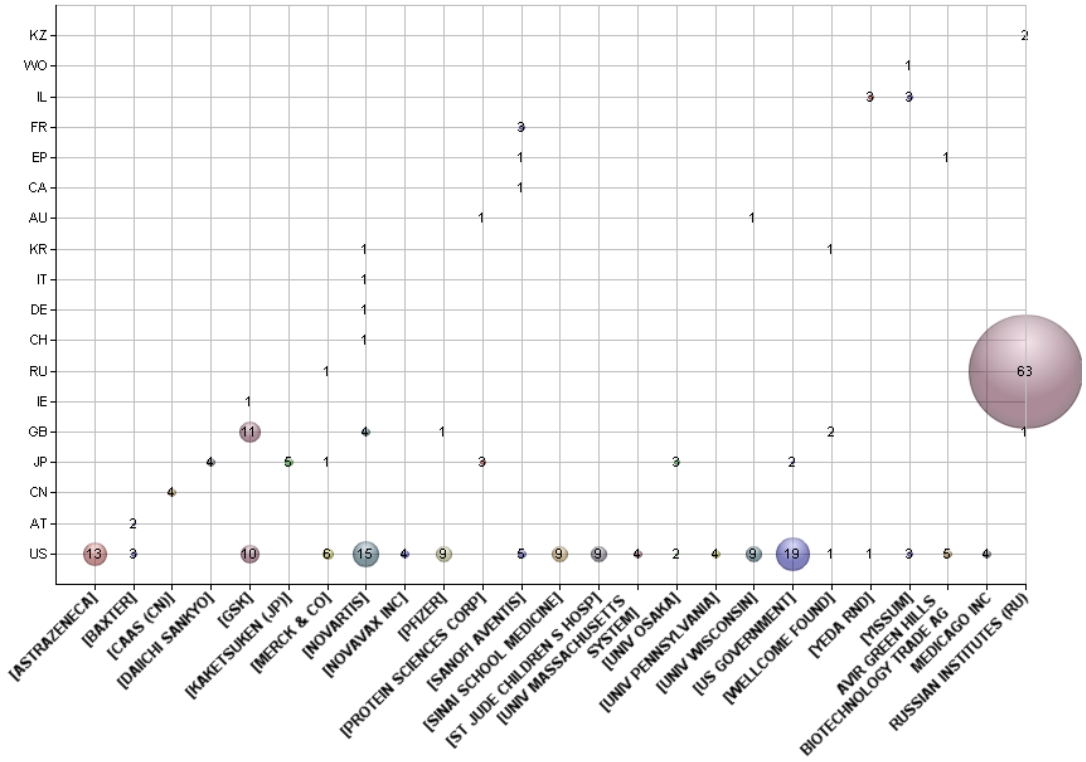


Figure 45 - Main applicants' preferred offices of first filings

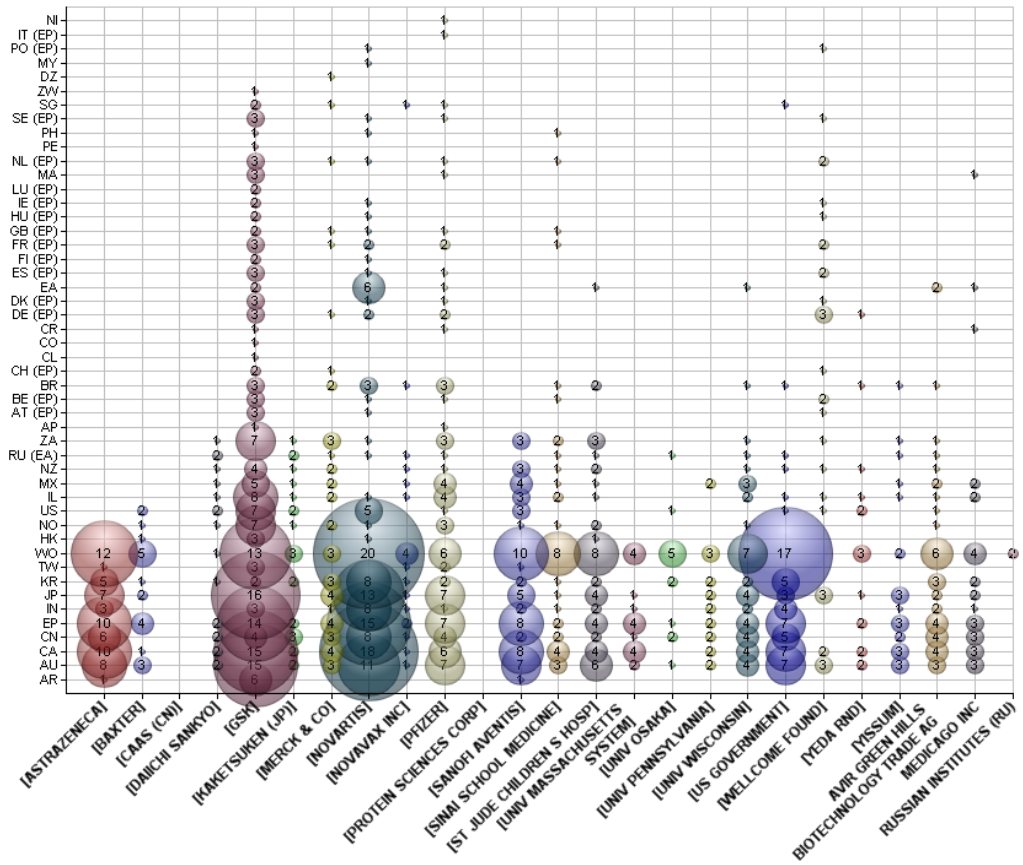


Figure 46 - Main applicants' preferred offices of second filings

The figure above outlines that Russian Institutes, the Chinese academy of agricultural sciences (CAAS) and Protein Sciences did not extend their patents.

The following graph details the evolution of office of first filing by applicant. The year corresponds to the first priority year of the patent family. Such a graph allows the identification of pioneer or emerging applicants in terms of filings.

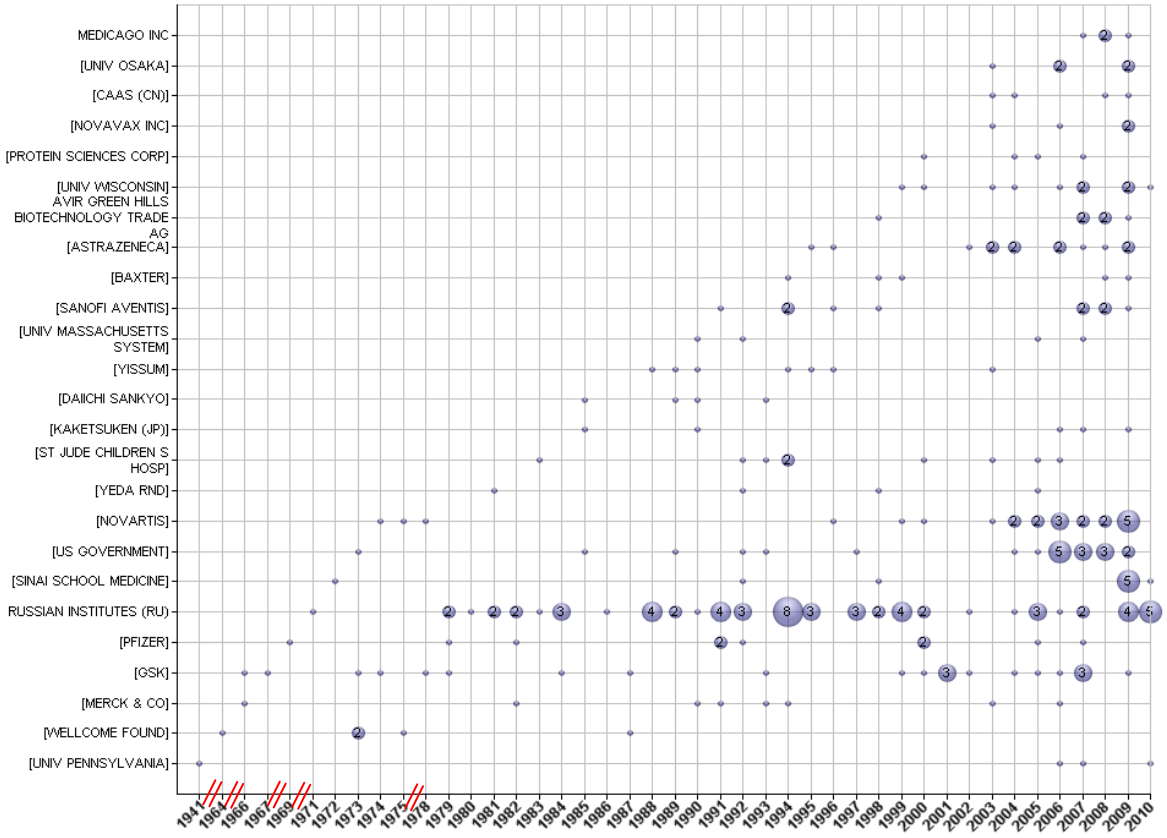


Figure 47 - Evolution of main applicants' filings (by year of first filing)

The University of Pennsylvania that was the first applicant to file a patent application about human influenza vaccines seems to have left the field a long time before filing again as of 2006. Among the most active applicants, the Russian scientific research institutes have had a strong and continuous activity since 1979 and all over the period. To a lesser extend, GSK have had also a continuous activity since the middle of the 1960s. Some other applicants, such as the US Government laboratories, Novartis, Sinai school of medicine or AstraZeneca, filed some patent applications before the 2000s but emerged in terms of filings only recently. In contrast, some players, such as Daiichi Sankyo might have stopped research on human influenza vaccines because no more patent applications have been filed since 1993.

The following table details the average family size by applicant. Please note that, because of the particular numbering of patent applications filed during the national phase of the European procedure (see section 4.2.3. for the detailed explanation), when a patent family contained a patent application filed via the EPO, the numbers delivered by the selected offices (during the national

phases) were not recorded. These numbers were counted only if no EP filing was part of the family. In addition, only one document per office was taken into account when calculating the family size in order not to count twice the patent application and the issued patent.

Applicants	Average family size	Standard deviation
RUSSIAN SCI RES INSTITUTIONS (RU)	1.0	0.2
NOVARTIS	7.0	5.2
GSK	9.4	6.6
US GOVERNMENT	3.9	2.9
ASTRAZENECA	5.8	3.0
PFIZER	8.9	6.0
UNIV WISCONSIN	5.2	5.1
SANOFI AVENTIS	7.3	3.8
ST JUDE CHILDREN S HOSP	6.1	5.5
SINAI SCHOOL MEDICINE	5.0	4.8
MERCK & CO	6.8	6.1
YISSUM	4.1	4.4
AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	7.5	5.2
BAXTER	5.0	2.1
WELLCOME FOUND	6.8	7.1
KAKETSUKEN (JP)	5.6	4.3
UNIV OSAKA	3.6	2.6

Table 35 - Average family size per applicant

These data show that Russian Scientific Reserch centers almost never extended their patents. In average, family sizes of each applicant are rather large but with high standard deviation without clear differences between industrial or institutional applicants.

4.2.7. Analysis of inventors

The table below lists the various inventors with their associated applicants.

Inventor	Number of filings	Assignee	Number of filings
Aleksandrova Galina	49	RUSSIAN INSTITUTES (RU)	44
		N/A	5
Rudenko Larisa	41	RUSSIAN INSTITUTES (RU)	36
		[BIODIEM]	1
		N/A	4
Klimov Aleksandr	29	RUSSIAN INSTITUTES (RU)	24
		US GOVERNMENT	1
		CENTERS FOR DISEASE CONTROL AND PREVENTION (US)	1
		N/A	4

Inventor	Number of filings	Assignee	Number of filings
Kiseleva Irina	20	RUSSIAN INSTITUTES (RU)	17
		N/A	3
Polezhaev Fial	14	RUSSIAN INSTITUTES (RU)	12
		N/A	2
Kawaoka Yoshihiro	13	UNIV WISCONSIN	10
		ST JUDE CHILDREN S HOSP	2
		US GOVERNMENT	1
		FLUGEN INC	1
Egorov Andrej	12	AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	5
		RUSSIAN INSTITUTES (RU)	4
		POLIMUN SCIENT IMMUNBIOLOGISCH	3
		UNIV WIEN	2
		SINAI SCHOOL MEDICINE	1
Larionova Natal	12	RUSSIAN INSTITUTES (RU)	12
Palese Peter	9	SINAI SCHOOL MEDICINE	7
		AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	1
		ISIS INNOVATION	1
		N/A	1
Garmashova Lyudmila	8	RUSSIAN INSTITUTES (RU)	6
		N/A	2
Medvedeva Tamilla	8	RUSSIAN INSTITUTES (RU)	6
		N/A	2
Romanova Yuliya	8	RUSSIAN INSTITUTES (RU)	6
		POLIMUN SCIENT IMMUNBIOLOGISCH	1
		UNIV WIEN	1
		AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	1
Smith Gale	8	NOVAVAX INC	4
		PROTEIN SCIENCES CORP	4
Garcia Sastre	7	SINAI SCHOOL MEDICINE	6
		AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	1
		ISIS INNOVATION	1
Gendon Yurij	7	RUSSIAN INSTITUTES (RU)	5
		N/A	2
Bogoch Elenore	6	N/A	6
Bogoch Samuel	6	N/A	6
Budilovskij Gennadij	6	RUSSIAN INSTITUTES (RU)	4
		N/A	2
Grunis Alla	6	RUSSIAN INSTITUTES (RU)	5
		N/A	1

Inventor	Number of filings	Assignee	Number of filings
Hanon Emmanuel	6	GSK	6
		SAECHSISCHES SERUMWERK	1
Kemble George	6	ASTRAZENECA	6
		US GOVERNMENT	2
Koval Tamara	6	RUSSIAN INSTITUTES (RU)	4
		N/A	2
Lonskaya Natalya	6	RUSSIAN INSTITUTES (RU)	6
Muster Thomas	6	AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	5
		SINAI SCHOOL MEDICINE	2
		UNIV WIEN	2
Webster Robert	6	ST JUDE CHILDREN S HOSP	5
		UNIV MASSACHUSETTS SYSTEM	1
		UNIV NAT AUSTRALIA	1
		AGRACETUS	1
		PFIZER	1
Bardina Elena	5	RUSSIAN INSTITUTES (RU)	5
Barrett Noel	5	BAXTER	5
Gavrilov Aleksandr	5	RUSSIAN INSTITUTES (RU)	5
Jin Hong	5	ASTRAZENECA	5
		US GOVERNMENT	1
Kistner Otfried	5	BAXTER	5
Lee Kwang hee	5	BIOTRION CO LTD	2
		HANIL SYNTHETICS INC	2
		PROTHEON CO LTD	2
		CHEIL JEDANG CORP	1
Lisovskaya Klara	5	RUSSIAN INSTITUTES (RU)	5
Murphy Brian	5	US GOVERNMENT	4
		ASTRAZENECA	2
		ST JUDE CHILDREN S HOSP	2
Nejime Kuniaki	5	DAIICHI SANKYO	3
		NISSHIN	2
		US GOVERNMENT	2
		SUMIKA CHEMICALS COMPANY	1
		KAKETSUKEN (JP)	1
		NATIONAL HEALTH RES INST (TW)	1
O hagan Derek	5	NOVARTIS	5
Arnon Ruth	4	YEDA RND	4
Borsanyi Anne	4	N/A	4
Couture Manon	4	MEDICAGO INC	4
Desheva Julia	4	RUSSIAN INSTITUTES (RU)	3
		BIODIEM	1
Deyan Luo	4	AMMS (CN)	3
		INST OF MICROBIOLOGY AND EPIDE	1
Doroshenko Elena	4	RUSSIAN INSTITUTES (RU)	4

Inventor	Number of filings	Assignee	Number of filings
Drinevskij Vladimir	4	RUSSIAN INSTITUTES (RU)	4
Galarza Jose	4	TECHNOVAX INC	3
		PFIZER	1
Garcon Nathalie	4	GSK	4
Grinbaum Evgeniya	4	RUSSIAN INSTITUTES (RU)	4
Hackett Craig	4	PROTEIN SCIENCES CORP	4
Malikova Emma	4	RUSSIAN INSTITUTES (RU)	4
Nabel Gary	4	US GOVERNMENT	4
Naumenko Z	4	RUSSIAN INSTITUTES (RU)	4
Neumann Gabriele	4	UNIV WISCONSIN	3
		FLUGEN INC	1
Penghui Yang	4	AMMS (CN)	3
		INST OF MICROBIOLOGY AND EPIDE	1
Seong Baik lin	4	PROTHEON CO LTD	3
		BIOTRION CO LTD	2
		CHEIL JEDANG CORP	2
Subbarao Kanta	4	US GOVERNMENT	4
		ASTRAZENECA	3
		ST JUDE CHILDREN S HOSP	1
Sung Young chul	4	POSTECH FOUNDATION	3
		GENEXINE LTD	2
		LG GROUP	1
		UNIV POHANG (POSTECH)	1
Vasileva Rozaliya	4	RUSSIAN INSTITUTES (RU)	4
Vezina Louis	4	MEDICAGO INC	4
Volvovitz Franklin	4	PROTEIN SCIENCES CORP	4
Voznesensky Andrei	4	PROTEIN SCIENCES CORP	4
Weiner David	4	UNIV PENNSYLVANIA	3
		VGX PHARMACEUTICALS	1
		N/A	1
Wilkinson Bethanie	4	PROTEIN SCIENCES CORP	4
Wolschek Markus	4	AVIR GREEN HILLS BIOTECHNOLOGY TRADE AG	4
		UNIV WIEN	2
Xiliang Wang	4	AMMS (CN)	3
		INST OF MICROBIOLOGY AND EPIDE	1
Yan Jian	4	UNIV PENNSYLVANIA	3
		VGX PHARMACEUTICALS	1
		N/A	1
Yang Chin fen	4	ASTRAZENECA	4
		US GOVERNMENT	2
Yang Zhi yong	4	US GOVERNMENT	4
Yoshihiro Kawaoka	4	UNIV WISCONSIN	4

Figure 48 - List of main inventors(≥4 patent or patent applications)

4.2.8. Regional focuses: Brazil, India, China

Very few patent families stems with Brazil, India or China as their office of first filing. No patent families stems with Brazil as office of first filing, only three with India and forty-four with China. The table below lists all patent families stemming from China and and India (None came from Brazil).

Priority number	Publication number	Title	Applicant
CN201010137416	CN102205131	A type of H1N1 influenza DNA vaccine preparation and its use	
CN201110046186	CN102160893	Yew polysaccharide adjuvant and influenza vaccine containing the adjuvant	
CN200410009866	CN1326998	Gene encoding hemagglutinin protein of H5 avian influenza virus and its application	CAAS (CN)
CN200910094223	CN101560503	Influenza A virus Vero cell adapted strain and application thereof	
CN201110090992	CN102166351	A type of H1N1 influenza vaccine and its application	
CN200810050378	CN101224301	Application of attenuated live vaccine virus in preparing AIDS and flu treatment medicine	
CN200910005076	CN101780275	Development of H5N1 subtype avian influenza cold-adaption attenuated live vaccines and application thereof	CAAS (CN)
CN200510097795	CN1923288	Hybrid yeast influenza vaccine	
CN201010116631	CN102153621	Novel H1N1 influenza NA protein B cell epitope and its application	
CN201010300602	CN102134279	Fusion protein and its encoding gene and application	
CN200810067900	CN101502649	Liposome influenza vaccine	SHENZHEN POLYTECHNIC
CN201010233022	CN101899101	One kind uses in flu virus Asia unit vaccine research the synthesis multi-peptides	
CN20031021807	CN100482788	High-yield recombinant influenza B virus strain and its application	CHINA CDC
CN200410054064	CN1739801	Influenza virus lysis vaccine and its prepn process	SHANGHAI INST OF BIOLOG PRODUC

Priority number	Publication number	Title	Applicant
CN201010140628	CN101857872	Replacement method of influenza A Virus antigenic determinant	ZHEJIANG ACADEMY OF MEDICAL SCIENCES
CN200810029130	CN101302499	Preparation of influenza virus vaccine seed strain	CAS (CHINA)
CN20021000031	CN1431020	Epiposition vaccine of gene engineering for influenza virus and its preparing method	UNIV TSINGHUA
CN200810225584	CN101397572	Method for rescuing influenza virus and bidirectional transcription vector special therefor	
CN200810247021	CN101450208	Nasal-spraying immune influenza multivalent vaccine and preparation method thereof	AMMS (CN)
CN200410021296	CN1270771	Influenza vaccine sucked or sprayed through nasal cavity preparation method	TIANCHENG BIOLOG PHARM MFG CO
CN200910217549	CN101732711	Preparation of nose-spraying flu immunization pentavalent or multivalent inactivated vaccine and application thereof	INST OF MICROBIOLOGY AND EPIDE
CN200410061206	CN1306960	Curtail hemagglutinin vaccine for preventing influenza virus and its preparing method	CAS (CHINA)
CN201010103495	CN101843901	Influenza virus vaccine using nanometer emulsion as adjuvant and method for preparing same	
CN200310100029	CN1644686	High yielded strain of mammalia influenza virus its recommbined strains and preparation and use thereof	CHINA CDC
CN200310107733	CN1261564	Artificial recombined influenza virus and its application	CAAS (CN)
CN200410092666	CN1775287	SARS influenza bivalent combined vaccine and its preparing process	KEXING BIOLOG PRODUCTS CO LTD
CN201010171774	CN101899461	One kind of code armor flu virus NP protein and M2e multi-peptide fusion gene	
CN20001021293	WO0226252	A VACCINE FOR INFLUENZA VIRUS AND ITS PREPARATION	UNIV TSINGHUA

Priority number	Publication number	Title	Applicant
CN200610112125	CN1911445	Grippe primary generation susliks kidney cell multivalent raccine and its preparation method	BEIKE BIOTECHNOLOGY
CN200710045654	CN101161285	Influenza virus cracking vaccine	SHANGHAI RONGSHENG BIO TECH CO
CN201010205088	CN101879312	Broad spectrum type influenza vaccine and preparation method thereof	BEIJING JINGYI TAIXIANG DEV CO LTD
CN200410061317	CN1660421	Bobtail bacterin of neuraminidase for preventing influenza virus and preparing method	CAS (CHINA)
CN200510051548	CN1827636	Protective polypeptide of human influenza A virus its use vaccine and diagnostic tool	CHINA CDC
CN200610017404	CN101015690	Development and application of wide spectrum influenza vaccine	HENAN BIOTECHNOLOGY RES CT
CN201110074214	CN102180927	Obtain samples of influenza virus-specific nucleic acid primers methods and their	
CN200810163763	CN101450207	Human influenza-poultry influenza combined vaccine and preparation method thereof	ZHEJIANG ACADEMY OF MEDICAL SCIENCES
CN200810247022	CN101450209	Transdermal immune influenza multivalent vaccine and preparation method thereof	AMMS (CN)
CN200910103514	CN101524538	Influenza-pandemic influenza bivalent combined vaccine and preparation method thereof	CHENGDU KANGHUA BIOLOG PRODUCT
CN200910063217	CN101624580	Recombinant baculovirus expressing manually modified and synthesized influenza A H1N1 virus HA-NA-M1 gene	UNIV HUAZHONG
CN200910272549	CN101716340	Establishment of method for preparing recombinant protein vaccine of type A H1N1 influenza virus	WUHAN CUSABIO ENGINEERING CO L
CN200810004757	CN101497877	Influenza all-virus attenuated live vaccine recombinant construction method and use thereof	HEBEI XINZHANG PHARMACEUTICAL

Priority number	Publication number	Title	Applicant
CN200610007909	CN1810961	Recombinant influenza virus and its prepn and application	AMMS (CN)
CN200810239333	CN101745107	Recombinant replication-defective adenoviral vector H5N1 subtype influenza genetic engineering vaccine	CAAS (CN)
CN200410010704	CN100393358	Preparation of horse family animal anti human poultry grippe immune globulin and its medicinal preparation	INST OF MILITARY VETERINARY
IN19670113235	IN113235	PROCESS FOR THE PREPARATION OF VIRAL SUSPENSIONS AND OF VACCINES FOR COMBATING INFLUENZA	RHODIA
IN2009DE01015	WO10134094	UNIVERSAL INFLUENZA VACCINE BASED ON RECOMBINANT MODIFIED VACCINIA ANKARA VIRUS (MVA)	PANACEA BIOTEC LTD
IN2006DE00369	WO07091165	Pharmaceutical composition useful for the treatment of peptic ulcer diseases	DOW CHEMICAL CSIR (IN)

Table 36 - List of patent families stemming from China and India

Appendix 1: Terminology

Patent family: all the documents having at least one priority in common belong to the same INPADOC patent family and strictly the same priority belong to the same FAMPAT patent family. INPADOC is an acronym for International Patent Documentation Center. INPADOC is an international patent collection founded by WIPO but produced and maintained by the European Patent Office. FAMPAT is a patent database created by Questel.

Patent publication: patent applications are generally published 18 months after the earliest priority date of the application. Prior to that publication, the application is confidential. After publication, depending upon local rules, certain parts of the application file may remain confidential, but it is common for all communications between an Applicant (or his agent) and the patent office to be publicly available.

Office of first filing (OFF): it is the country where the first patent application (the earlier priority) was filed.

Office of second filing (OSF): it is the offices where subsequent family members of a patent were filed.

Continuation: a continuation application is a patent application filed by an applicant who wants to pursue additional claims to an invention disclosed in an earlier application of the applicant that has not yet been issued or abandoned. It is claiming priority based on the filing date of the parent application.

Continuation-in-part: a continuation-in-part application is a patent application that repeats substantional portion of an invention disclosed in an earlier application and adds subject matter not disclosed in this parent application. It is claiming priority based on the filing date of the parent application.

Divisional: A divisional patent application is a patent application which contains matter from an earlier application but claims a distinct or independent invention extracted from the parent application. Divisional applications are generally used in cases where the parent application may lack unity of invention (i.e. parent application describes more than one invention) and the applicant is required to split the parent into one or more divisional applications each claiming only a single invention. A divisional application is retaining its parent's filing date and is generally claiming the same priority.

Granting: the procedure for granting patents varies widely between countries according to national laws and international agreements. However, a patent application always includes one or more claims defining the invention which must be new, inventive and industrially applicable.

PCT (WO): the Patent Cooperation Treaty (PCT) is an international patent law treaty concluded in 1970. Any contracting state to the Paris Convention for the Protection of Industrial Property (1883) can become a member of the PCT. It provides a unified procedure for filing patent applications to protect inventions in each of its contracting states. A patent application filed under the PCT is called an international application, PCT application.

European patent (EP): the Convention on the Grant of European Patents signed October 5, 1973, commonly known as the European Patent Convention (EPC) and sometimes known as the Munich Convention, is a multilateral treaty instituting the European Patent Organisation (EPO) and providing an autonomous legal system according to which European patents are granted. The term European patent is used to refer to patents granted under the European Patent Convention. However, after granting, a European patent is not a unitary right, but a group of essentially independent nationally-enforceable patents.

Eurasian patent (EA): The Eurasian Patent Organization (EAPO) set up by the Eurasian Patent Convention (EAPC) was signed and ratified by nine countries (Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Turkmenistan) in 1994 and came into force in 1995. The Convention allows the filing of one patent application in the Russian language with an automatic designation of all Member States. After the grant of a Eurasian Patent, the patentee shall indicate in which Member States he desires to maintain the patent.

ARIPO (AP): ARIPO is the African Regional Industrial Property Organization for English-speaking Africa. The Agreement between the member countries (Botswana, Gambia, Ghana, Kenya, Lesotho, Liberia (from 24 March 2010), Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe) was signed on December 9, 1976. A protection can alternatively be obtained on an individual basis in any of these countries via a national application in such country.

OAPI (OA): OAPI is the African Intellectual Property Organization for French-speaking Africa. The Agreement between the member countries (Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Guinea, Guinea Bissau, Ivory Coast, Mali, Mauritania, Niger, Senegal, and Togo) was signed on September 13, 1962. It is not possible to obtain protection in any of these countries other than by way of an OAPI application.

Appendix 2: Previous Patent Landscape Reports on vaccines & Links

A background study was performed in order to collect publicly available patent studies that already existed on vaccines against infectious diseases, as well as articles and presentations. These studies were used to collect information (such as useful keywords to build patent queries) before starting this patent landscape. The list of these reports is presented below:

- Patent Landscaping for Vaccines: Patent information, tools and methodologies. WHO/ WIPO/ WTO symposium, Medicines, Feb. 2011. Friede M.

- Patent data mining: A tool for accelerating HIV vaccine innovation. Vaccine 29 (2011) 4086–4093. Clark et al.

-The Impact of Intellectual Property, University Licensing Practices, and Technology Transfer on Regional Manufacturing of and Access to the HPV Vaccine in Resource-Poor Regions. Undergraduate Honors, 2009. Padmanabhan S.

- Intellectual property, technology transfer and manufacture of low-cost HPV vaccines in India. Nat Biotechnol. 2010 Jul;28(7):671-8. Padmanabhan et al.

- Patent Landscape of Countermeasures Against Smallpox and Estimation of Grant Attraction Capability Through Patent Landscape Data. Recent Patents on Anti-Infective Drug Discovery, Volume 5, Number 3, November 2010 , pp. 240-254(15). Mayburd et al.

- Vaccine Partnerships and Intellectual Property Management. 2008. Haanes EJ.

- Recent patent applications in antiviral vaccines. Nat Biotechnol. 2005 Nov;23(11):1370.

- "A review of production technologies for influenza virus vaccines, and their suitability for deployment in developing countries for influenza pandemic preparedness" conducted by the World Health Organization - Initiative for Vaccine Research,

- the "Working Paper on Patent issues related to influenza viruses and their genes", prepared by WIPO at the request of the World Health Organization,

- the "WIPO Patent search report on pandemic influenza preparedness (PIP)-related patents and patent applications", prepared by the International Bureau,

- Access to vaccine technologies in developing countries: Brazil and India. Vaccine 25 (2007) 7610–7619. Milstien et al.

Useful general information on vaccines can be found on a dedicated WHO website[17].

An important compilation of patent landscape reports is available on a WIPO website[18], in particular reports related HIV, malaria, Influenza[19] and adjuvants[20].

[17] http://www.who.int/topics/vaccines/en/

[18] http://www.wipo.int/patentscope/en/programs/patent_landscapes/pl_existing_reports.html

[19] http://www.patentlens.net/daisy/influenza/4132.html
http://www.boliven.com/boliven_landscapes/ip_report/Influenza_landscape

[20] http://www.patentlens.net/daisy/adjuvants/Introduction.html

Appendix 3: Command line of the different databases used in the queries

Patbase command language		Orbit command language	
Boolean operator **(A Boolean search request consists of a group of words, phrases, or macros linked by connectors)**			
AND	Operator used between two terms or queries →Both terms must be present in the field or document searched	ET	Operator used between two terms or queries →Both terms must be present in the field or document searched
OR	Operator used between two terms or queries → Either word can be present in the field or document searched	OU	Operator used between two terms or queries → Either word can be present in the field or document searched
AND NOT	Operator used between two terms or t queries →Excluded results from a search	SAUF	Operator used between two terms or t queries →Excluded results from a search
Truncation **(truncation and wildcards are useful when searching keywords that may have plurals or are derivatives of a word)**			
*	Unlimited truncation: matches any number of characters	+	Unlimited truncation: matches any number of characters
?	Wilcard character : matches exactly one character (any position in the term searched)	?	Wilcard character : matches exactly one character (any position in the term searched)
%	Wilcard character : matches one or zero characters (allows to find a word even if it is misspelled)	_	Wilcard character : matches one or zero characters or a [space] (allows to find a word even if it is misspelled)

#	Stemming: extends a search to cover grammatical variations on an English word Wilcard character : matches one or zero characters (allows to find word variants such as plurals, singular forms, past tense, present tense)		
Proximity operator (allows to specify that one word must occur within n words of the other)			
WF*n*	Operator used between two words: Word 1 and word 2 are located within n words in this order	*n*AV	Operator used between two words: Word 1 and word 2 are located within n words in this order
W*n*	Operator used between two words: Word 1 and word 2 are located within n words in either order	*n*M	Operator used between two words: Word 1 and word 2 are located within n words in either order
[space]	The two words are adjacent in exact order	[space]	The two words are adjacent in exact order
near	Operator used between two words: Word 1 and word 2 are located within 5 words in either order	PHR	Operator used between two terms (words or queries): Term 1 and term 2 are located in the same sentence in either order
Field Qualifiers (allows to target a search term to a particular field)			
TI=	Qualifiers used at the beginning of the query→ the search is performed in the titles of the document.	/TI	Qualifiers used at the end of the query→ the search is performed in the titles of the document.
TA=	Qualifiers used at the beginning of the query→ the search is performed in the titles and abstracts of the documents.	/BI	Qualifiers used at the end of the query→ the search is performed in the titles and abstracts of the documents.
CL=	Qualifiers used at the beginning of the query→ the search is performed in the claims of the documents.	/CLMS	Qualifiers used at the end of the query→ the search is performed in the claims of the documents.

TAC=	Qualifiers used at the beginning of the query→ the search is performed in the titles, abstracts and claims of the documents.	/BI/CLMS	Qualifiers used at the end of the query→ the search is performed in the titles, abstracts and claims of the documents.
[RU]:FT=	Qualifiers used at the beginning of the query→ the search is performed in the full text of Russian documents		
[JP]:FT=	Qualifiers used at the beginning of the query→ the search is performed in the full text of Japanese documents in non latin text.		
[KR]:FT=	Qualifiers used at the beginning of the query→ the search is performed in the full text of Korean documents in non latin text.		
[CN]:FT=	Qualifiers used at the beginning of the query→ the search is performed in the full text of Chinese documents in non latin text.		
FN=	Qualifiers used at the beginning of the query→ the search is performed in the inpadoc patent family numbers (number series devised by the database producer).	/FAN	Qualifiers used at the end of the query→ the search is performed in the FamPat patent family numbers (number series devised by the database producer).
PN=	Qualifiers used at the beginning of the query→ the search is performed in the publication numbers.	/PN	Qualifiers used at the end of the query→ the search is performed in the publication numbers.
IC=	Qualifiers used at the beginning of the query→ the search is performed in the International Patent Classification.	/IC	Qualifiers used at the end of the query→ the search is performed in the International Patent Classification.
JCI=	Qualifiers used at the beginning of the query→ the search is performed in the Japanese Classification.	/FI	Qualifiers used at the end of the query→ the search is performed in the Japanese Classification.
UC=	Qualifiers used at the beginning of the query→ the search is performed in the US Classification.	/PCLO	Qualifiers used at the end of the query→ the search is performed in the US Classification.

Appendix 4: Comparisons of the coverage of Patbase and Orbit databases

		Patbase coverage					Orbit coverage				
CC	Authority	Publications	Biblio data	Full text data	From	To	Publications	Biblio data	Full text data	From	To
AP	ARIPO	Unpublished Patent Applications	X		03/07/1971	06/30/2011	Publ. Application	X		03/07/1971	6/30/2011
		Patents	X		07/03/1985	06/30/2011	Patent	X		10/02/1990	6/30/2011
		Utility Models	X		06/06/2002	06/06/2002	Utility Model	X		06/06/2002	06/06/2002
AR	Argentina	Patents	X		02/08/1973	11/08/2006	Patent IPC from No. 200987 (PUBL. DATE 750206) onwards. No inventors; titles in Spanish	X		02/11/1965	8/18/1995
		Patent Applications	X		03/26/1997	09/28/2011	Patent Applications	X		11/20/1996	9/29/2011
		Utility Model Applications	X		03/20/1996	09/28/2011	Utility Model	X		03/20/1996	8/29/2011
AT	Austria						Publ. application. Titles in German	X	X	05/01/1914	9/15/2006
							Europ. Patent	X	X	11/15/1980	11/15/2011
		Patents	X		08/25/1899	11/15/2011	Patent	X	X	8/25/1899	4/15/2007
		Utility Models	X		07/25/1994	11/15/2011	Utility Model	X	X	7/25/1994	11/15/2011
		Patent Applications	X		05/01/1914	11/15/2011	Publ. Application	X	X	11/02/1965	11/15/2011
							Patent (new Law)	X	X	04/15/2007	11/15/2011

AU	Australia	Unpublished Patent Applications	X		01/06/1994	08/28/2003	Publ. application	X		3/14/1922	8/25/2005
		Patent Applications	X		03/14/1917	06/16/2011	Patent, Amended Patent	X		07/06/1938	03/01/2007
		Designs	X		03/07/2005	07/14/2006	Design	X		10/09/1986	7/14/2006
		Patents	X		06/07/1938	06/16/2011	Patent applications prior to acceptance	X		05/24/2001	6/16/2011
							Patent applicatons that were accepted	X		05/24/2001	6/16/2011
							Patent applicatons that were accepted but were subsequently amended and therefore needed to be republished.	X		05/24/2001	6/16/2011
BA	Bosnia	Patent Applications	X		12/28/1998	09/14/2001	Patent Application	X		12/28/1998	9/14/2001
		Patents	X		03/06/1998	08/02/1999	Patents rights inscribed into the registry on a basis of recognised right of former SZP until 1992-03-01.	X		03/06/1998	08/02/1999
BE	Belgium						Old Law Until Publ. Date 790702 (approx. No. 873263) only one foreign priority. From 700702 IPC up to subclass. From appl. date 790101 (No. 873264) onwards applicant, inventor and title in French or Dutch	X	X	9/15/1875	12/07/1999
		Patent Applications	X		01/26/1993	03/01/2011	EP transformed patents	X	X	12/07/1979	08/10/1988

		Patents	X		10/15/1862	10/04/2011	New Law	X	X	3/31/1987	10/04/2011
BG	Bulgaria	Patent Applications	X		06/15/1993	08/31/2010	Patent applications and patents	X		2/15/1973	5/31/200
		Patents	X		02/15/1973	08/31/2010	Patent application (from december 1993 onwards)	X		6/15/1993	8/31/2010
		Utility Model Applications	X		02/15/1973	10/31/2006	Patent (from december 1993 onwards)	X		05/31/1995	8/31/2010
		Utility Models	X		09/30/1994	06/29/2007					
		Granted Registered Utility Models	X		10/31/2007	11/30/2009	Utility models	X		01/18/1994	8/31/2010
BR	Brazil	Patents	X		04/22/2008	11/01/2011	Patent	X	X	01/02/1973	11/01/2011
		Utility Model Applications	X		08/05/1975	11/01/2011	Utility Model	X	X	08/05/1975	11/01/2011
							Additional Inventions Certificate	X	X	1/17/1995	11/01/2011
		Patent Applications	X		04/25/1972	11/01/2011	Application of certificate of addition of invention published without search report	X	X	05/12/2009	10/04/2011
BY	Belarus							X		30/09/1997	12/30/2003
CA	Canada	Patents	X		01/06/1920	11/01/2011	Patents	X	X	10/16/1874	10/09/1990
		Patent Applications	X		01/02/1973	11/05/2011	Filed applications and granted patents number > 1275150 and > 2000000	X	X	10/16/1990	10/11/2011
		Reissues	X		04/17/1973	08/22/2007	Filed application and granted patent Number > 2000000, for new applications filed from 10/1/1989 onwards	X	X	06/12/1990	11/05/2011
CH	Switzerland	Patent Applications	X		06/30/1891	10/31/2011	Publ. application	X	X	02/12/1964	8/31/1977
							Patent of addition	X	X	21/1/1886	5/16/1908
		Patents	X		01/09/1888	10/31/2011	Patent	X	X	11/1/1888	2/14/1975

							Patent (until 06/30/2008)	X	X	9/1/1889	11/30/2006
							Partial withdrawals and annullments of CH/EP patents	X	X	9/30/1998	5/31/2007
							Publication of patent application (new law 07.01.2008)	X	X	1/15/2009	10/31/2011
							Patent (New Law 01.07.2008)	X	X	07/01/2008	10/31/2011
CL	Chile	Patent Applications	X		01/07/2005	10/24/2008	Patent application	X		01/07/2005	10/24/2008
		Patents	X		01/07/2005	06/03/2005	Granted patent	X		01/07/2005	06/03/2005
		Industrial design application	X		01/07/2005	10/17/2008	Industrial Design application	X		01/07/2005	10/24/2008
		Industrial Design Applications	X		01/07/2005	10/17/2008					
		Utility Model Applications	X		01/14/2005	10/17/2008	Utility Model application	X		01/07/2005	10/17/2008
		Utility Models	X		03/18/2005	06/03/2005	Utility model	X		3/18/2005	06/03/2005
CN	China						Patent (old)	X	X	10/09/1985	12/28/1988
		Patent Applications	X	X	09/10/1985	11/09/2011	Unexamined patent appl., open to public inspection; Translation of an international Application	X	X	01/04/1989	11/09/2011
		Patents	X	X	01/06/1993	11/09/2011	Patent	X	X	01/04/1989	11/09/2011
		Utility Model Applications	X	X	04/09/1985	12/30/1992	Utility model (old)	X	X	04/09/1985	12/28/1988
		Utility Models	X	X	01/06/1993	11/09/2011	Utility model (new)	X	X	11/18/1992	11/09/2011
		Designs	X	X	09/10/1985	10/26/2011					
CO	Colombia	Patent Applications	X		02/13/1995	08/22/2011	Patent Application	X		2/13/1995	8/22/2011
CR	Costa Rica	Patent Applications	X		07/13/1988	12/30/2010	Patent Application	X		01/04/2007	7/30/2010
		Utility Model Applications	X		07/02/1996	10/28/2010	Utility model application (from 05/94/1983 onwards)	X		01/09/2009	04/12/2010

		Industrial Design Applications	X		04/10/1996	12/14/2010	Industrial Design application	X		05/04/2009	5/27/2010
CS	Czecho-slovakia	Patent Applications	X		02/26/1982	12/28/1992	Publ. application (Since 880816 titles in English)	X		9/15/1982	12/28/1992
		Patents	X		08/15/1957	11/12/2003	Patent From No. 178501 onwards applicant, inventor and titles in English	X		4/15/1964	3/17/1993
CU	Cuba	Patent Applications	X		03/12/1968	05/28/2009	Patent (former collection) Number series not complete	X		12/03/1968	01/06/1997
		Patents	X		11/11/1968	09/21/2011	Patent (current collection)	X		10/19/2005	9/21/2011
CY	Cyprus	Patents	X		05/06/1921	04/06/2011	Number series not complete	X		06/05/1921	04/06/2011
CZ	Czech Republic	Patent Applications	X		01/13/1993	11/09/2011	Publ. application	X		11/12/1991	11/09/2011
		Patents	X		03/17/1993	11/09/2011	Patent	X		8/15/1985	11/09/2011
		Utility Models	X		12/16/1992	11/09/2011	Utility Model	X		12/16/1992	11/09/2011
DD	Germany (EX_GDR)	Patent Applications	X		05/07/1992	04/22/1999	Patent from No. 127690 onwards applicant, inventor and titles in German	X		05/08/1952	4/22/1999
		Patents	X		12/06/1965	07/15/1999	Economic and exclusiv patent	X		1/30/1980	02/01/1989
		Utility Models	X		10/06/1956	12/05/1960	public notice of inspection of patent application	X		05/07/1992	05/07/1992
DE	Germany	Patent Applications	X	X	12/21/1921	11/17/2011	Patent till 730104 only one publication stage (no granted patents)	X	X	8/22/1954	11/17/2011
		Patents	X	X	08/26/1877	11/17/2011	Patent	X	X	06/07/1951	1/13/1983
							Granted Patent	X	X	12/18/1852	12/27/1998

							Publlication of filing or grant of certificate	X	X	7/19/1984	6/16/2011
		Utility Models	X	X	06/26/1928	11/17/2011	Utility model	X	X	6/26/1928	10/06/2011
		EP/WO Patents	X		12/17/1987	03/31/2011	Notification of the publication of the international application in German language (title page only)	X	X	12/27/1998	11/17/2011
DK	Denmark	Patent Applications	X		08/22/1949	10/09/2011	Filed application Data of unpublished applications abandoned in 1994	X	X	8/24/1973	12/23/1993
							Publ. Application (filed before 1.1.2000) Date of gazette given in statistics, correct publication date given in records	X	X	8/22/1949	07/01/2010
							Publ. Application (filed after 1.1.2000) Date of gazette given in statistics, correct publication date given in records	X	X	01/07/2000	09/10/2011
		Patents	X		03/25/1895	10/24/2011	Patent	X	X	3/25/1895	10/24/2011
		Utility Models	X		11/27/1992	09/14/2007	Translation of EP patent	X	X	01/08/1990	10/24/2011
		Utility Model Applications	X		08/28/1992	10/14/2011	Utility model	X	X	8/28/1992	10/14/2011
DO	Dominican Republic	Patent Applications	X		10/31/2001	09/30/2011	Patent application	X		5/31/2002	9/30/2011
		Utility Model Applications	X		12/31/2001	04/15/2011	Utility model application	X		1/15/2007	5/30/2007
		Designs	X		09/30/2005	09/15/2011	S	X		6/15/2006	9/15/2011
DZ	Algeria	Patents	X		09/28/2000	10/08/2005	Patent of Invention	X		9/28/2000	10/08/2005
EA	Eurasian	Patent Applications	X		07/01/1996	08/30/2011	Publ.	X		07/01/1996	8/30/2011

	patent office						application/Published/Search Report				
		Patents	X		03/31/1997	08/30/2011	Patent,Amended specification	X		07/01/1996	8/30/2011
EC	Ecuador	Patents	X		10/01/1990	06/30/2011	Patent	X		10/01/1990	6/30/2011
		Utility Models	X		10/01/1990	02/28/2011	Utility Model	X		10/01/1990	6/30/2011
		Industrial Designs	X		10/29/1990	02/28/2011	Industrial design application	X		5/25/1992	6/30/2011
EE	Estonia	Patent Applications	X		12/15/1995	10/17/2011	Published Patent Application	X		12/15/1995	10/17/2011
		Patents	X		02/15/1996	10/17/2011	Granted Patents	X		2/15/1996	10/17/2011
		Utility Models	X		10/17/1994	10/17/2011	Registered Utility Models	X		10/17/1994	10/17/2011
EG	Egypt	Patents	X		01/31/1976	06/26/2011	Patent	X		1/31/1976	6/26/2011
EP	European Patent Office	Patent Applications	X	X	12/20/1978	11/16/2011	Publ. application	X	X	12/20/1978	11/16/2011
		Patents	X	X	01/09/1980	11/16/2011	Patent	X	X	01/01/1980	11/16/2011
ES	Spain	Unpublished Patent Applications	X		05/16/1919	06/01/1993	Patent	X	X	5/16/1919	06/01/1993
		Patent Applications	X		01/01/1981	11/17/2011	Patent (Concordances) Patents	X	X	01/01/1981	12/16/1992
		Patents	X		01/08/1977	11/16/2011	Patent (Law 1986)	X	X	08/01/1987	11/17/2011
							Utility model	X	X	05/01/1959	06/01/1991
		Utility Model Applications	X		10/01/1987	11/17/2011	Utility model	X	X	09/01/1996	07/01/1999
		Utility Models	X		05/01/1959	11/17/2011	Utility model (New law 1986)	X	X	01/01/1988	11/17/2011
FI	Finland	Unpublished Patent Applications	X		05/09/1978	10/31/2011	Filed application Data of unpublished application	X	X	6/29/1842	07/01/1976
		Patent Applications	X		03/30/1973	11/15/2011	Publ. application Date of gazette given in statistics; correct publication date given in data records	X	X	07/03/1975	10/31/2011

		Patents	X		06/29/1842	04/24/2006	Patent	X	X	5/31/1968	11/15/2011
		Unpublished Utility Model Applications	X		01/02/1992	10/31/2011	Utility model application	X	X	01/02/1992	10/31/2011
		Utility Models	X		02/03/1992	10/31/2011	Utility model	X	X	02/03/1992	10/31/2011
FR	France	Patent Applications	X	X	03/07/1969	11/11/2011	Addition No IPC, no inventors, no applicants, no titiles	X	X	10/07/1902	10/20/1972
		Patents	X		02/28/1891	11/11/2011	Medicament No applicants, inventors and titles	X	X	07/10/1960	7/27/1973
		Utility Model Applications	X	X	01/07/1972	11/11/2011	Patent old system (without applicant, inventors and titles)	X	X	11/28/1898	8/14/1981
		Utility Models	X		01/12/1973	11/11/2011	Patent or utility model with title Applicant, inventor and title for 1st publication stage only applicant and inventor for second publication stage From publication date 850531 onwards titles and inventors also for the second publication stage	X	X	07/10/1911	11/11/2011
GB	United Kingdom	Unpublished Patent Applications	X		02/09/1983	10/19/2011	Filed application Data of unpublished application	X	X	02/09/1983	10/19/2011
		Patent Applications	X	X	01/04/1979	11/16/2011	Before 1916	X	X	8/12/1840	12/30/1921
		Patents	X	X	07/04/1782	11/16/2011	Before 1949	X	X	01/03/1916	12/29/1978
							Law 1949	X	X	4/30/1969	08/12/2003
							Law 1978	X	X	01/04/1979	11/16/2011
							Corrected publication published	X	X	09/03/1962	11/02/2011
GC	Gulf Coop.	Patents	X		10/30/2002	03/31/2011	Granted Patent	X		10/30/2002	3/31/2007

	Council										
GE	Georgia	Patent Applications	X		04/10/2006	04/10/2006					
		Patents	X		01/10/2000	09/10/2010	Patent (2nd publ)	X		01/10/2000	04/10/2000
GR	Greece	Patent Applications	X		12/16/1988	10/13/2011	Patent Application (new law)	X		10/31/1988	10/13/2011
		Patents	X		12/10/1920	09/30/2011	Patent	X		10/12/1920	9/30/2011
							Translation of claims of EP patent application	X		10/18/1988	1/31/2002
							Translation of EP patent	X		9/29/1989	1/31/2002
							Patent application (old law)	X		07/04/1977	2/23/1988
		Utility Model Applications	X		01/19/1990	01/31/2002	Utility model application	X		1/19/1990	1/31/2002
		Utility Models	X		12/16/1988	02/12/2002	Utility model	X		12/16/1988	02/12/2002
GT	Guatemala	Patent Applications	X		06/29/1966	08/20/2007	Patent Application	X		6/29/1966	8/20/2007
HK	Hong Kong	Patents	X		10/03/1997	06/03/2011	Patent	X		03/05/1976	3/30/2008
							Standard Patent	X		10/03/1997	06/03/2011
		Short Term Patents	X		05/01/1998	06/03/2011	Short term patents	X		05/01/1998	06/03/2011
HN	Honduras	Patent Applications	X		01/13/2005	02/27/2009	Patent application	X		1/13/2005	21/27/2010
HR	Croatia	Patent Applications	X		08/11/1994	10/31/2011	Patent	X		08/11/1994	10/31/2011
		Patents	X		12/31/1995	10/31/2011	Trans. of EP patent into Croatian	X		3/31/2007	10/31/2011
HU	Hungary	Unpublished Patent Applications	X		01/28/1990	02/28/2011	Deferred application numbers	X		03/02/1971	10/28/2000
		Patent Applications	X		03/02/1970	08/29/2011	Application number	X		3/28/1990	8/29/2011
		Patents	X		07/07/1913	08/29/2011	Examined Patent application	X		12/28/1983	11/28/2000
							Patent number From no. 170759 onwards applicant, inventor, title in English	X		1/29/1973	8/29/2011
		Utility Model Applications	X		09/28/1992	08/29/2011	Utility model application	X		3/28/1992	2/28/2011

		Unpublished Utility Model Applications	X		03/28/1992	02/28/2011	Utility model	X		8/28/1992	8/29/2011
ID	Indonesia						A	X		11/26/1988	01/03/2002
		Patents	X		07/29/1992	12/27/2001	Patent	X		7/29/1992	10/30/1996
		Patent Applications	X		11/26/1988	01/03/2002	Simple Patent	X		7/22/1996	12/27/2001
IE	Ireland	Short Term Patent Applications	X		01/13/1993	08/31/2011	Publ. application.	X		01/11/1995	8/31/2011
		Patent Applications	X		11/29/1990	08/31/2011					
		Short Term Patents	X		06/16/1993	03/05/2008					
		Patents	X		05/02/1945	11/11/2009	Patent	X		05/02/1945	02/03/2010
IL	Israel	Unpublished Patent Applications	X		06/20/1968	08/31/2011	Filed application Data of unpublished application	X		6/20/1968	8/31/2011
		Patent Applications	X		01/25/1968	08/31/2011	Patent	X		1/25/1968	8/31/2011
IN	India	Patent Applications	X		01/11/2005	11/18/2011	Patent	X	X	02/05/1912	10/28/2011
		Patents	X		02/05/1912	11/11/2011	Patent specification	X	X	1/25/1968	12/10/2010
		Designs	X		05/15/2009	11/18/2011					
IS	Iceland	Patent Applications	X		07/10/1926	08/23/2011	Patent application made available to the Public	X		02/05/1912	8/23/2011
		Patents	X		01/08/1927	09/15/2011	Patent specification	X		10/18/1996	9/15/2011
IT	Italy	Unpublished Patent Applications	X		01/02/1978	09/28/2006	Filling application	X		01/02/1978	11/04/2003
		Patent Applications	X		05/17/1990	11/16/2011	Published patent application	X		9/17/1990	11/08/2011
		Patents	X		12/20/1927	09/20/2010	Patent Titles in Italian, IPC up to subclass level	X		5/19/1953	8/30/2011
		Unpublished Utility Model Applications	X		01/02/1978	11/04/2003	Utility model application (old)	X		12/20/1927	10/03/1990
		Utility Model Applications	X		05/29/1989	11/15/2011	Patent for Utility model	X		1/13/1978	6/20/1991

		Utility Models	X		05/12/1978	12/23/2010	Utility model	X		1/13/1978	12/23/2010
							Published utility model application	X		6/13/1990	11/15/2011
JP	Japan	Patent Applications	X	X	01/16/1971	10/27/2011	Unexam. application From 50033701 (publication date 750401) onwards with IPC symbols from 51111001 to 6402910 titles in English	X	X	1/23/1971	01/06/1989
							Non-official translation of JP-A documents, not issued by Patent Office	X	X	05/09/1972	09/08/2005
							Unexam. Application	X	X	1/16/1971	11/04/2011
							Examined application	X	X	1/16/1971	01/06/1989
							Examined application	X	X	09/02/1946	3/29/1996
							("Old law") Granted Patent	X	X	01/06/1971	9/27/1995
		Patents	X	X	10/26/1928	10/26/2011	Registered patent	X	x	7/26/1979	11/09/2011
							PCT translations (before 1989)	X	X	7/26/1979	12/22/1988
							PCT translations (before 2000)	X	X	01/12/1989	12/21/1999
		Utility Model Applications	X		01/07/2000	07/31/2008	PCT translations (from 2000)	X	X	01/11/2000	9/22/2011
		Utility Models	X		02/06/1913	06/16/2010	Unexamined utility models	X	X	09/13/1971	11/04/2011
		Registered utility models	X	X	03/31/1983	10/20/2011	Granted utility models	X	X	2/28/1931	8/18/2004
KE	Kenya	Patents	X		07/11/1975	09/01/1989	Patent	X		07/11/1975	09/01/1989
KR	Korea Republic of	Patent Applications	X	X	12/09/1978	11/18/2011	Patent specification	X	X	01/08/1978	6/30/2011
		Patents	X	X	01/08/1978	10/06/2011	Official Gazette of the unexamined patents	X	X	12/09/1978	11/11/2011
		Utility Model Applications	X	X	11/27/1978	11/18/2011	Official Gazette of the unexamined utility models	X	X	9/17/1981	9/16/2011

		Utility Models	X	X	01/10/1978	06/30/2011					
		Design Applications	X	X	01/14/2009	01/10/2011	Utility model specification	X	X	01/10/1978	6/30/2011
KZ	Kazakhstan	Patent Applications	X		08/15/2001	05/15/2008	1 document was inserted into the database, no further delivery foreseen				
		Patents	X		12/10/1993	03/15/1995		X		1/15/2004	5/15/2008
LT	Lithuania						Patent application (until 1994)	X		3/25/1994	12/27/1994
		Patent Applications	X		03/25/1994	10/25/2011	Patent application (from 1995)	X		7/25/1996	10/25/2011
		Patents	X		08/25/1994	10/25/2011	Patent	X		8/25/1994	10/25/2011
							Reregistrations of SU patents	X		10/15/1992	4/25/1994
LU	Luxembourg	Patent Applications	X		07/08/1952	10/24/2011					
		Patents	X		03/15/1929	09/26/2006	Patent	X		06/02/1945	10/24/2011
LV	Latvia	Patents	X		10/20/1994	03/20/2011	Patent	X		03/10/1994	3/20/2011
		Patent Applications	X		03/10/1994	05/20/2002	Reregistrations of SU patents	X		06/10/1993	9/20/1998
MA	Morocco						Patent of Invention	X		07/06/1977	06/01/2011
		Patents	X		07/06/1977	09/01/2011	Granted Patent	X		07/01/2011	01/09/2011
MC	Monaco	Patents	X		12/13/1957	03/30/2011	Patent	X		12/13/1957	3/30/2011
MD	Moldova	Patent Applications	X		01/31/1994	12/31/2010	Patent application	X		9/30/1994	12/31/2010
		Patents	X		09/30/1994	12/31/2010	Patent, Decision of grant	X		1/31/1994	12/31/2010
		Utility Model Applications	X		08/31/1994	05/31/2009	Utility model application	X		10/31/1994	1/31/2009
		Utility Models	X		01/30/1995	12/31/2010	Utility model	X		8/31/1994	5/31/2009
		Plant Patent Applications	X		02/28/2003	06/30/2004	Granted short-term patent for invention	X		1/31/2009	12/31/2010
MN	Mongolia	Patents	X		02/15/1984	06/15/1989	Patent From No. 111 onwards applicant, inventor and title in English	X		11/20/1972	6/15/1989
MT	Malta	Patents	X		06/25/1968	05/08/1992	Patent	X		06/25/1968	05/08/1992
MW	Malawi	Patents	X		05/09/1973	10/12/1994	Patent	X		05/09/1973	10/12/1994

MX	Mexico						Patent of invention - From 1976 onwards	X		10/14/1980	10/01/1993
		Patent Applications	X		10/14/1980	06/06/2011	Patent application	X		02/03/1992	06/06/2011
		Patents	X		04/01/1992	01/10/2011	Patent of invention - from 1991 onwards	X		5/25/1991	11/19/2010
		Utility Models	X		10/09/1992	05/16/1994	Certificate of invention	X		01/02/1980	6/27/1991
MY	Malaysia						Reregistered GB patent	X		12/31/1953	3/31/2009
		Patents	X		12/31/1953	12/31/2010	Patent	X		10/26/1988	3/16/1989
		Utility Models	X		03/30/1996	03/30/1996	Laid open patent application	X		1/015/2010	12/31/2010
NI	Nicaragua	Patents	X		11/05/2003	03/24/2009	Patent	X		11/05/2003	3/24/2009
NL	Netherlands	Patent Applications	X		07/01/1913	08/10/2011	Unexamined application	X		2/17/1924	03/10/2011
		Patents	X		10/16/1908	08/11/2011	Registered specification laid open (patent law April 1995)	X		07/04/1995	2/16/2010
		SPC Applications	X		02/16/1993	04/01/2010	Patent application (from 20-02/2010 onwards)	X		2/20/2010	08/10/2011
		Granted SPCs	X		07/01/1993	04/01/2010	Patent B-documents (examined applications) as well as C-documents (granted patents) are stored (C-documents starting with publication date 790917)	X		2/17/1924	2/23/2011
							Patent (patent law April 1995)	X		07/01/1913	03/03/2011
							Patent (from 20-02-2010 onwards)	X		3/14/2011	08/11/2011
							Suppl. protection certificate application	X		01/01/2007	04/01/2010
							Granted suppl. protection certificate				
NO	Norway	Unpublished Patent	X		04/01/1986	12/09/2005	Filed application	X		06/02/1988	12/09/2005

		Applications					Data of unpublished application				
		Patent Applications	X		01/04/1915	09/09/2011	Public application	X		12/08/1966	07/01/1975
							Public application Date of gazette given in statistics. Correct publication date given in data records.	X		12/30/1974	09/09/2011
							Examined application; granted patent	X		1/19/1909	1/15/2004
		Patents	X		01/19/1909	09/26/2011	Patent	X		3/27/1991	9/26/2011
		SPC Applications	X		01/05/2004	09/26/2011	Suppl. protection certificate application, Granted suppl. protection certificate	X		01/05/2004	8/22/2011
		Granted SPCs	X		06/01/2004	07/25/2011	Document laid open for public inspection	X		02/10/2000	5/16/2011
NZ	New Zealand	Patents	X		03/06/1978	06/30/2011	Public application Titles in English, IPC symbols from 831216 onwards	X		03/06/1978	6/30/2011
OA	OAPI	Patents	X		01/15/1966	04/13/2007	Patent	X		1/15/1966	12/13/2006
PA	Panama	Patent Applications	X		05/20/1996	07/27/2010	Patent application	X		5/20/1996	02/12/2010
PE	Peru	Patent Applications	X		04/19/1992	09/30/2011	Patent application	X		4/19/1992	9/30/2011
		Utility Models	X		01/25/2002	09/16/2011	Utility Model application	X		05/11/1998	9/16/2011
PH	Philippines	Patents	X		07/03/1975	06/02/1999	Patent	X		12/02/1981	06/02/1999
		Utility Models	X		12/02/1981	12/23/1997	Utility model	X		12/02/1981	12/23/1997
PL	Poland	Patent Applications	X		09/26/1977	10/24/2011	Public application	X		9/26/1977	10/24/2011
		Patents	X		10/30/1930	10/31/2011	Patent From publication date 800731 (No. 110100) onwards titles in English	X		2/28/1973	10/31/2011

		Utility Model Applications	X		01/08/1996	10/24/2011	Utility model application	X		01/08/1996	10/24/2011
		Utility Models	X		01/31/1996	09/30/2011	Granted utility model	X		8/29/1997	9/30/2011
PT	Portugal	Patent Applications	X		11/01/1971	09/30/2011	Public application	X		01/11/1971	9/29/2011
		Patents	X		03/12/1976	09/29/2011	Patent	X		04/03/1977	9/29/2011
							Availability of national translation of European patent	X		4/28/2000	9/30/2011
		Utility Model Applications	X		06/23/1967	09/19/2011	Published utility model application	X		6/23/1967	7/25/2011
		Utility Models	X		02/13/1969	07/25/2011	Granted utility model	X		2/13/1969	07/02/2010
							Translation of EP patent into Portugese	X		1/31/1992	9/19/2011
RO	Romania	Patent Applications	X		04/29/2011	10/28/2011	Patent From publication date 15.10.77 onwards applicant, inventor and title in French	X		08/01/1907	10/28/2011
		Patents	X		01/20/1973	10/28/2011	Patent Titles in English	X		10/05/1989	10/28/2011
							U1, U2	X		4/29/2011	10/28/2011
							A0	X		4/29/2011	10/28/2011
RU	Russia	Patents	X		02/15/1993	10/10/2011	Patent	X	X	2/15/1993	10/27/2011
		Patent Applications	X		11/10/1995	10/10/2011	Application for Invention	X	X	7/27/1996	10/10/2011
		Utility Models	X		12/25/1994	10/10/2011	Certificate for Utility Models	X	X	12/25/1994	10/10/2011
RS	Republic of Serbia	Patent Applications	X		10/27/2006	08/31/2011	A	X		10/27/2006	8/31/2011
		Patents	X		12/15/2006	08/31/2011	B	X		12/15/2006	8/31/2011
		Petty Patents	X		10/27/2006	08/31/2011	U	X		10/27/2006	8/31/2011
SE	Sweden	Unpublished Patent Applications	X		11/30/1973	01/11/2005	Patent application filed	X	X	11/30/1973	01/11/2005
		Patent Applications	X		04/01/1968	04/19/2010	Public application	X	X	11/05/1940	11/08/2011

							Document laid open for public inspection	X	X	06/07/1966	3/02/011
							Abstract available to the public	X	X	04/07/1973	7/22/2010
							Patent specification (first level, from 1 to 227869)	X	X	9/20/1890	07/07/1970
		Patents	X		04/15/1971	11/08/2011	Patent (from 300001onwards)	X	X	9/20/1919	9/16/2008
							Patent (from 500001 onwards)	X	X	3/21/1994	11/01/2011
SG	Singapore						Patent	X		2/25/1983	12/22/1995
		Patent Applications	X		08/17/1990	09/29/2011	Transitional appication for re-registration	X		8/18/1995	12/22/1995
							Patent, (under patent act of 1995)	X		8/17/1990	9/29/2011
SI	Slovenia	Short Term Patents	X		12/31/1992	08/31/2011	Patent (before year 2000)	X		11/27/1992	12/31/1999
		Patents	X		11/27/1992	10/28/2011	Patent	X		2/29/2000	9/30/2011
							Translation of the claims of EP patents	X		10/31/1997	9/30/2011
SK	Slovakia	Patent Applications	X		07/07/1993	11/04/2011	Patent application	X		07/07/1993	11/04/2011
		Patents	X		12/08/1993	11/04/2011	Patent	X		12/08/1998	11/04/2011
							Utility model	X		04/05/2011	11/04/2011
SM	San Marino	Patent Applications	X		02/16/2000	09/09/2011	Publication of application	X		2/16/2000	09/09/2011
		Patents	X		10/17/2001	09/09/2011	Granted patent / Granted patent for PCT transfers	X		2/16/2000	09/09/2011
		Design Applications	X		04/05/2001	12/06/2006	Design / Model (first publication)	X		04/05/2001	12/06/2006
		Designs	X		06/25/2003	12/06/2006	Revalidation Design / Model	X		04/05/2001	09/09/2011
SU	U.S.S.R.	Patents	X		10/31/1940	09/10/2011	Patent	X		12/31/1928	09/10/2011
							From 770630 onwards applicant, inventor transliterated from Cyrilic to Latin,				

							English titles				
SV	El Salvador	Patent Applications	X		03/10/1970	10/13/2011	Patent	X		03/10/1970	03/11/2011
TH	Thailand	Patent Applications	X		08/13/1980	09/19/2011					
		Patents	X		07/28/1982	09/22/2011					
TJ	Tajikistan	Patent Applications	X		10/28/1998	06/05/2007	Patent Application	X		10/20/1998	06/05/2007
		Patents	X		07/16/1996	07/16/2007	Patent, Reregistration of SU Patent	X		10/20/1998	7/16/2007
		Utility Models	X		11/14/1998	05/06/2005	Utility Model Registration	X		11/14/1998	05/06/2005
							Petty Patent	X		10/14/2005	17/16/2007
TR	Turkey	Patent Applications	X		06/21/1996	08/23/2010	Patent titles in Turkish, no inventors, IPC down to subclass level since 850801 (Doc. No. 20671)	X		01/01/1973	9/23/1997
		Utility Model Applications	X		07/21/2000	08/23/2010	Patent Application (some 96xxxx and 97xxxxx numbers only 6 instead of 7 digits)	X		3/21/1997	8/23/2010
		Utility Models	X		06/21/1996	08/23/2010	Utility Model	X		6/21/1996	8/23/2010
TT	Trinidad and Tobago	Patents	x		06/16/1994	12/08/1995					
TW	Taiwan	Patent Applications	X		05/01/2003	11/16/2011	Laid open application fro patent or patent of addition	X	X	01/05/2003	11/01/2011
		Designs	X		05/01/1974	11/11/2011					
		Patents	X		05/01/1974	11/11/2011	Patent	X	X	1/21/1991	12/21/2010
		Utility Models	X		03/11/1974	11/11/2011	Granted Utility Model	X	X	01/01/2000	12/21/2009
UA	Ukraine	Patents	X		01/07/1987	05/26/2008	Granted Patent	X		07/01/1987	5/26/2008
		Utility Models	X		10/16/2000	05/26/2008	Utility Model	X		10/16/2000	5/26/2008
US	U.S.A.						Reissue	X	X	4/23/1839	11/08/2011
							Defensive publication	X	X	02/04/1969	07/05/1988

							Titles in English				
							TVPP (patent application)	X	X	1/28/1975	4/20/1976
		Patents	X	X	07/13/1836	11/15/2011	Patent	X	X	10/11/1932	11/15/2011
							Plant patent	X	X	08/02/2001	11/08/2011
							Plant patent application	X	X	08/02/2001	11/10/2011
							S.I.R.	X	X	12/03/1985	09/06/2011
		Patent Applications	X	X	03/15/2001	11/17/2011	Published application (pre-grant)	X	X	3/15/2001	11/17/2011
		Designs	X	X	06/16/1908	11/15/2011	Design Patent	X	X	4/25/1916	11/15/2011
UY	Uruguay	Patent Applications	X		02/23/2000	10/31/2011	Patent application	X		2/23/2000	10/31/2011
		Industrial Design Applications	X		01/31/2002	10/31/2011	Industrial design application	X		01/31/2002	10/31/2011
		Utility Model Applications	X		01/31/2002	10/31/2011	Utility model application	X		1/31/2002	10/31/2011
UZ	Uzbekistan	Patents	X		12/30/1997	12/30/1997					
VN	Viet Nam	Patents	X		12/22/1986	10/25/2010	Inventors Certiivates and patents	X		07/06/1984	4/25/1997
		Utility Models	X		09/24/1989	10/25/1996	Utility Solution	X		9/24/1989	10/25/1996
X	W.I.P.O (P.C.T.)	Patent Applications	X	X	10/19/1978	11/17/2011	Public application	X	X	10/19/1978	11/10/2011
							Later or corrected publication	X	X	08/02/1979	11/17/2011
YU	Yugoslavia	Patent Applications	X		02/28/1973	05/28/1992	Public application	X		2/28/1973	5/28/1992
		Patents	X		09/30/1964	11/13/1981	Patent	X		2/28/1973	5/28/1992
		Patent Applications	X		03/03/2006	12/15/2006					
		Patents	X		03/03/2006	12/15/2006	Applicant, inventor, title until publ. date 761231 in Serbo-Cratian, from 770228 (No. 33426) onwards title in English				
YU	Serbia and Montenegro						Publication of patent application	X		03/03/2006	12/15/2006
							Registered patent	X		01/08/1996	5/25/2006
							Petty patent	X		03/03/2006	12/15/2006

ZA	South Africa	Patents	X		09/06/1968	10/27/2010	Patent	X		09/06/1968	10/27/2010
ZM	Zambia	Patents	X		10/16/1968	05/25/1994	Patent	X		10/16/1968	5/25/1994
ZW	Zimbabwe	Patent Applications	X		09/03/1980	01/25/1995	Public application (Titles in English, IPC up to subclass level)	X		09/03/1980	1/25/1995

Appendix 5: Queries to retrieve worldwide patent and patent applications dealing with active ingredients of vaccines against infectious diseases

1. Classification code based queries

To understand the query language, please refer to appendices.

QUERY 1: IPC codes

IC=(A61K39/00? OR A61K39/1* OR A61K39/2* OR A61K39/02 OR A61K39/04 OR A61K39/05 OR A61K39/07 OR A61K39/08 OR A61K39/09 OR A61K39/0?? OR A61K39/40 OR A61K39/42)

25144 results

QUERY 2: USPC codes

UC=(424/185.1 OR 424/185.1 OR 424/186.1 OR 424/187.1 OR 424/188.1 OR 424/189.1OR 424/19?.1% OR 424/20?.1 OR 424/21?.1 OR 424/22?.1 OR 424/23?.1 OR 424/24?.1 OR 424/25?.1 OR 424/26?.1 OR 424/270.1 OR 424/271.1 OR 424/272.1 OR 424/273.1 OR 424/813 OR 424/814 OR 424/815 OR 424/816 OR 424/817 OR 424/818 OR 424/819 OR 424/820 OR 424/821OR 424/822 OR 424/823 OR 424/824 OR 424/825 OR 424/826 OR 424/827 OR 424/828 OR 424/829 OR 424/830 OR 424/831 OR 424/832)

10792 results

QUERY 3: ECLA codes

EC=(A61K39/00A OR A61K39/00B OR A61K39/00C OR A61K39/002 OR A61K39/005 OR A61K39/008 OR A61K39/01? OR A61K39/02? OR A61K39/02?? OR A61K39/04 OR A61K39/05 OR A61K39/07 OR A61K39/08* OR A61K39/09* OR A61K39/1* OR A61K39/2* OR A61K39/40 OR A61K39/42)

7493 results

QUERY 4: Japan FI

JCI=(A61K39/00? OR A61K39/0?? OR A61K39/02 OR A61K39/04 OR A61K39/05 OR A61K39/07 OR A61K39/08* OR A61K39/09* OR A61K39/1* OR A61K39/2*)

5032 results

→ As mentioned in the search strategy introduction, the combination of these queries built with classification codes created the pool 1.

QUERY 5: combination of classification codes based queries

query 1 OR query 2 OR query 3 OR query 4

Pool 1=28299 results

2. Keyword-based query – Pool 1

To understand the query language, please refer to appendices.

QUERY 6: query used to clean the pool 1

TAC=(vaccine% OR vaccin% OR vaccina* OR vacina* OR vacuna* OR impstoff* OR impftoff* OR vakzine OR vaksine OR immunis* OR immuniz* OR immunogenic OR immunogen% OR prevent* OR prophyla* OR protect*) OR DSC=(vaccine% OR vaccin% OR vaccina* OR impstoff* OR vaksine) OR TAC=((elicit* OR generat* OR induc* OR trigger*) W5 (immun* response)) OR FT=(疫苗) OR FT=(백신) OR FT=(ワクチン) OR FT=(вакцина)

→ These results were crossed with *pool 1* in order to eliminate all patents and patent applications that clearly do not deal with vaccines and obtain *pool 2*

QUERY 7: *pool 2*

query 5 AND query 6

Pool 2=22745 results

3. Keyword-based query – Pool 2A

To obtain *pool 2A*, *pool 2* was crossed with high relevant keyword-based queries. Many keywords were tested to build the following queries of keywords that retrieve a high percentage of relevant patents and patent applications.

QUERY 8: TAC=((immunis* OR immuniz*) WF1 against) AND TAC=(seq id)

QUERY 9: TA=((prevent* OR protect*) W10 (vaccin* OR antigen* OR immunis* OR immuniz*))

QUERY 10: TAC=(vaccin% OR vaccine%) AND TAC=(seq id)

QUERY 11: TA=(Bacterin*)

QUERY 12: TA=((attenuat* OR inactivat* OR killed OR live OR virulent OR avirulent) AND (Strain% OR *virus OR bacter* OR viral))

QUERY 13: TA=((Elicit* OR Generat* OR Induc* OR Trigger*) W5 (Response))

QUERY 14: TA=((conjugate* WF1 (vaccin% OR vaccine% OR vaccina*)) AND NOT schedul*)

QUERY 15: TA=(subunit WF1 (vaccin% OR vaccine% OR vaccina*)) AND NOT TI=((adjuvants for) OR (vaccine adjuvants) OR dose OR intranasal OR somatostatin OR cream OR amphipat*)

QUERY 16: TI=(recombinant WF2 (vaccin% OR vaccine% OR vaccina*))

QUERY 17: TA=((vaccin* OR immuniz* OR immunis*) W5 against)

→ These queries of highly relevant keywords were combined (query 18) and then crossed with *pool 2* to obtain *pool 2A* (query 19)

QUERY 18: combination of high relevant keyword-based queries

query 8 OR query 9 OR query 10 OR query 11 OR query 12 OR query 13 OR query 14 OR query 15 OR query 16 OR query 17

51608 results

QUERY 19: *pool 2A*

query 7 AND query 18

Pool 2A=11276 results

→ Then *pool 2A* (containing 11276 patents and patent applications) was cleaned with queries of keywords containing combinations of typical irrelevant keywords to obtain the first group of relevant patents and patent applications.

Many keywords were tested to build the following typical irrelevant queries of keywords that cleaned pool 2A.

QUERY 20: TAC=(((cancer OR tumo%r OR carcinom*) W2 (antigen* OR peptid*)))

QUERY 21: TI=adju* AND NOT ((TI=(adjuvanted OR adjuvated OR adjuvanting OR (adjuv* with))) OR PN=(US2009110699 OR US2003091595 OR WO9848836 OR US5733555 OR US2004101534 OR US2002172692 OR US2004101534 OR US2002172692 OR US2004151734 OR CN101690810 OR CN1562363 OR CN101063142 OR US2002131980 OR US6573245 OR US4567042 OR US2006104943 OR US2003064078 OR WO10094663 OR US2009220522 OR US2011195091 OR WO0056358 OR US4285930 OR CN101745104 OR CN101024080 OR WO09069447 OR WO09069448 OR US2002058046))

QUERY 22: TI=(deliver* AND NOT (meningococcal OR papilloma OR tuberculosis OR anthrax OR epstein OR anguillarum OR (hiv vaccine)))

QUERY 23: TI=((cell line%) OR cultur* OR matri*) AND NOT (TI=(vaccin* OR immunogenic OR attenuat* OR avirulent OR inactivat*) OR AB=(vaccin* AND (attenuat* OR immuniz* OR immunis*)) OR CL=(vaccin* AND (immuniz* OR immunis* OR seq OR immunoprotec*)))

QUERY 24: (TI=(stabilizer) AND NOT TAC=((immunogenic composition*) OR (vaccin* preparation) OR (vaccin* composition*) OR (live WF2 vaccin*))) OR (TI=(stabili* AND (formulation OR cassette OR conformation OR antibody*))) OR (TA=(stabili* AND packaging) AND NOT TI=(vaccin* composition*)) OR (TI=stabili* AND NOT TAC=(vaccin* OR immunogenic OR inactivat* OR attenuate*))

QUERY 25: TI=(device% OR needle* OR microneedle* OR inject* OR apparatus* OR pen OR semiconductor* OR stent* OR catheter* OR magnetic OR automatic) AND NOT (TA=(((vaccin* composition%) OR (immunogenic composition%)) AND infect*) OR (TAC=(seq id) AND TI=vaccin*) OR

TI=(vaccin* against) OR TI=(injectable vaccine) OR TI=((viru* OR vira* OR viro* OR viri*) WF1 vaccin*) OR TA=prophylac* OR TI=attenuat*)

QUERY 26: TI=(cream% OR tablet% OR aqueous OR solvent% OR gel% OR powder* OR oil# OR water OR emulsi* OR dry OR dried) AND NOT (TAC=(immuniz* OR immunis* OR ((elicit* OR generat* OR induc*) WF3 immun*)) OR TA=(vaccin*) OR TA=(bacterin*) OR TAC=((attenuated OR avirulent) AND strain*))

QUERY 27: TI=(crohn OR alzheimer OR (immune disease%) OR (autoimmune disease) OR neurotoxicity OR amyloid* OR arthritis)

QUERY 28: TI=cancer* AND NOT TI=(hpv OR papilloma)

QUERY 29: TI=(allergen* OR (adenoviral vectors) OR (adenovirus-based methods))

QUERY 30: (TA=probiotic OR TI=allerg*) AND NOT TI=vaccin*

QUERY 31: (TA=((graft* OR xenograft* OR implant% OR transplantation* OR immunosuppressor OR rejection OR (down regulation))) AND NOT ((TAC=(((vaccin* composition%) OR (immunogenic composition%)) AND infect*)) OR (TAC=(seq id)) OR TI=((vaccin* against) OR ((viru* OR vira* OR viro* OR viri*) WF1 vaccin*)) OR (TA=prophylac*) OR (TAC=(elicit* W5 response)) OR TI=(attenuat* OR (immune response))))

QUERY 32: (TI=((model%)) AND NOT (TAC=(seq id) OR (TI=(prevent*)) OR (TA=(antigen* AND (immune response))) OR (TA=(vaccine against))))

QUERY 33: (TI=((bioreactor% OR reactor% OR industrial OR (large scale) OR (mass production))) OR (AB=((bioreactor% OR reactor%)) AND (TI=(method OR process))))

QUERY 34: (IC=A61P35 AND TAC=((treat* OR therap*) AND NOT (prophyl* OR prevent*)))

→ These queries of irrelevant keywords were combined (query 35) and then crossed with *pool 2A* to obtain the first group of relevant patents and patent applications (query 36)

QUERY 35: combination of typical irrelevant queries of keywords

query 20 OR query 21 OR query 22 OR query 23 OR query 24 OR query 25 OR query 26 OR query 27 OR query 28 OR query 29 OR query 30 OR query 31 OR query 32 OR query 33 OR query 34

More than 100 000 results

QUERY 36: first group of relevant and validated patents and patent applications

query 19 AND NOT query 35

9762 results

→At this point, a first group with a total of 9762 relevant patents and patent applications was identified

4. Keyword-based query – Pool 2B

To obtain *pool 2B*, *pool 2A* was removed from *pool 2*. Then, an iteration of queries of keywords that alternatively retrieved relevant documents or eliminated irrelevant ones were implemented, decreasing progressively the number of remaining documents to analyze in *pool 2B.* Gradually, these steps led to a new group of relevant patents and patent applications.

QUERY 37: *pool 2B*

query 7 AND NOT query 18

11474 results remaining to analyze

→ P*ool 2B* (containing 11474 patents and patent applications) was first cleaned with the keyword search queries containing combinations of irrelevant keywords (query 38)

QUERY 38: iteration 1 – elimination of irrelevant patents and patent applications using the typical irrelevant queries of keywords

query 37 AND NOT query 35

9058 results remaining to analyze

After this step and for the next steps of the iteration process, relevant queries of keywords (that should only retrieve relevant patents and patent applications) retrieved also irrelevant patents and patent applications. These irrelevant patents and patent applications were identified by intellectual screening and then saved in a folder in order to remove them easily (folder "irrelevant patents"). To simplify the presentation of the present search strategy, this pool of irrelevant INPADOC patent families was removed at the next step (query 39).

QUERY 39: iteration 2 – elimination of folder "irrelevant patents"

query 38 AND NOT **folder "irrelevant patents"**

8594 results remaining to be analyzed

QUERY 40: iteration 3 – recovery of a first group of relevant patents and patent applications

query 39 AND TAC=(prevent* WF9 infect*) AND TA=(vaccine* OR antigen* OR immunogen*)

335 relevant families identified and removed from the query 39

8259 results remaining to be analyzed

QUERY 41: iteration 4 – recovery of a second group of relevant patents and patent applications

query 40 AND TA=((vaccine* composition*) OR (immunogenic* composition*)) AND TAC=((prevent* OR protect*) WF9 infect*)

21 relevant families identified and removed from the query 40

8238 results remaining to be analyzed

QUERY 42: iteration 5 – recovery of a third group of relevant patents and patent applications

query 41 AND TA=(elicit* OR generat* OR induc* OR trigger*) W5 (re%ponse*)

66 relevant families identified and removed from the query 41

8172 results remaining to be analyzed

For the next step, in order to simplify the presentation, iteration steps that could be grouped were presented in the same query (query 43, query 44 and query 45).

QUERY 43: iteration 6 – elimination of irrelevant patent families using a series of irrelevant queries of keywords presented below

- TI=(assay% OR immunoassay% OR microassay%) AND NOT TAC=vaccin*
- TAC=(large scale) W5 (produc* OR manufactur*)
- TAC=(enhanc* immun*)
- TAC=autoimmun* OR (auto immun*)
- TAC=allerg*
- TAC=inflammat*
- TA=cytokine*
- TAC=((modulat* OR enhanc*) WF2 immun*) OR immunomodu* OR (immuno modu*) OR immunostimu* OR (immuno stimu*)
- TAC=immunopotentia* OR (immuno potentia*) OR (immune potentiatio*)
- TA=(scleros* OR leukemi* OR leukaemi* OR lymphom* OR tumor* OR tumour* OR diabet* OR head*) AND NOT (HPV OR papilloma*)
- TAC=(treat* OR therap*) AND NOT (vaccin* OR prevent* OR prophyla* OR immuniz* OR immunis*)
- TA=(anticancer* OR (anti cancer*) OR cancer* OR neoplasm* OR melanoma* OR antineoplas* OR (anti neoplas*) OR antitumor* OR (anti tumor*) OR antitumour* OR (anti tumour*) OR obesity OR healing) AND NOT (HPV OR papilloma*)

query 42 AND NOT series of irrelevant keyword-based queries presented above

5618 results remaining to be analyzed

QUERY 44: iteration 7 – recovery of a fourth group of relevant patent families using a set of relevant queries of keywords presented below

- TAC=(elicit* OR generat* OR induc* OR trigger*) WF5 (immune re%ponse*)
- TAC=((prevent* OR protect*) WF5 infect*) AND TA=(vaccin* OR immunogen* OR antigen* OR immuniz* OR immunis* OR prophylac*)
- TA=((virus like particle*) OR vlp OR vlps) AND TAC=(vaccin* OR immunogen* OR antigen* OR immuniz* OR immunis* OR prophylac*)
- TAC=((immunogenic composition*) OR (vaccine* composition*) OR (immunizing composition*) OR (immunising composition*)) AND (immuniz* OR immunis* OR prophylac*

OR prevent* OR protect* OR (immune respons*) OR vaccinat* OR ((elicit* OR generat* OR induc* OR trigger*) WF5 re%ponse*))

- TAC=(elicit* OR generat* OR induc* OR trigger*) WF5 (immune OR re%ponse*)
- TAC=immunogen% AND (virus* OR infect* OR parasite* OR bacteri* OR mycobacteri* OR salmone* OR hiv OR influenz*) AND (protect* OR prevent*)
- TAC=((conjugate% OR glycoconjugate%) WF1 (vaccine* OR antigen*)) AND (virus* OR infect* OR parasit* OR bacteri* OR mycobacteri* OR salmone* OR HIV OR influenz*)
- TAC=((conjugate% OR glycoconjugate%) WF1 (vaccine* OR antigen*)) AND (virus* OR infect* OR parasit* OR bacteri* OR mycobacteri* OR salmone* OR HIV OR influenz*)
- (TAC=(((immunizi* OR immunisi*) WF1 (subject% OR host% OR patient% OR man% OR human% OR woman% OR animal%)) AND (virus* OR infect* OR parasit* OR bacteri* OR mycobacteri* OR salmone* OR HIV OR influenz*)))
- (TAC=((protective OR protection) W1 (antigen% OR immunity OR antigenic)))
- (TA=((strain* OR antigen%) AND (vaccin* OR immuniz* OR immunis*)))

query 42 AND NOT series of relevant keyword-based queries presented above

1624 relevant families identified and removed from the query 43

3994 results remaining to be analyzed

QUERY 45: iteration 8 – elimination of irrelevant patent families using a new series of irrelevant keyword-based queries presented below

- TAC=monoclonal
- TI=antibod*
- TA=antibod* AND NOT TI=(immunogenic OR immunization OR immunisation OR immunogen% OR prophyla* OR vaccine* OR vaccino*)
- TI=(detect* OR diagnos*) AND NOT (immunogenic OR immunization OR immunisation OR immunogen% OR prophyla* OR vaccine* OR vaccino*)
- TI=(medicament% OR medecine% OR compound%)

query 44 AND NOT series of irrelevant keyword-based queries presented above

2883 results remaining to be analyzed

QUERY 46: iteration 9 – recovery of a fifth group of relevant patents and patent applications

query 45 AND TAC=((stimulat*) WF5 (immune re%ponse*)) AND NOT (treat* OR therap*)

14 relevant families identified and removed from the query 45

2869 results remaining to be analyzed

QUERY 47: iteration 10 – elimination of irrelevant patent families

query 46 AND NOT TA=(treat* OR therap*) AND NOT TAC=(vaccin* AND (prevent* OR prophyla* OR immuniz* OR immunis* OR immunogenic))

2255 results remaining to be analyzed

QUERY 48: iteration 11 – recovery of a sixth group of relevant patents and patent applications

query 47 AND TA=(immunogenic WF1 influenza)

2 relevant families identified and removed from the query 47

2253 results remaining to be analyzed

At this stage no further keyword-based queries were sufficiently helpful to eliminate or retrieve irrelevant or relevant patent families. A deep review was performed on a sample of the patent families remaining to analyze in order to estimate the percentage of relevant patent families present. As this percentage was inferior to 10%, it was decided in accordance with the WIPO to eliminate the whole pool of remaining patent families.

→ This concluded the iteration process concerning pool 2B. A second group of 2062 relevant patents and patent applications was validated

5. Investigations to validate the search strategy

Other IPC codes were investigated to confirm and validate the fact that only a tiny fraction of the relevant patents and patent applications were not classified within the classification codes selected.

As IPC codes cover the major part of patents and patent applications comparing to other type of classification codes, the next steps were only performed using IPC codes. By screening the IPC classification, it appeared that the main group C07K14 gathered patent families claiming peptides. As antigens are mostly from peptide origin, it was decided to investigate this major group. However, this classification does not only cover patents claiming vaccine applications; these classification codes had therefore to be combined with other IPC codes (or keywords) such as A61P31 or A61P33 that are related to potential vaccine application. These IPC codes are presented below.

International Patent Classification (IPC):

Selection of subclasses of subgroup C07K14 corresponding to peptides having more than 20 amino acids specific to infectious diseases

Examples of selected subclasses of subgroup C07K14: C07K 14/005 (from viruses), C07K 14/21 (from Pseudomonadaceae)

Examples of unselected subclasses of subgroup C07K14: C07K 14/49 (Platelet-derived growth factor (PDGF)), C07K 14/65 (Insulin-like growth factors (Somatomedins), e.g. IGF-1, IGF-2)

A61P31 (Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics) and A61P33 (Antiparasitic agents) and their respective sub-classes

Note that these IPC codes are related to infectious diseases but despite their combination are still not fully specific to vaccines (there are still patents claiming therapeutic peptides, immunomodulators …)

QUERY 49: Other IPC codes investigated

(IC=(C07K14/00? OR C07K14/0?? OR C07K14/01 OR C07K14/02 OR C07K14/03 OR C07K14/04 OR C07K14/05 OR C07K14/06 OR C07K14/07 OR C07K14/08 OR C07K14/09 OR C07K14/1?% OR C07K14/2?% OR C07K14/3?% OR C07K14/40 OR C07K14/44% OR C07K14/45*)) AND (IC=(A61P31 OR A61P33))

5778 results

From these results were removed all the results retrieved through by the classification codes selected and already analyzed (query 5).

QUERY 50: Other IPC codes investigated without the classification codes already analyzed

query 49 AND NOT query 5

1279 results

Then, this result was crossed with the combination of queries of high relevant keywords (query 18) and cleaned with the combination of queries of irrelevant keywords (query 35) in order to highlight the potentially relevant patent families.

QUERY 51: Other IPC codes investigated – potential relevant patent pool

(query 50 AND query 18) AND NOT query 35

77 results

This result shows that very few relevant patents and patent applications were not retrieved by the first selection of classification codes (query 5).

Although the volume of relevant patents and patent applications retrieved through the other IPC codes investigated was not representative comparing to the volume of the global database, these patent families were included in the final database.

This analysis therefore confirmed and validated the formerly set up search strategy.

6. Final database

The final database on vaccines against infectious diseases, created 23rd November 2011, contained 11818 relevant INPADOC patent families.

Appendix 6: Map of filings

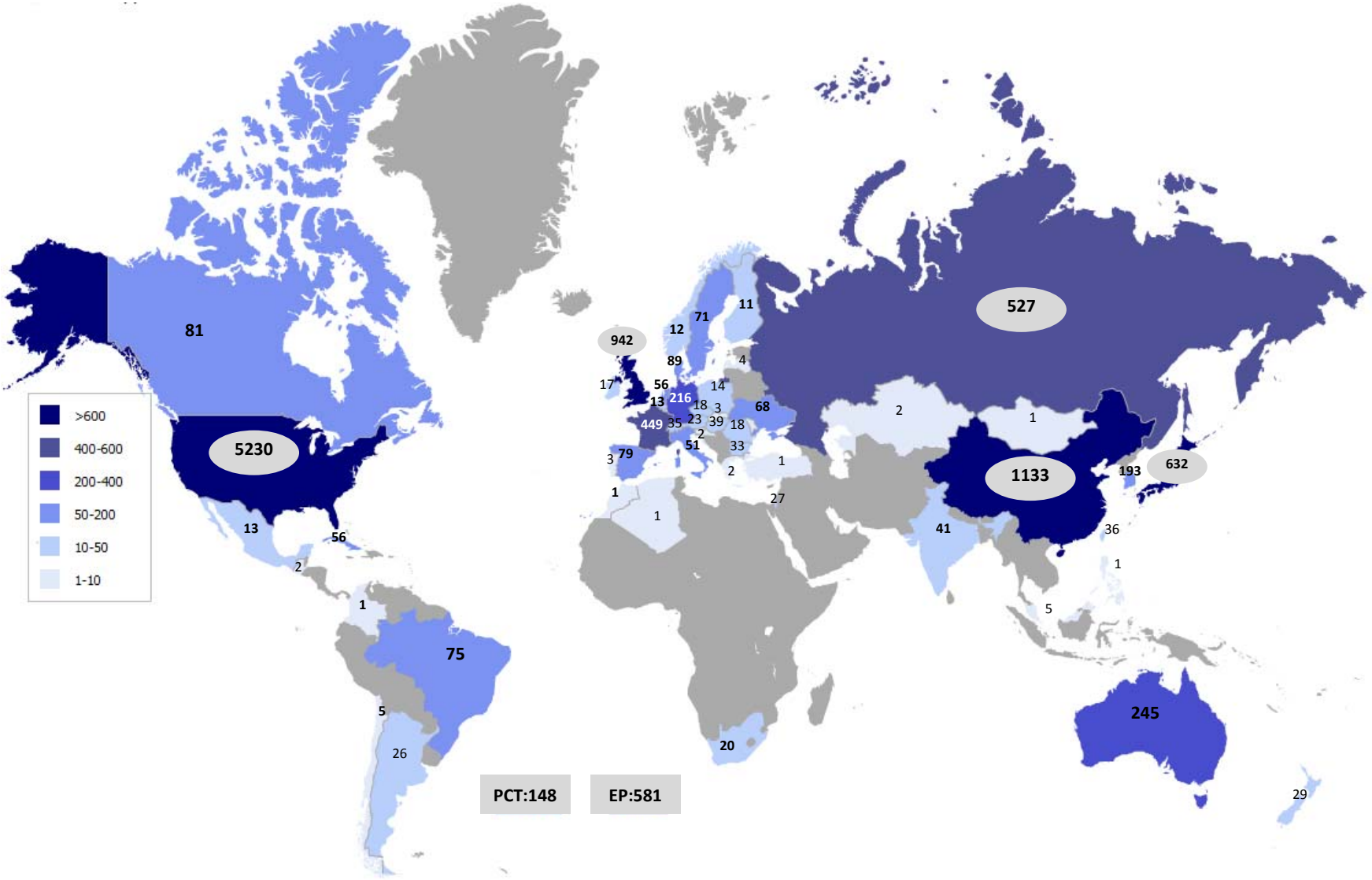


Figure 1 - Map of offices of first filing for patent and patent applications claiming active ingredients of vaccines against infectious diseases

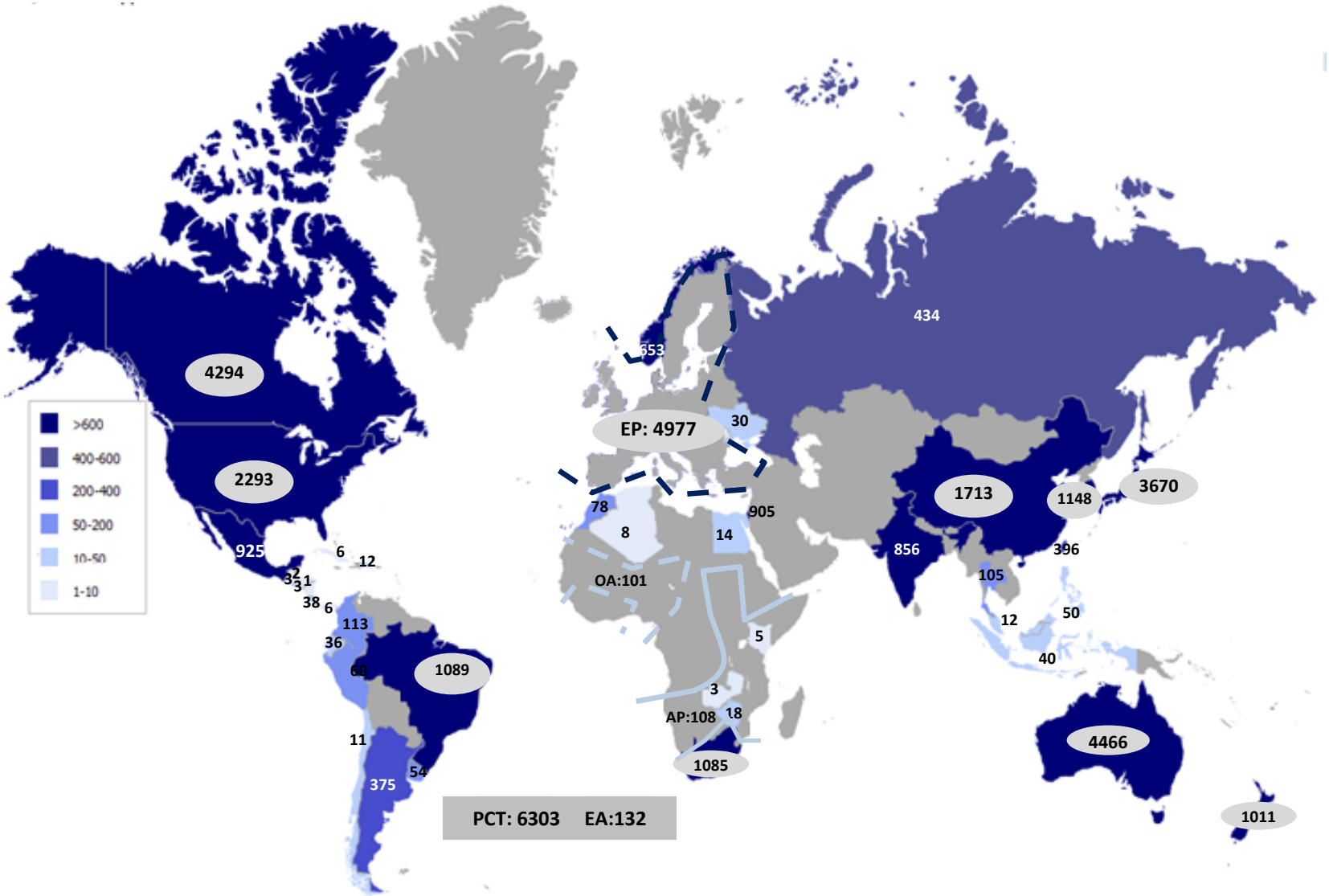


Figure 2 - Map of offices of second filings for patent and patent applications claiming active ingredients of vaccines against infectious diseases

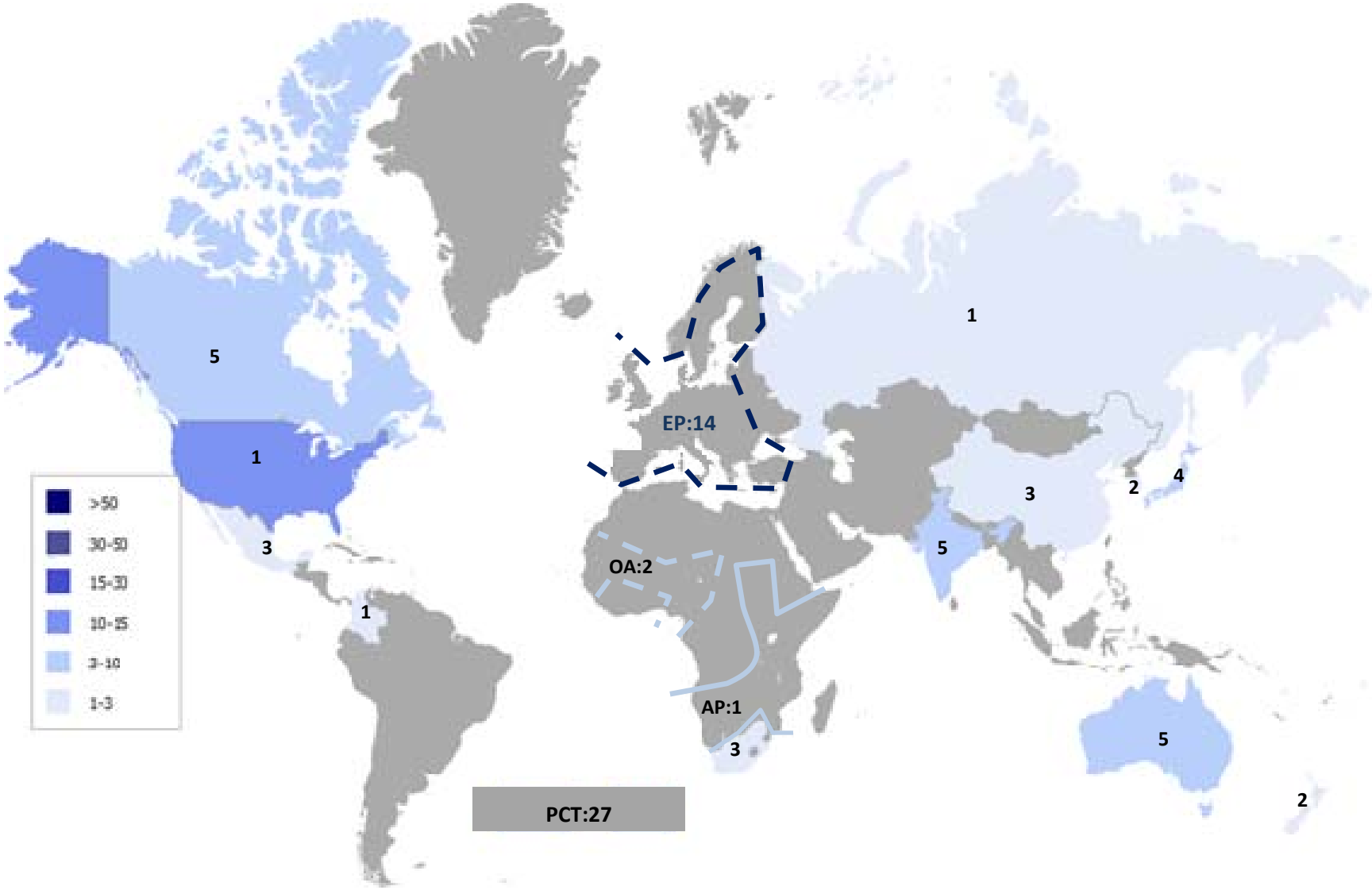
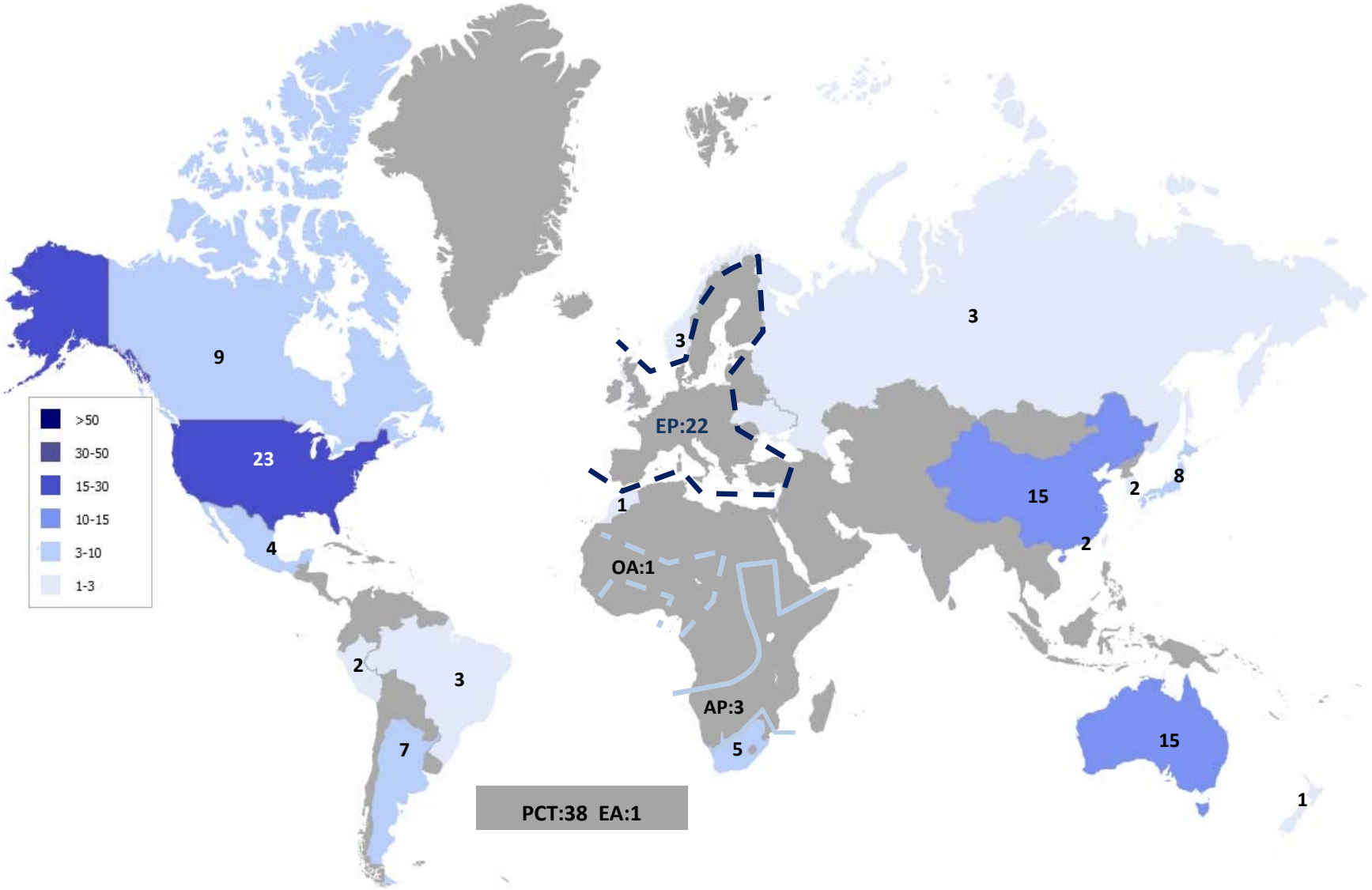
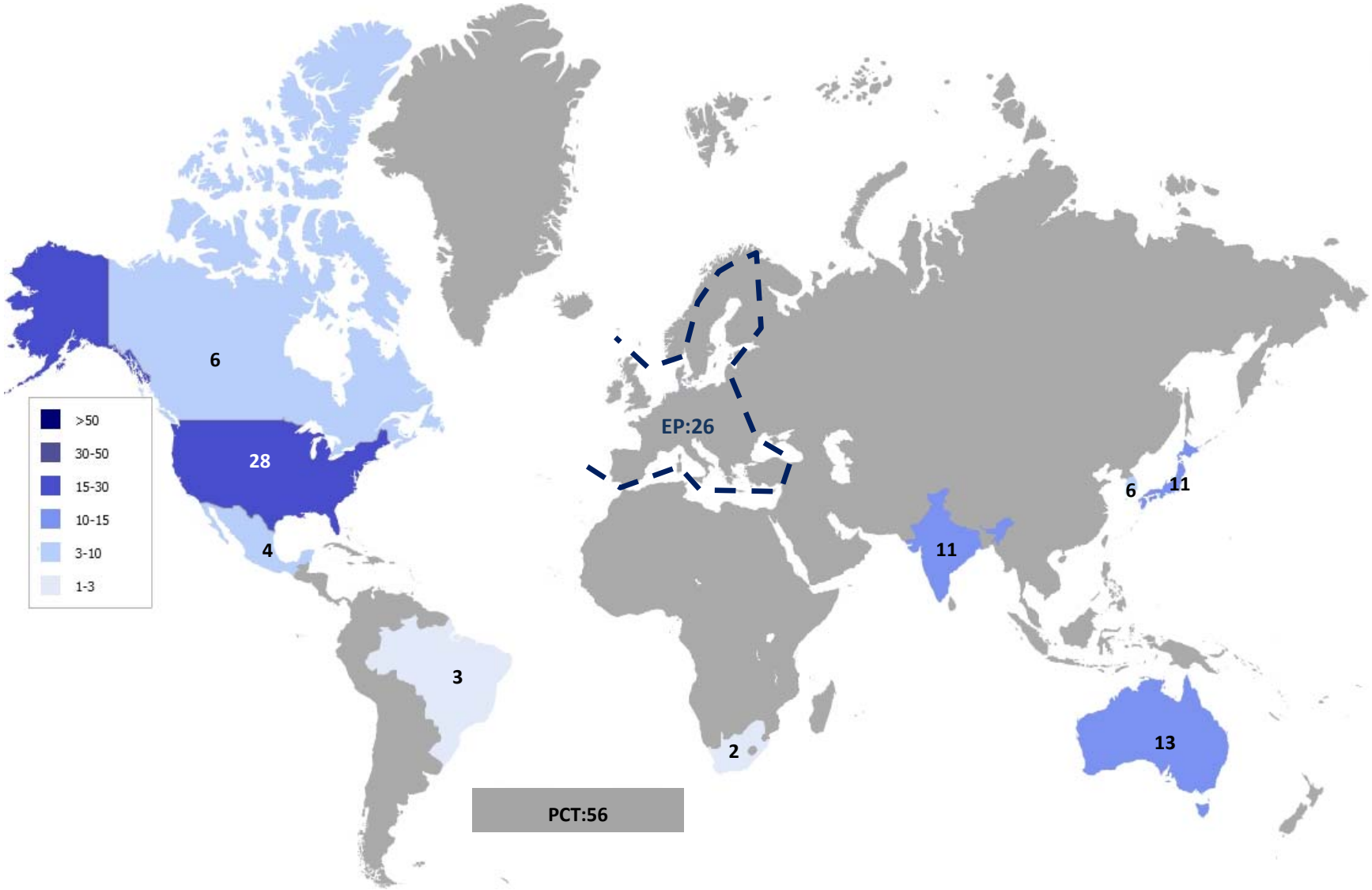

>50
30-50
15-30
10-15
3-10
1-3
5
1
3
1
EP:14
OA:2
AP:1
3
PCT:27
1
3
2
4
5
5
2

Figure 3 - Map of offices of second filings for patent and patent applications filed in priority in Brazil claiming active ingredients of vaccines against infectious diseases



Map of offices of second filings for patent and patent applications filed in priority in India claiming active ingredients of vaccines against infectious diseases



Map of offices of second filings for patent and patent applications filed in priority in China claiming active ingredients of vaccines against infectious diseases

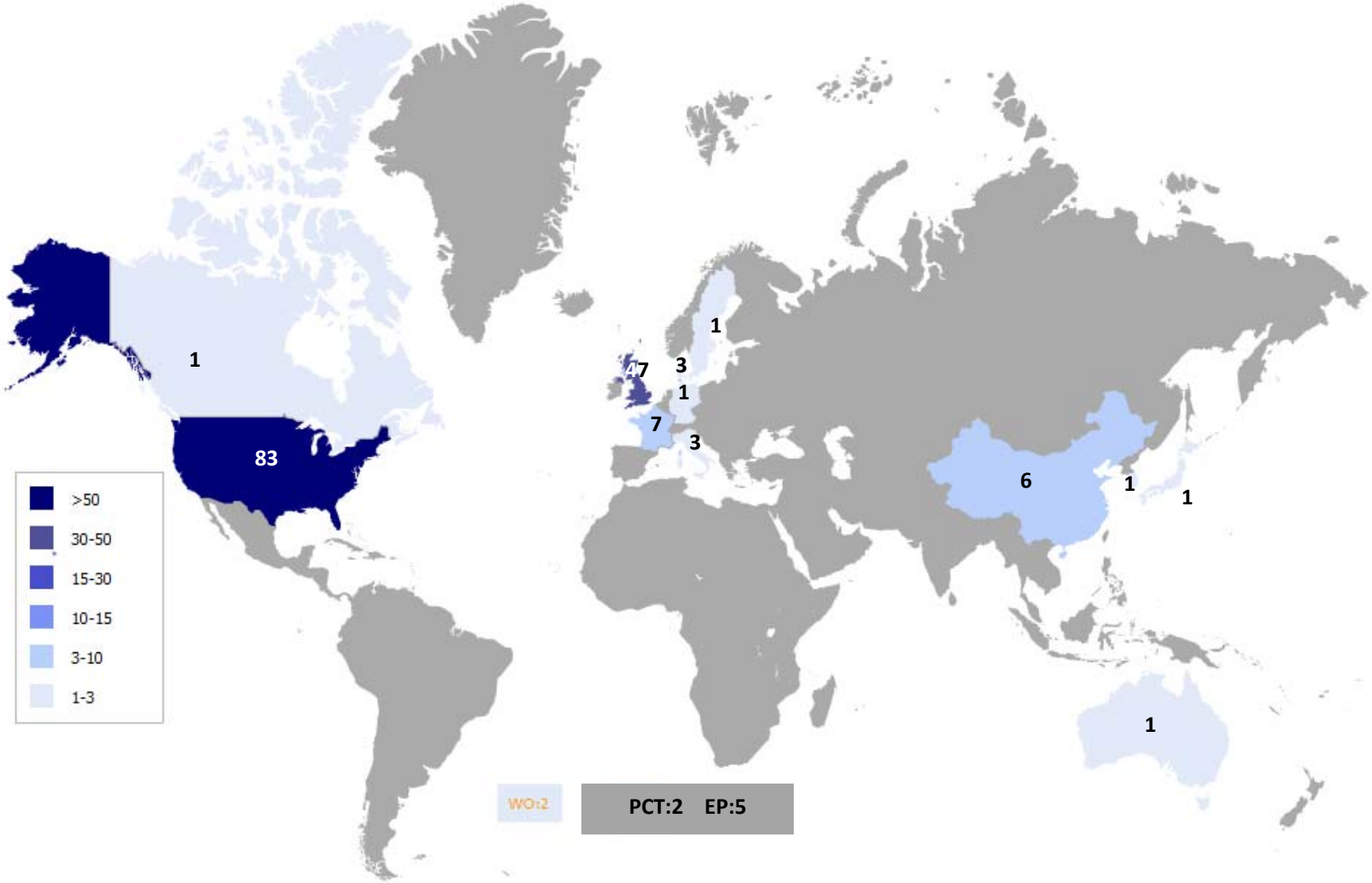


Figure 4 - Map of offices of first filing for patent and patent applications claiming active ingredients of human pneumococcal conjugate vaccines

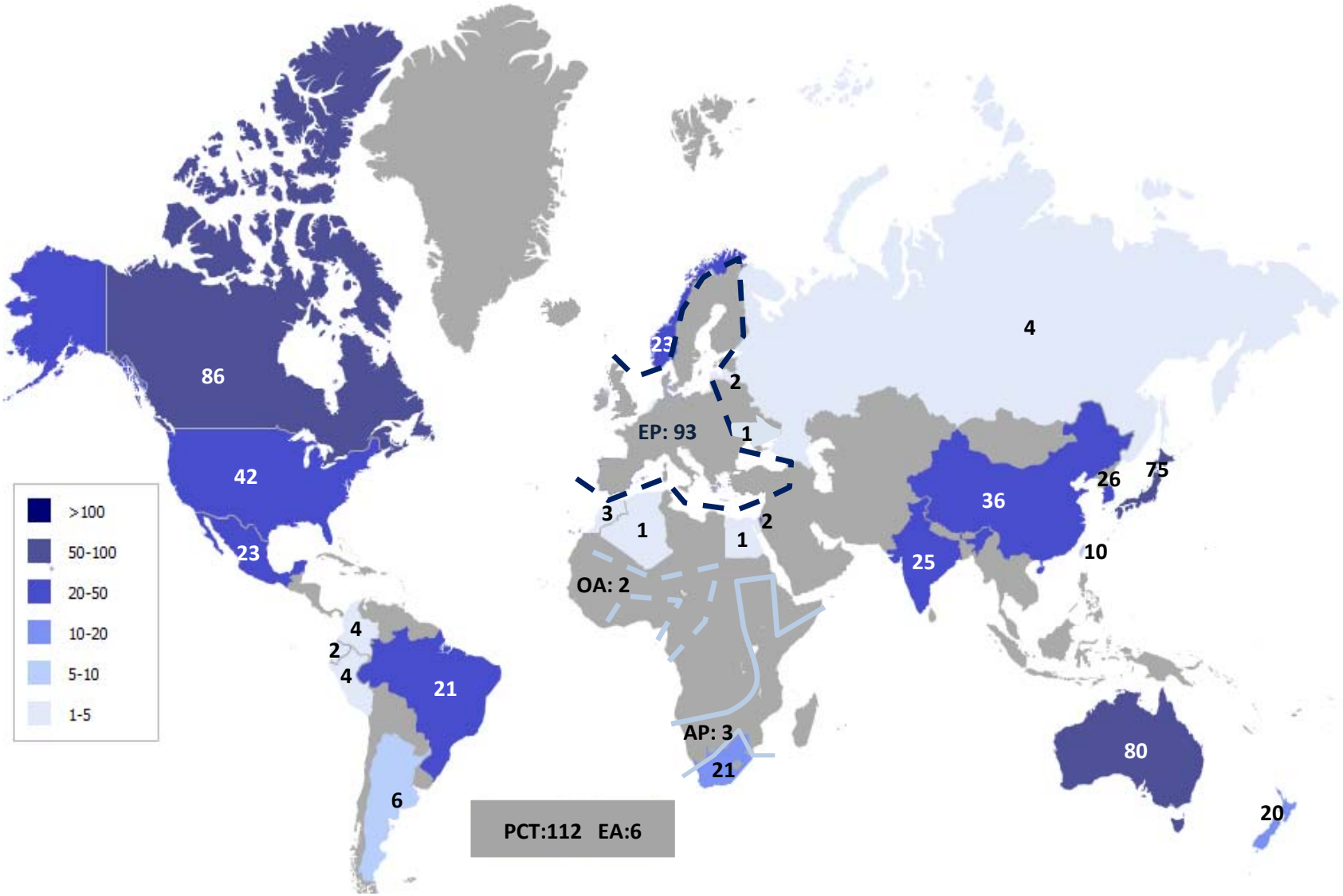


Figure 5 - Map of offices of second filings for patent and patent applications claiming active ingredients of human pneumococcal conjugate vaccines

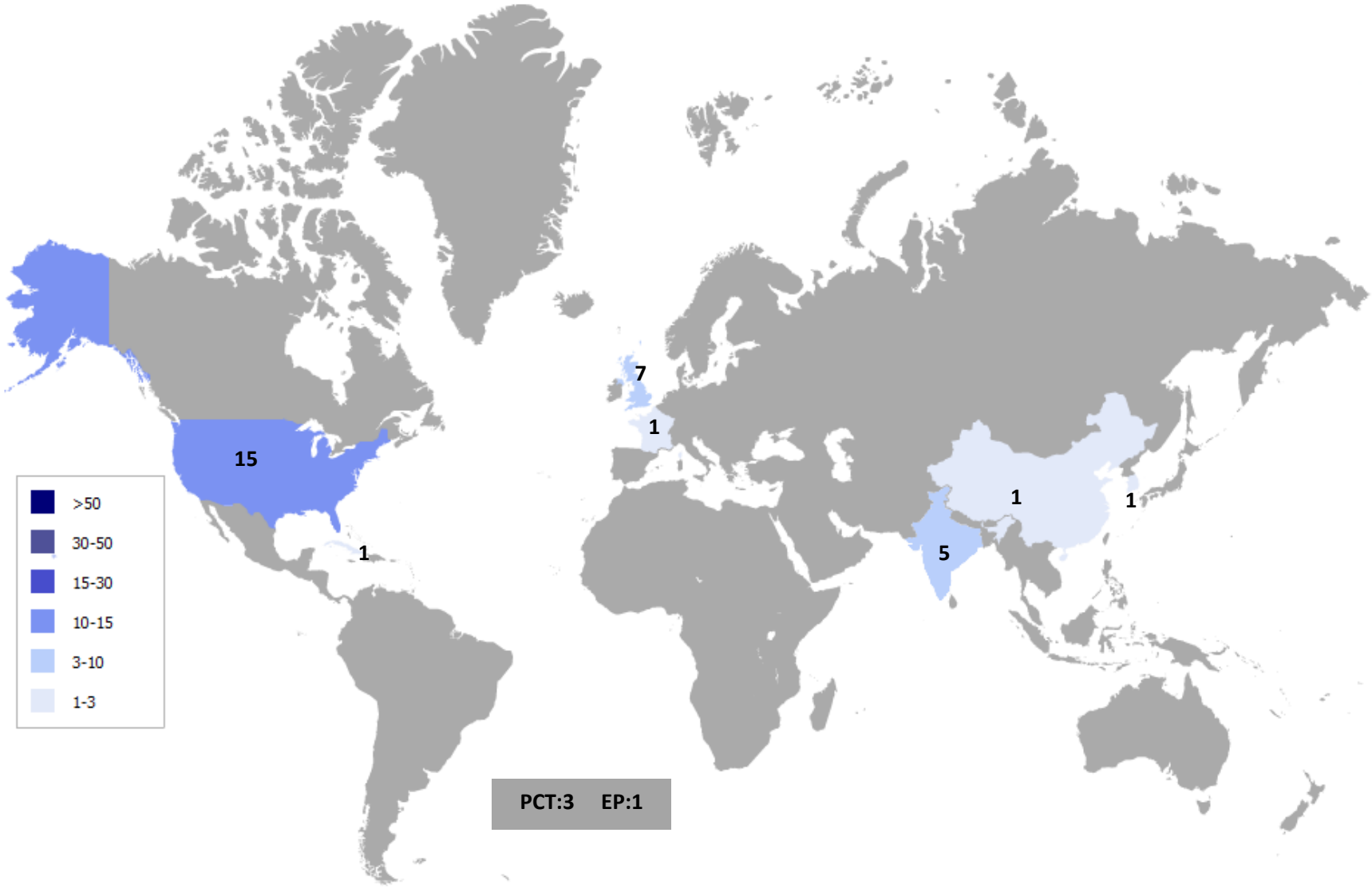


Figure 6 - Map of offices of first filing for patent and patent applications claiming active ingredients of human typhoid conjugate vaccines

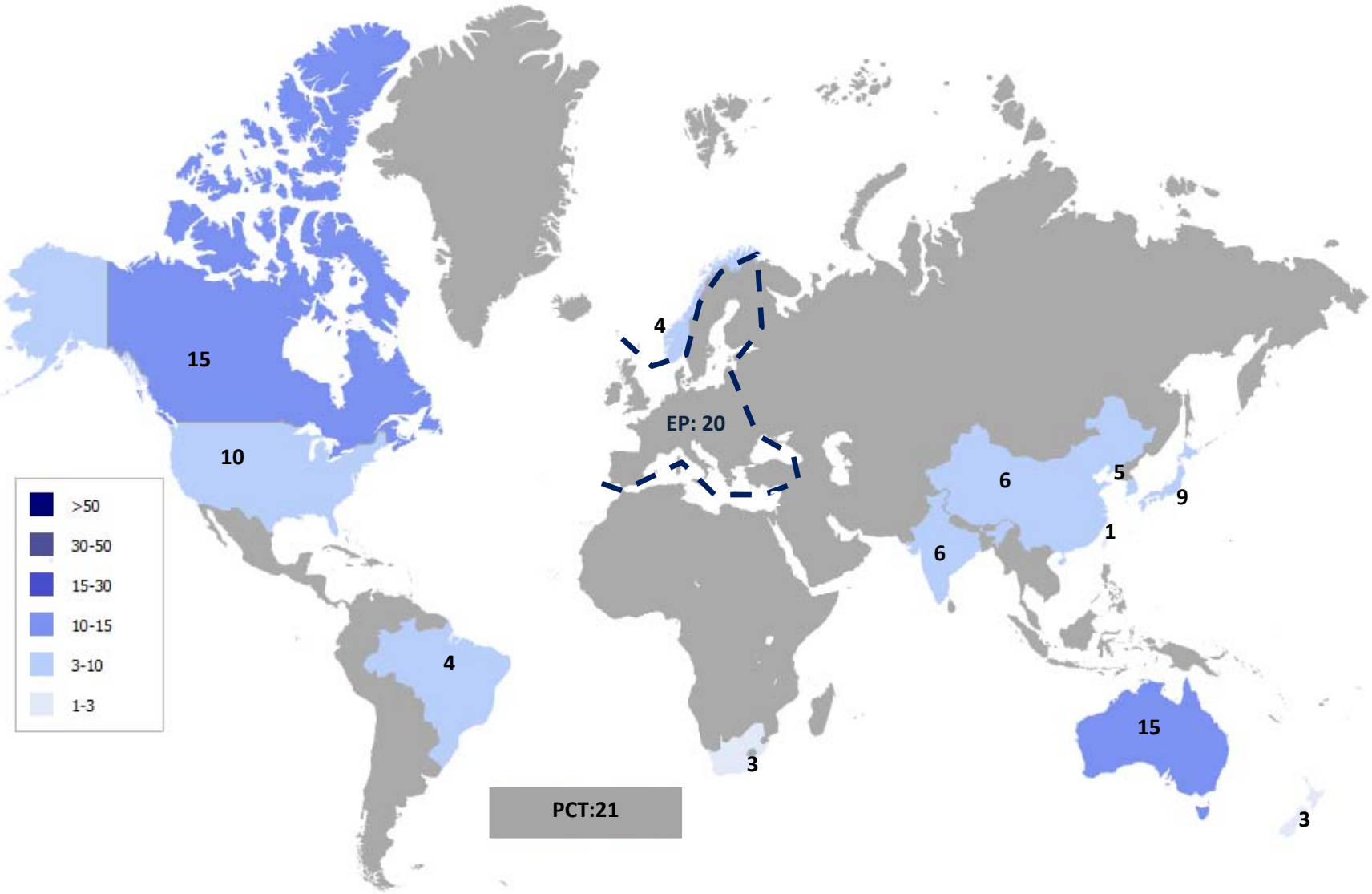


Figure 7 - Map of offices of second filings for patent and patent applications claiming active ingredients of human typhoid conjugate vaccines

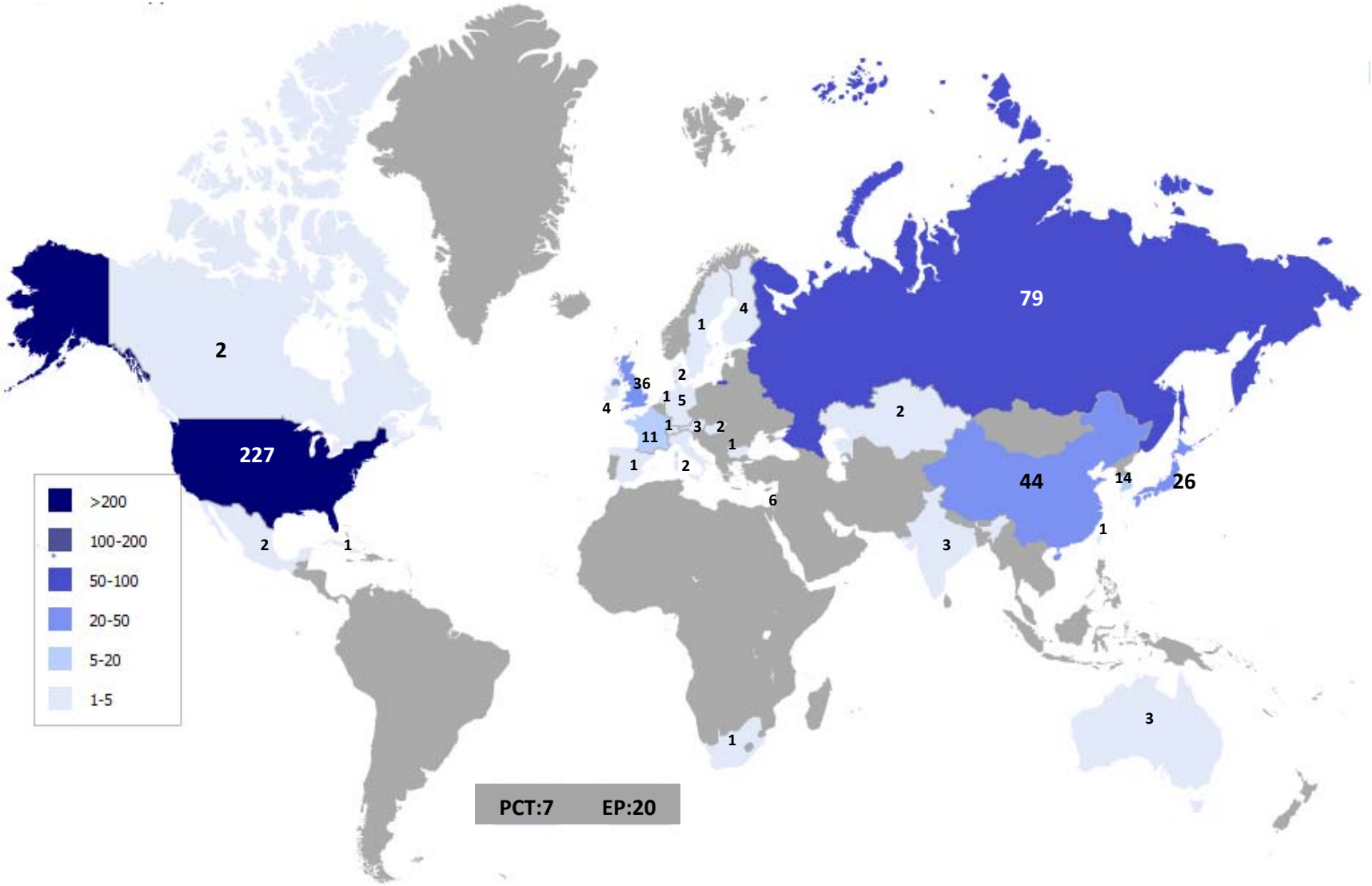


Figure 8 - Map of offices of first filing for patent and patent applications claiming active ingredients of human influenza vaccines

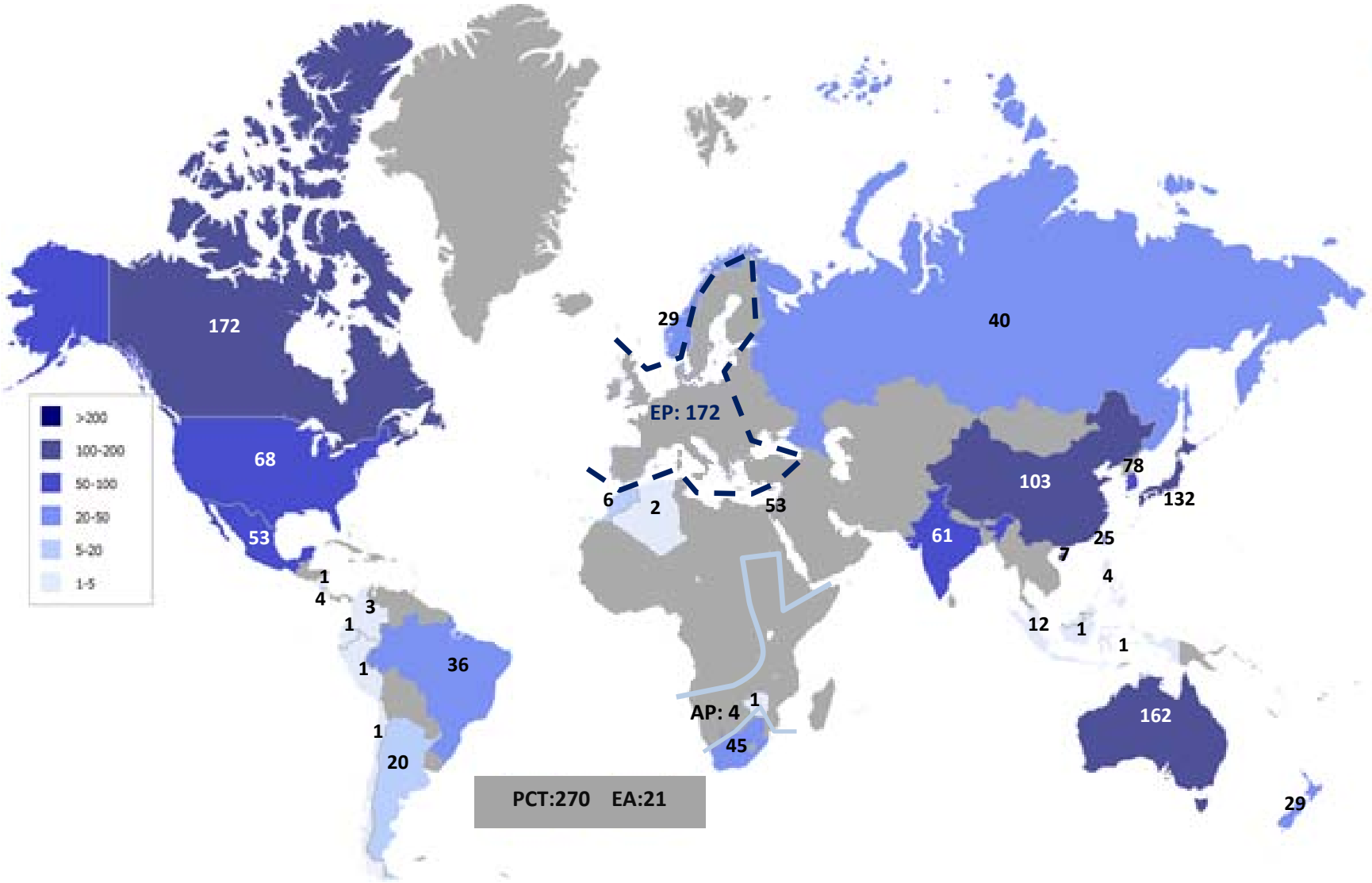


Figure 9 - Map of offices of second filings for patent and patent applications claiming active ingredients of human influenza vaccines

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