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VACCINE TECHNOLOGY IN HUMAN AND ANIMAL HEALTH:

MARKET ASSESSMENT AND INTELLECTUAL PROPERTY LANDSCAPE

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1. EXECUTIVE SUMMARY

IP Pragmatics is a technology and IP commercialisation consultancy, with broad expertise across the Life Sciences, Human Health, Animal Health, Agritech, and Food & Nutrition. The intention of this white paper is to provide an overview of the market developments across the vaccine technology commercial and patent landscapes comparing and contrasting the human and animal health markets.

This white paper aims to give an overview of the vaccine technology industry for both human and animal health through a combination of market research and patent landscaping. It looks at current and future applications of the vaccine technology in industry sectors in which IP Pragmatics have their expertise: Life Science Research, Animal Health, and Human Health. The paper also incorporates details of the key organisations, factors affecting the market, licensing and collaboration.

Vaccination has been one of the most effective tools to prevent infectious disease, which makes it key in global healthcare. Vaccination also plays a vital role in animal health in preventative health and disease control programmes in animals. Similar to human health, there is a drive for innovation through research and development in this field, especially with the risk of endemic outbreaks of zoonotic diseases which pose a risk to not only animal health but also human health. Recent outbreaks of COVID-19 and African Swine Fever (ASF) have highlighted how new diseases can impact when there are no effective vaccines.

In both human and animal health conventional vaccines developed by the attenuation or inactivation of the pathogen are widely adopted. Both industry sectors have also embraced new vaccine technologies including subunit vaccines, nucleic acid vaccines, viral vectored vaccines, toxoid vaccine and the use of virus-like particles. In animal health there is also the drive to develop DIVA vaccines that allow the Differentiation of Infected animals from Vaccinated Animals, which is crucial in disease control when used as part of an eradication policy.

The animal health vaccine market is considerably smaller than the human health market and more complex because of the large number of different species for which vaccines are administered. However, this has not stopped it adopting many of the newer vaccine technologies. Both sectors are dominated by a small number of global players, with the human vaccine market being more concentrated and dominated by three major players. Only one company, Merck & Co, has significant interests in both animal and human health vaccines.

The significant challenges to human and animal health from managing COVID-19 and ASF, respectively, in the absence of vaccines to either disease is driving research and development changes. This has spurred industry, academia and global funding agencies to seek new ways to collaborate to rapidly adapt existing vaccine technology platforms to address these new threats.

2. INTRODUCTION

According to the World Health Organisation (WHO) global vaccine action plan, there has been an increase in global vaccine coverage since 2010, and with population growth, approximately 4.9 million more infants are receiving three doses of diphtheria, tetanus toxoid and pertussis vaccine. In addition to this, government expenditure on national immunisation programmes has increased about one-third from 2010 to 2018 in both low and middle income countries, which in turn has encouraged further research and development in this field[1].

Vaccination is also key in animal health, playing a vital role in preventative health and disease control programmes in animals. Similar to human health, there is a drive for innovation through research and development in this field, especially with the risk of endemic outbreaks of zoonotic diseases, which pose a risk to not only animal health but also human health.

In both human and animal health conventional vaccines are developed by the attenuation or inactivation of the pathogen. To date this method of vaccine development has been very successful, resulting in the eradication of small pox, and severely reducing the disease burden of a number of other infectious diseases including polio, tetanus, diphtheria and measles. There are, however, disadvantages to these methods of vaccine development. With live attenuated vaccines there is the risk of reversion, which in the case of highly pathogenic and uncharacterized organisms is a significant problem. When it comes to inactivated vaccines, there is the issue of not inducing a sufficient protective immune response, or having undesired effects. This has been shown in Respiratory Syncytial Virus (RSV) where formalin-inactivation induced exacerbated disease upon wild type RSV infection, and in the case of Ebola where there is an insufficient immune response following inactivation. As a result of this there has been a drive to develop new more versatile approaches to vaccine development[2].

New vaccine technologies include subunit vaccines, nucleic acid vaccines, viral vectored vaccines, toxoid vaccine and the use of virus-like particles. In animal health there is also the drive to develop DIVA vaccines that allow the Differentiation of Infected animals from Vaccinated Animals, which is crucial in disease control when used as part of an eradication policy.

3. MARKET OVERVIEW

This section provides an overview of the market sizes and development of the market for vaccines in both human and animal health.

In 2017 the global vaccine market was valued at around $35.7 billion, with a predicted compound annual growth rate (CAGR) of 5.5% between 2017 and 2022; reaching nearly $46.6 billion by 2022. The human vaccine market makes up a larger proportion of this market valued at $29 billion in 2017, potentially reaching $38.1 billion in 2022 with a CAGR of 5.6%. Although smaller, the animal vaccine market was valued at $6.7 billion in 2017, growing to potentially $8.5 billion by 2022 with a 4.8% CAGR[3].

Segment	2016	2017	2022	CAGR%
Human vaccines	27,600	28,970	38,050	5.6
Animal Vaccines	6,420	6,730	8,500	4.8
Total	34,020	35,700	46,550	5.5

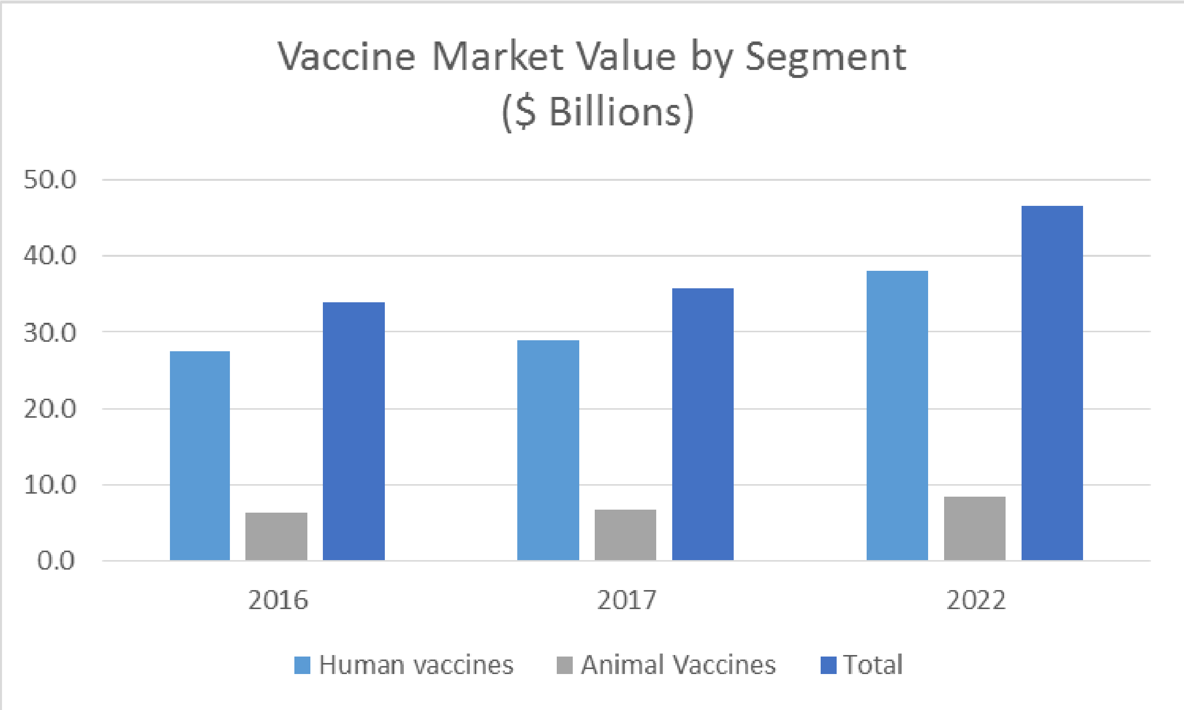

Figure 1. Human and Animal vaccine market segments value (US $ Billions).

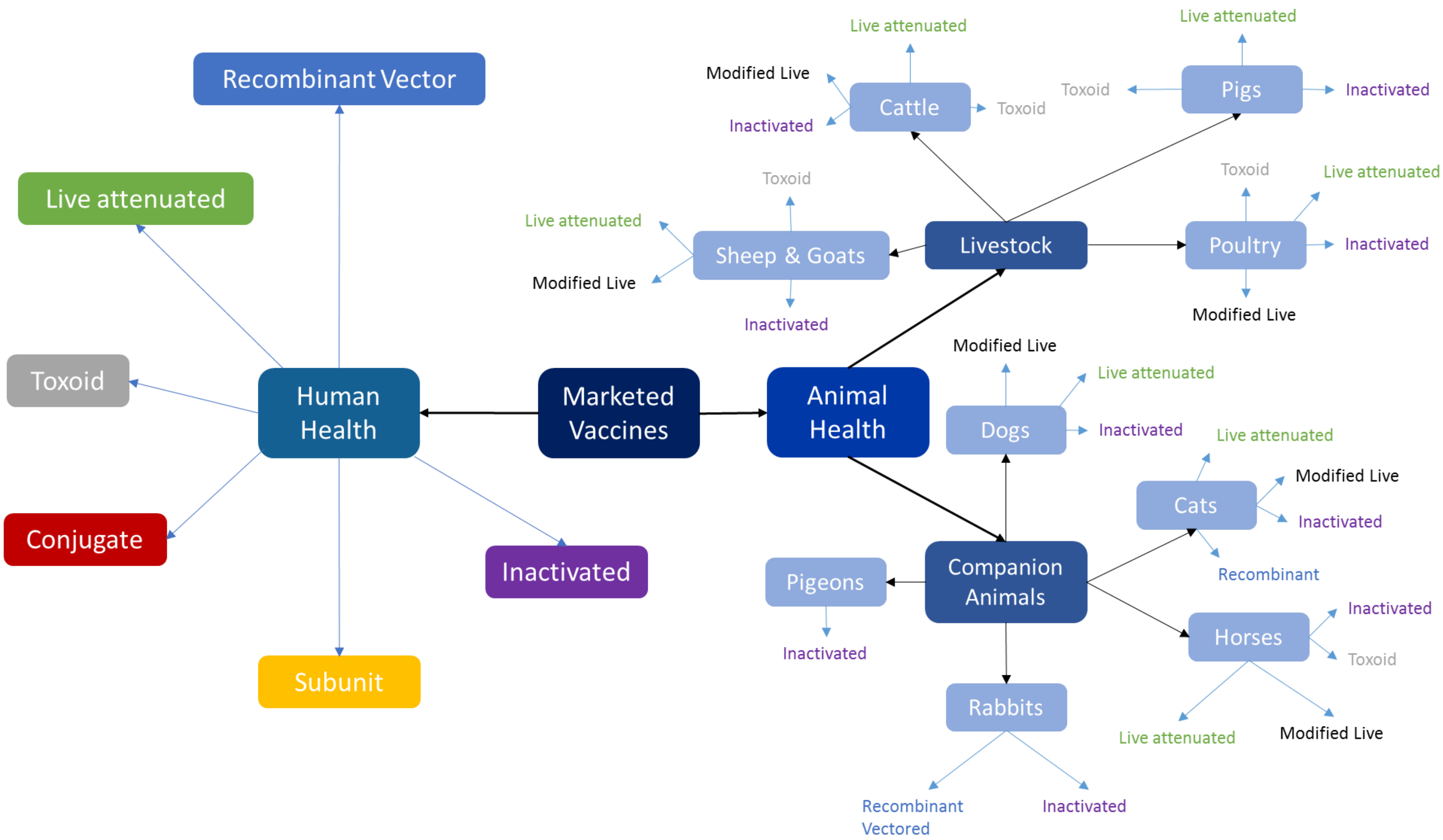

Figure 2. Overview of vaccines type in different market areas. Split into Human and Animal Health. Animal Health is split into companion animals and livestock.

3.1 HUMAN VACCINE MARKET

The total human vaccine market was valued at $28.9 billion in 2017 and is expected to grow to a value of about $38 billion by 2022, with a CAGR of 5.6%. When the market is split by vaccine type, conjugate vaccines have the largest market share with a CAGR of 8.0% and an expected value of $11.5 billion by 2022. Other vaccine types with large market growth include recombinant DNA vaccines, inactivated vaccines and subunit vaccines.

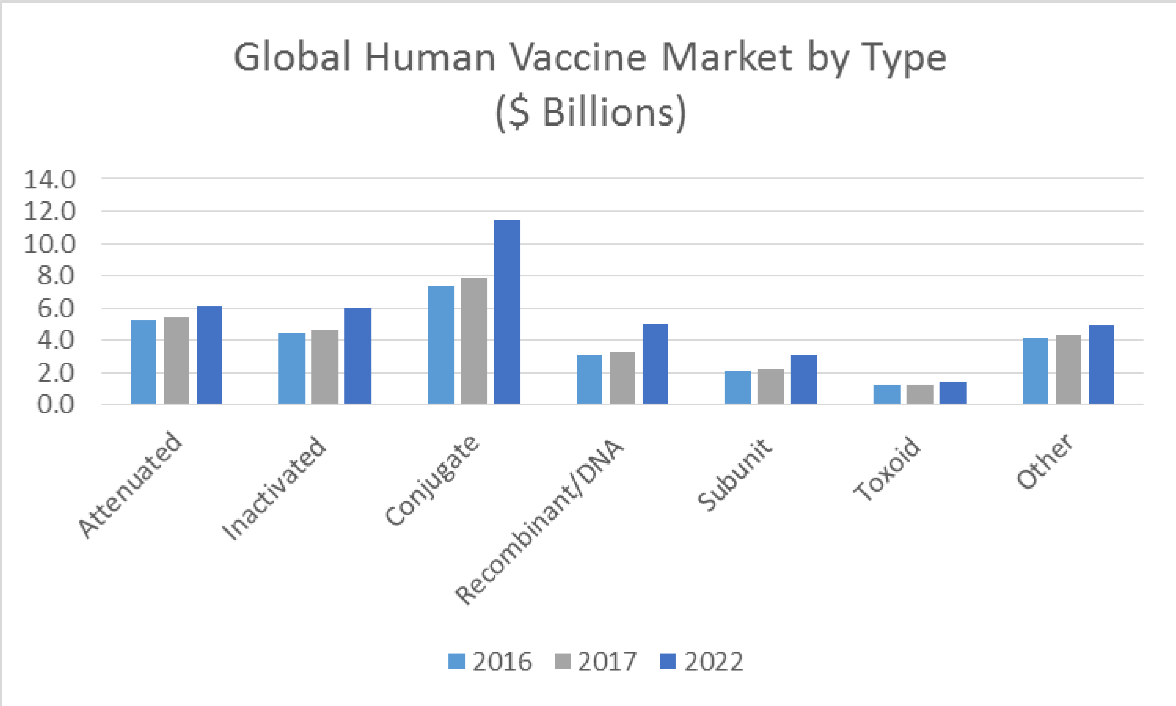

Figure 3. Overview of global human vaccine market split by vaccine type (US $ Billion).

Although the market for attenuated and inactivated vaccines is expected to total roughly $6 billion each by 2022, the CAGR is much lower than the other novel vaccine technologies. Attenuated vaccines CAGR at 2.3%, whereas conjugate vaccines and recombinant/DNA vaccines has a CAGR of 8.0% and 8.9%, respectively, reflecting the greater opportunity modern research methods present to develop these types of vaccine.

Type	2017 ($ Millions)	2022 ($ Millions)	CAGR % 2017-2022
Attenuated vaccines	5446	6088	2.3
Inactivated vaccines	4635	6012	5.3
Conjugate vaccines	7836	11490	8.0
Recombinant/DNA vaccines	3259	4985	8.9
Subunit vaccines	2202	3082	7.0
Toxoid vaccines	1246	1446	3.0
Other vaccines	4346	4947	2.6
TOTAL	28970	38050	5.6

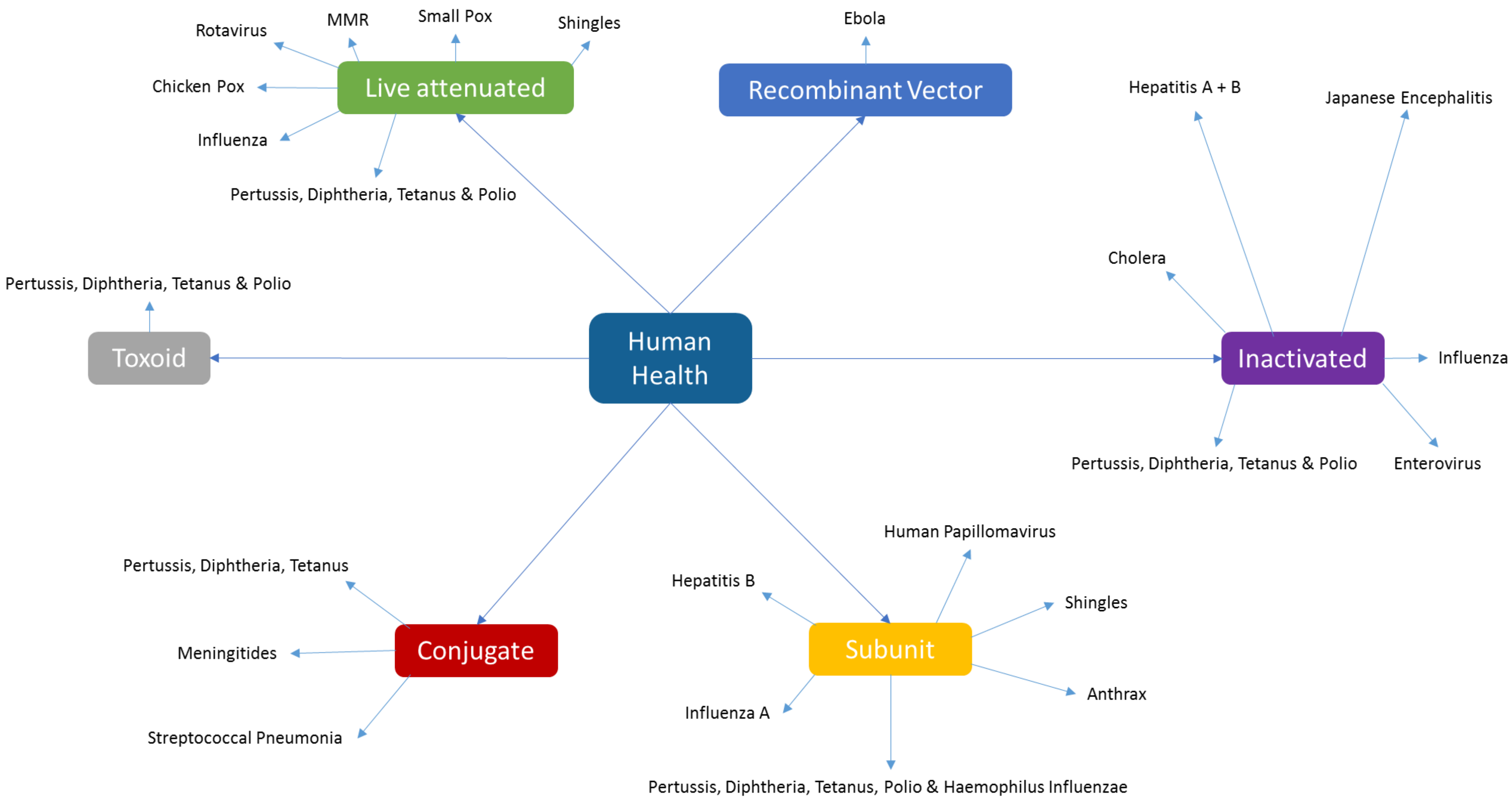

Figure 4. Examples of human vaccines currently used split by vaccine type.

The human vaccine market can be split into three age groups: paediatric, adolescents & adults, and geriatrics. The largest segment is paediatric vaccines with an estimated value of $24.8 billion by 2022. This market size is a result of global paediatric vaccination programmes. According to the WHO financing from domestic budgets allocated to immunisation programmes has risen over the past 10 years. In addition, there has been an increase in international resources dedicated to immunisation[1].

Age Group	2017 ($ Millions)	2022 ($ Millions)	CAGR % 2017-2022
Paediatric	19097	24790	5.4
Adolescents and adults	8726	11815	6.2
Geriatric	1147	1445	4.7
TOTAL	28970	38050	5.6

The main paediatric vaccines include DTwP (diphtheria, tetanus and whole-cell pertussis), measles and oral polio vaccines. Enhanced paediatric vaccines include; DTaP (diphtheria, tetanus and acellular pertussis), inactivated poliovirus and vaccines for *Hemophilus influenza* type B, hepatitis A and B and MMR (measles, mumps and rubella). In addition to this there are increasing numbers of multivalent paediatric vaccines as detailed below:[4]

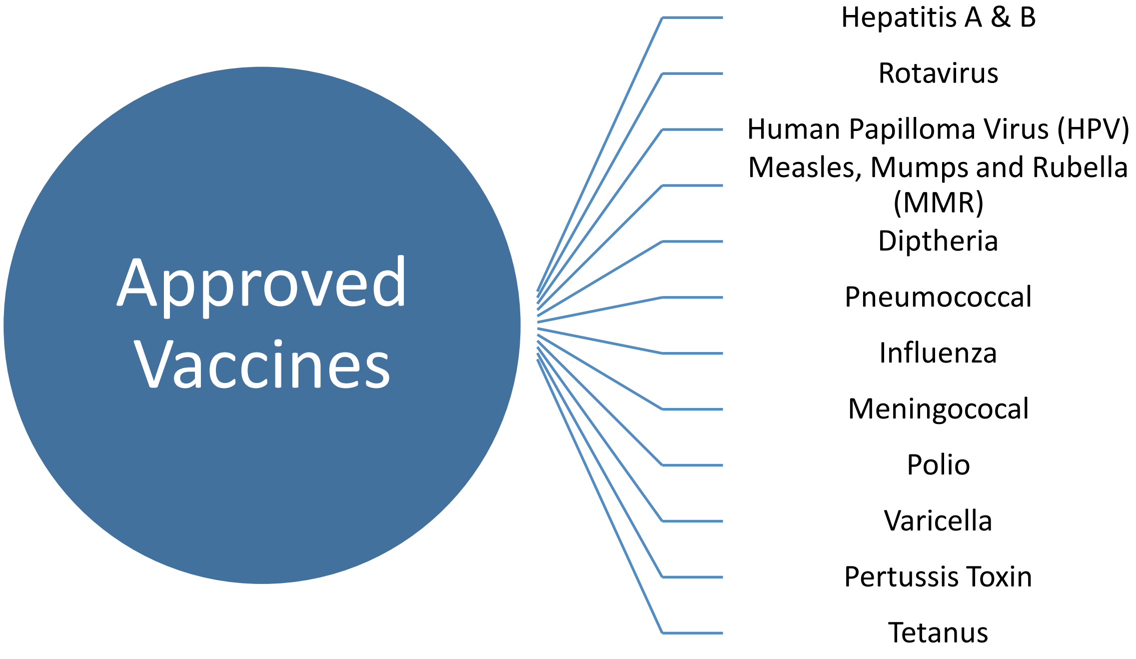

Figure 5. Approved multivalent paediatric vaccines.

The WHO outlines the recommended routine vaccinations for all age groups including children, adolescents and adults. These recommendations are outlines below[5].

Vaccine	Age Group	Additional Information	Vaccination Programmes
BCG	Children		ALL
Hepatitis B	Children/ Adults (if not previously immunised)		ALL
Polio	Children		ALL
DTP containing vaccine	Children, boost in adolescents		ALL
Haemophilus Influenzae type B	Children	Not reccomended for children >5 years old	ALL
Pneumococcal (Conjugate)	Children		ALL
Rotavirus	Children	Not reccomended if >24 months old	ALL
Measle	Children	Combination Vaccine	ALL
Rubella	Children / women of child-bearing age if not previously vaccinated		ALL
HPV	Adolescent female	Target 9-14 year old girls	ALL
Japanese Encephalitis	Children		CERTAIN REGIONS
Yellow Fever	Children		CERTAIN REGIONS
Tick-Borne Encephalitis	All		CERTAIN REGIONS
Typhoid	All		HIGH-RISK POPULATIONS
Cholera	All		HIGH-RISK POPULATIONS
Meningococcal	A – Children C/Quadrivalent – All		HIGH-RISK POPULATIONS
Hepatitis A	All		HIGH-RISK POPULATIONS
Rabies	All		HIGH-RISK POPULATIONS
Dengue	All		HIGH-RISK POPULATIONS
Mumps	Children	Combination vaccines	OTHER
Seasonal Influenza	All	Priority for higher risk groups	OTHER
Varicella	All		OTHER

The global focus on peadactric vaccination programmes is a key reason for the increasing support for vaccine development and is one of the reasons for the overall market growth.

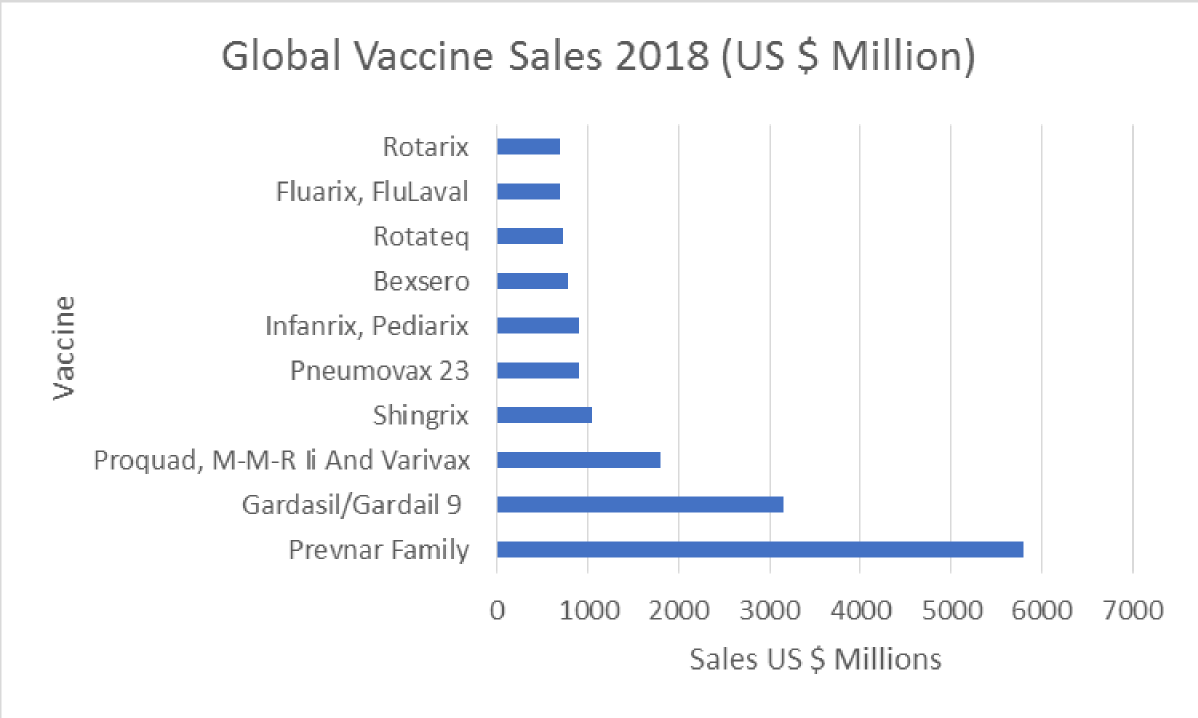

Figure 6. Top 10 vaccines based on global vaccine sales in 2018 (US $ Million).

The top selling vaccines are all manufactured by 3 key players, Pfizer Inc, Merck & Co Inc and GlaxoSmithKline Plc. When you split these vaccine sales by target age group, eight of these ten vaccines are targetted to the paediatric market, and these are all vaccines recommended in paediatric vaccination schemes globally[6].

Vaccine	Company	Target	Age Group
Prevnar Family	Pfizer Inc	Pneumococcal	Paediatric/Geriatric
Gardasil/Gardail 9	Merck & Co Inc	HPV	Adolescents
Proquad, M-M-R Ii And Varivax	Merck & Co Inc	MMR	Paediatric
Shingrix	GlaxoSmithKline Plc	Shingles	Adult/Geriatric
Pneumovax 23	Merck & Co Inc	Pneumococcal	Paediatric/Geriatric
Infanrix, Pediarix	GlaxoSmithKline Plc	DTaP and Hep B	Paediatric
Bexsero	GlaxoSmithKline Plc	Meningococcal B	Paediatric
Rotateq	Merck & Co Inc	Rotavirus	Paediatric
Fluarix, FluLaval	GlaxoSmithKline Plc	Influenza	Paediatric/Adult
Rotarix	GlaxoSmithKline Plc	Rotavirus	Paediatric

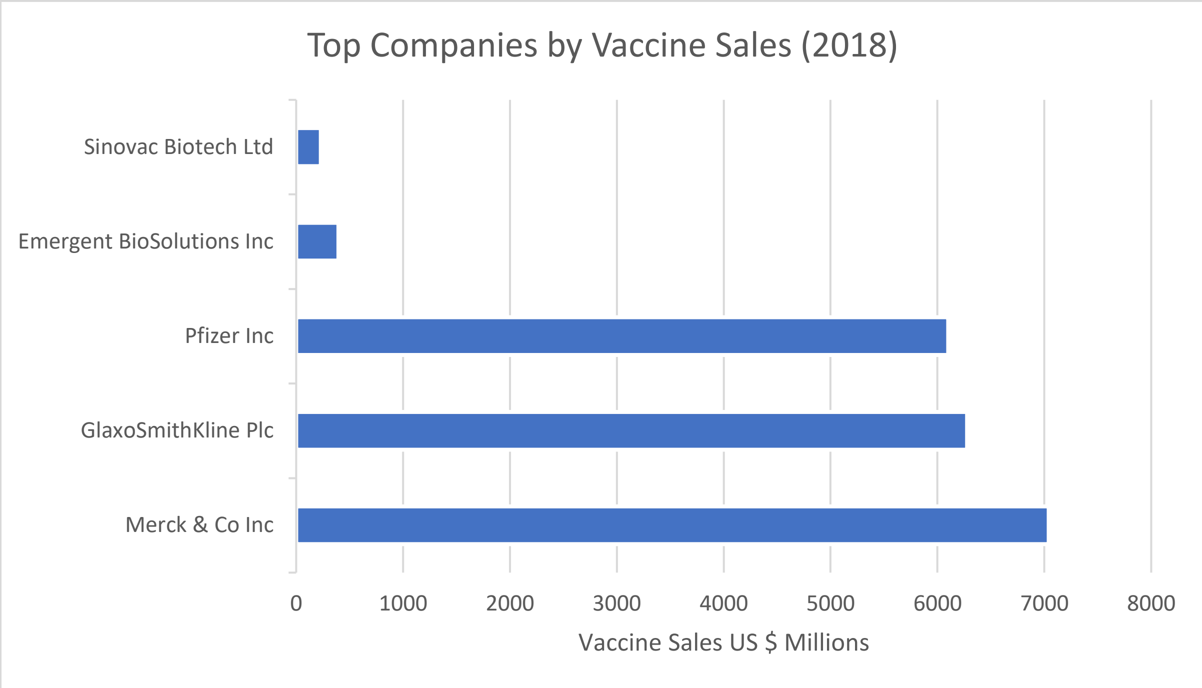

Figure 7. Top companies based on vaccine sales in 2018 (US $ Millions).

Vaccine Technology Application in Human Health

When looking at vaccine technology used in human health, the different areas of development in vaccine technology can be split into the categories summarised below.

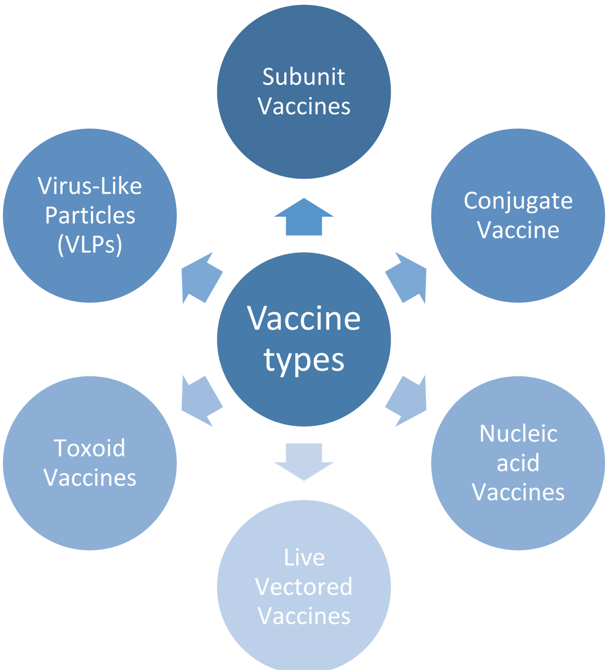

Figure 8. Vaccine development areas in Human Health, split by vaccine type.

Subunit vaccines

Subunit vaccines are based on small pathogen-derived components that tend to lack the native 'danger' signal required to stimulate the immune response. Therefore, subunit vaccines need to be able to provide the equivalent signal to stimulate an effective immune response. Most subunit vaccines stimulate this response by mimicking the size of the native pathogen, or through the use of immunostimulant vaccine adjuvants[7]. There are several subunit vaccines currently available and commonly used in human health, which are outlined below.

Vaccine	Company	Target	Sales (2018) US $ Million
Gardasil	Merck & Co Inc	HPV	3151
Shingrix	GlaxoSmithKline Plc	Shingles	1045
BioThrax	Emergent BioSolutions Inc	Anthrax	278
Cervarix	GlaxoSmithKline Plc	HPV	184
Hepilsav-B	Dynavax Technologies Corp	Hep B	7

Conjugate Vaccines

Conjugate vaccines are similar to subunit vaccines and usually contain more than one component. They are often used to combine a weak antigen with a strong antigen as a carrier to illicit a more potent immune response. Conjugate vaccines have been used for *Streptococcus pneumoniae*[8]. Current conjugate vaccine examples in human health are outlined below.

Vaccine	Company	Target	Sales (2018) US $ Million
Prevnar	Pfizer Inc	Pneumococcal	5802
Pneumovax 23	Merck & Co Inc	Pneumococcal	908
Infanrix, Pediarix	GlaxoSmithKline Plc	Diphtheria/Tetanus	907
Bexsero	GlaxoSmithKline Plc	Meningococcal	779
Rotarix	GlaxoSmithKline Plc	Rotavirus	695

Viral Vector Vaccines

Live vectored vaccines offer several distinct advantages over the conventional inactivated subunit vaccine. By replicating in the host, they more accurately mimic natural infection and they are often easy to administer, stimulating a more comprehensive immune response and therefore result in long-lived immunity. Due to these advantages, there is significant research and development into vaccine delivery using live vectors.

Most live vectors used are viral vectors, which are typically based on large DNA viruses. The most common viral vector used experimentally is the orthopoxvirus vaccinia, which was successfully used to vaccinate against small pox, consequently leading to eradication of the disease. Other common viral vectors used include Modified Vaccinia Ankara (MVA), Chimpanzee Adenovirus Oxford University (ChAdOx) and Pox virus. In human health, current vaccines include an adenovirus vectored Ebola vaccine, as well as Pertussis, Diphtheria, and Tetanus vaccines.

Vaccine	Company	Target	Sales (2018) US $ Million
Ad5-EBOV vaccine	CanSino Biologics Inc	Ebola	unavailable

Toxoid Vaccines

Some bacteria release toxins, which are recognised by the immune system. Toxoid vaccines use toxins that have been rendered harmless to elicit an immune response. Currently combination vaccines for Pertussis, Tetanus, and Diphtheria represent the available toxoid vaccines in human health, the details of which are outlined below.

Vaccine	Company	Target	Sales (2018) US $ Million
Infanrix, Pediarix	GlaxoSmithKline Plc	Pertussis/Diphtheria/Tetanus	907
Boostrix	GlaxoSmithKline Plc	Pertussis/Diphtheria/Tetanus	689
Tetrabik	Mitsubishi Tanabe Pharma Corp	Pertussis/Diphtheria/Tetanus	76

Nucleic Acid Vaccines (DNA)

Nucleic Acid Vaccines involve the direct immunisation with DNA or RNA encoding the antigen(s) of interest. The main advantage is the simplicity and purity with which they can be produced[9]. Nucleic acid vaccines can be manufactured rapidly, by custom gene synthesis, with vaccination resulting in *in situ* antigen expression in its native configuration.

Virus-like Particles (VLPs)

Virus-like particle (VLP) vaccines are multi protein structures that mimic the organisation and confirmation of the native virus, while lacking the viral genome. This technology has the potential to yield safer and cheaper vaccine candidates. VLP vaccines have the advantage of being able to be worked on at a lower containment level than the live pathogen itself, with the potential to retain key immunogenic antigens that may be altered by inactivation, and which could be more potent immunogens compared to subunits[10,11]. Currently HPV and Hepatitis B vaccines contain VLPs.

Vaccine	Company	Target	Sales (2018) US $ Million
Gardasil	Merck & Co Inc	HPV	3151
Recombivax HB®	Merck & Co Inc	HBV	N/A

Pipeline Analysis

Pipeline analysis performed on GlobalData highlighted that over 600 pipeline vaccines in development are subunit vaccines out of around 1,500, and almost 300 vaccines are recombinant vector vaccines, showing the shift in vaccine development from the traditional inactivated and live attenuated vaccines to novel vaccine technologies. This is outlined in the graph below.

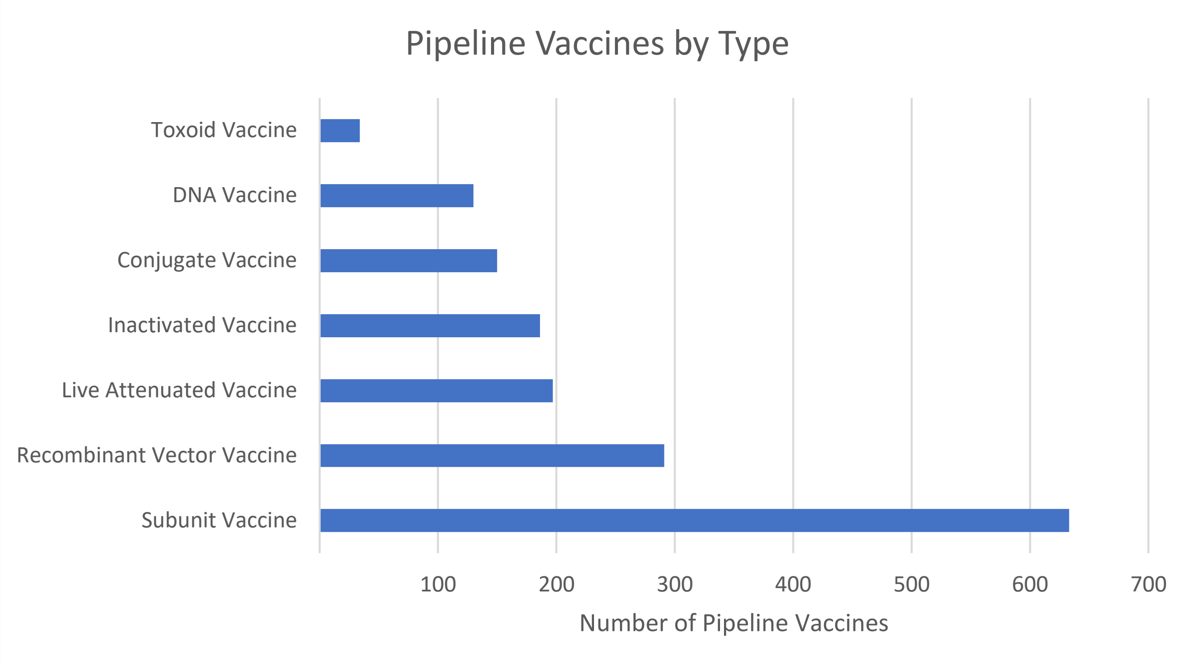

Figure 9. Current distribution of pipeline vaccines in development by vaccine type.

3.2 ANIMAL VACCINE MARKET

Turning to the animal vaccine market in more detail, the largest segment for animal vaccine products is food-producing (livestock) animal vaccines[3]. In 2017 the animal vaccine market was estimated to be worth $6.7 billion, with production animals generating the largest revenue, accounting for 64% of the market. Sales of animal vaccines are anticipated to grow at a compounded rate of 4.8% from 2017 through 2022, reaching $8.5 billion. Growth is a result of increased vaccine use in developing regions of the world.

Type	2017 ($ Millions)	2022 ($ Millions)	CAGR % 2017-2022
Food-producing animal vaccines (porcine, bovine, poultry, ovine, fish vaccines)	4307	5440	4.8
Companion animal vaccines (canine, feline, and equine vaccines)	2258	2873	4.9
Other animal vaccines (rabbit, pigeon vaccines etc)	165	187	2.5
Total	6730	8,500	4.8

When analysing the global animal vaccine market by region the United States held 31% of the market share in 2016 with a value of $1.9 billion and a CAGR of 3.1% from 2016 to 2021. However the fastest predicted growth is in Asia Pacific with a CAGR of 5.1 % over this perdiod and a predicted value of $1.69 billion by 2021. Europe accounted for approximately 24% of the market share in 2016 with an estimated value of $0.9 billion

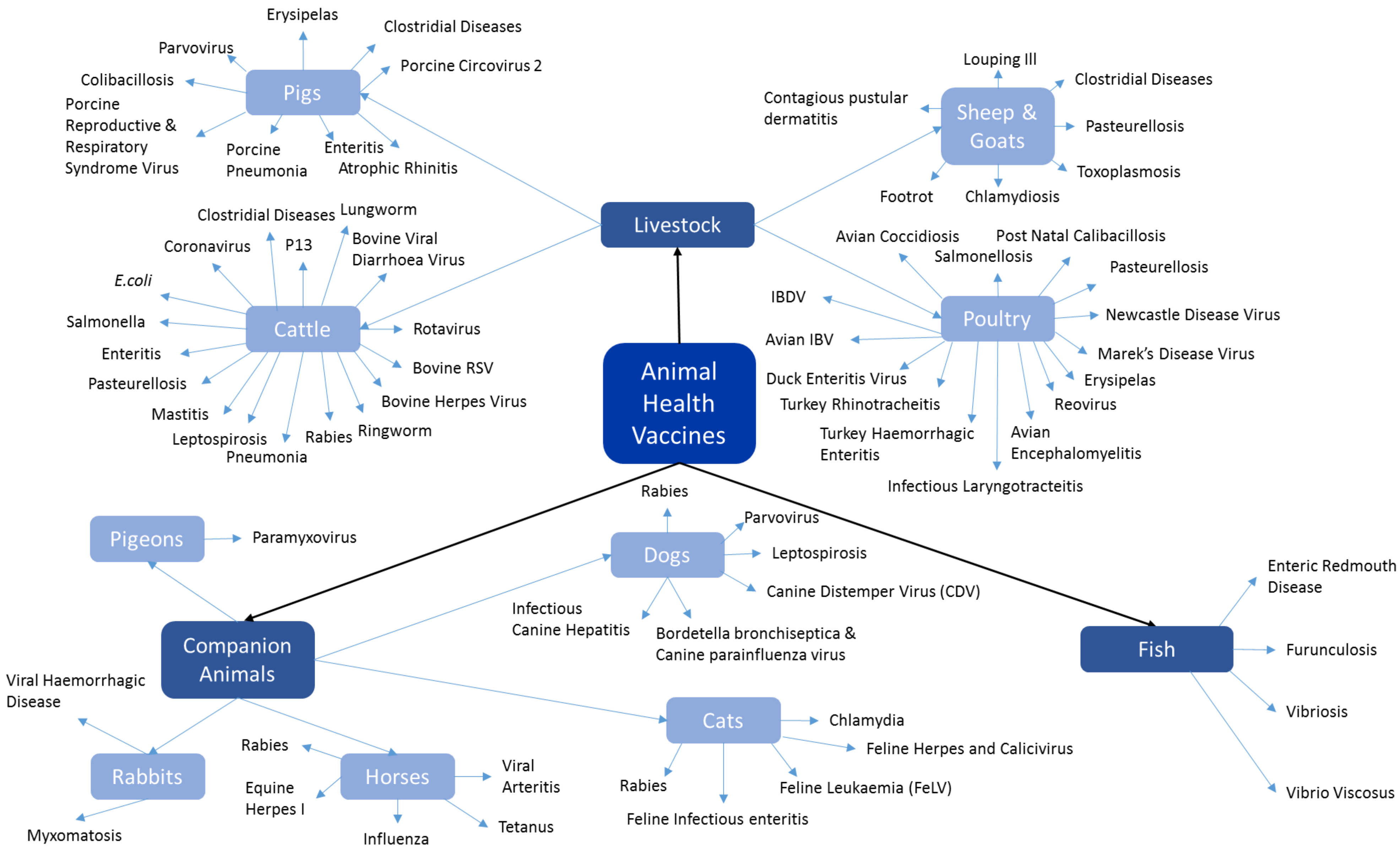

Figure 10. Current recommendations for animal health vaccines split by species according to NOAH.

Vaccine Technology Application in Animal Health

Animal health can be seperated into companion animals, food producing animals, and other animals (including fish). As with human health, traditional vaccines in animal health are largely based on inactivated or live attenuated viruses, and can be ineffective and have the same disadvantages as they do in human health. Current vaccines from the key players in the animal health vaccine market are outlined in **Appendix 1**, split into companion animal and livestock vaccines.

In animal health vaccination is important for a number of reasons. As well as protecting the individual animals, it is also important for herd immunity. Herd immunity is the protection offered to a wider community of animals, pets or farm animals, when a high enough proportion of animals are vaccinated the prevelence of disease is reduced. In addition to this, the vaccination of animals against zoonotic diseases is critical to protecting human health. Vaccinating susceptible animals that may be a reservoir of infectious diseases can prevent the spread of disease to the human population[12].

Similar to human health, innovation in vaccine technology is driving research and development for new animal health vaccines. These novel vaccine technologies have been summarised in the figure below:

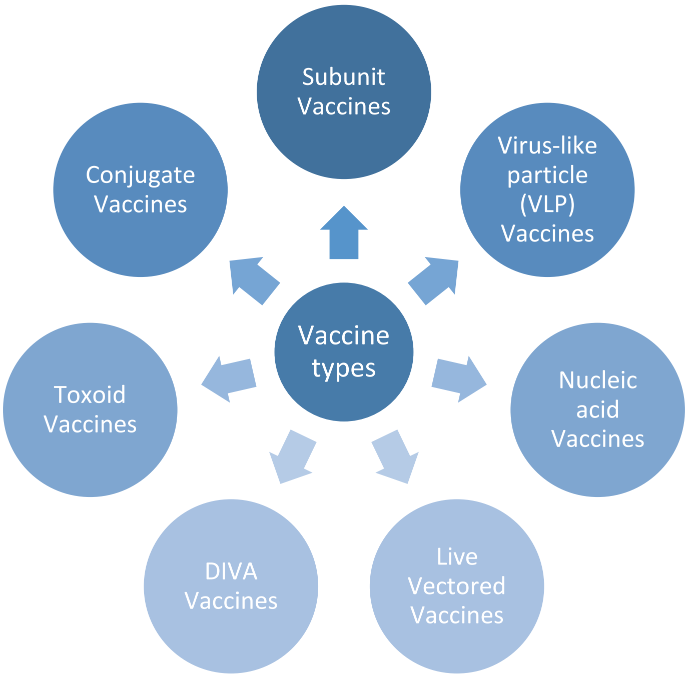

Figure 11. Vaccine development areas in animal health, split by vaccine type.

Subunit Vaccines

Many subunit vaccines have been developed in animal health; two leading examples are outlined below.

Vaccine	Manufacture	Species	Pathogen
Porcilis PCV®	Merck	Pigs	Porcine Circovirus[13]
Porcilis	Merck	Pigs	*Actinobacillus pleuropneumoniae*

Virus-like particle (VLP) Vaccines

VLPs have been generated as animal virus immunogens against a broad spectrum of viruses, some of which are outlined below:

- Porcine Circovirus
- Newcastle disease virus
- Avian Influenza virus
- Rift valley fever virus
- Bluetongue virus
- African horse sickness virus[14]

Nucleic Acid Vaccines

In animal health there are currently a number of nucleic acid vaccines on the market. The current DNA vaccines include some of those outlined below.

Vaccine	Manufacture	Species	Pathogen
Equine West-Nile Innovator®	Zoetis	Horses	Equine West Nile Virus
Salmonids Apex-IHN®	Novartis	Fish	Infectious Haematopoietic Necrosis Virus.
Canine Oncept®	Merial	Dogs	Canine Melanoma

There have been new advancements in nucleic acid vaccines, one of which is replicon vaccines. Replicon vaccines are self-amplifying viral RNA sequences, and in addition to encoding the antigen of interest, they contain all the elements required for RNA replication. Therefore, vaccination with replicons results in viral RNA replication with the host cell, endogenously expressing the protein of interest at high levels. There are a number of potential replicons vectors, the most common of which it an alphavirus-based vector, which is a single stranded, positive sense, enveloped RNA virus. Others include other positive-stranded RNA viruses such as members of the *Flaviviridae, Picornaviridae*, and *Arteriviridae*[11].

GlaxoSmithKline plc has developed self-amplifying mRNA (SAM) technology, which pre-clinical research has shown to elicit potent and robust protective immune responses against various pathogens. Phase I clinical trials are expected in 2020 for the use of SAM technology in Rabies, with the hope to produce many different vaccines against a variety of pathogens with the same process[15].

Live Vectored Vaccines

There are a number of live vectored vaccines currently in development in animal health, examples of which are outlined below.

Disease	Antigen	Use for	Tested in	Vector
Middle East respiratory syndrome (MERs)[16]	MERS-CoV spike glycoprotein	Camels, Human	Mice, Humans, Camel	MVA or ChAdOx[17]
African Swine Fever Virus (ASFV)[18]	Multiple ASFV proteins	Pigs	Pigs	MVA
Avian Influenza[19]	HA	Birds	Mice	Pox

Disease	Antigen	Use for	Tested in	Vector
Equine Influenza[20]	HA or NP	Horses	Horses	MVA or Pox
Rabies[21]	Viral glycoprotein G			Pox
Feline Leukaemia Virus (FeLV)[22]	Env and gag	Cats	Cats	Pox

In addition to viral vectors there are also bacterial and protozoal vectors in use. Bacterial vectors have developed from studies into the use of Bacillus Calmette-Guerin, as a vector in the immunisation against tuberculosis (TB) in humans. The advantage of this vector is that it is inexpensive to produce and relatively heat stable. Protozoal vectors are based on a live protozoan parasite genetically modified to deliver antigens in poultry, an example of the use of this vector includes coccidiosis infection[23].

DIVA Vaccines

Unlike human vaccine development, in veterinary vaccine development there needs to be a consideration into differentiating infected from vaccinated animals (DIVA). These new vaccine technologies can be used as a valuable tool in disease control and eradication programs. Examples of veterinary DIVA vaccines include: Pseudorabies, classical swine fever virus, and bovine rhinotracheitis[23]. There are also many DIVA vaccines currently in development, including vaccines targeting bovine viral diarrhoea virus.

Toxoid Vaccines

Toxoid vaccine are also used in animal health, an example of a which is the *Crotalus atrox* toxoid (Western Diamond rattlesnake) vaccine used in the US[24].

Conjugate Vaccines

Conjugate vaccines are also in development for use in animal health. These include vaccines against *Streptococcus suis* and meningococcal in cattle.

4. KEY PLAYERS

For the purpose of this white paper the top 10 companies have been identified in human health based on each company's sales reported on GlobalData. For animal health, the key players were determined by the major companies producing current licensed animal health vaccines. Merck & Co is the only company that appears as a key player in both sectors, including in both the major segments of the animal health market. Other animal health companies were previously part of pharmaceutical companies before being spun out – for example Zoetis from Pfizer.

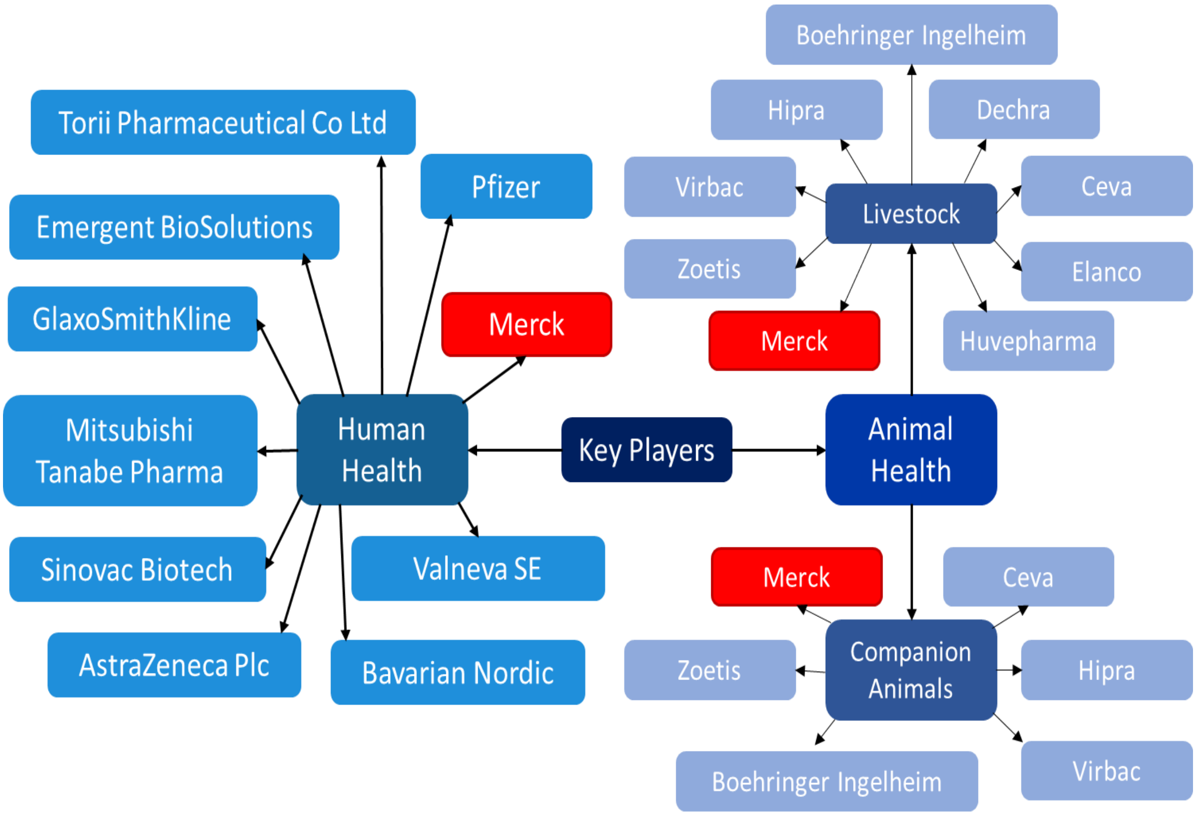

Figure 12. Key players in both human and animal health vaccines.

4.1 HUMAN VACCINES

The top 10 companies based on company vaccine sales are shown in the figure below.

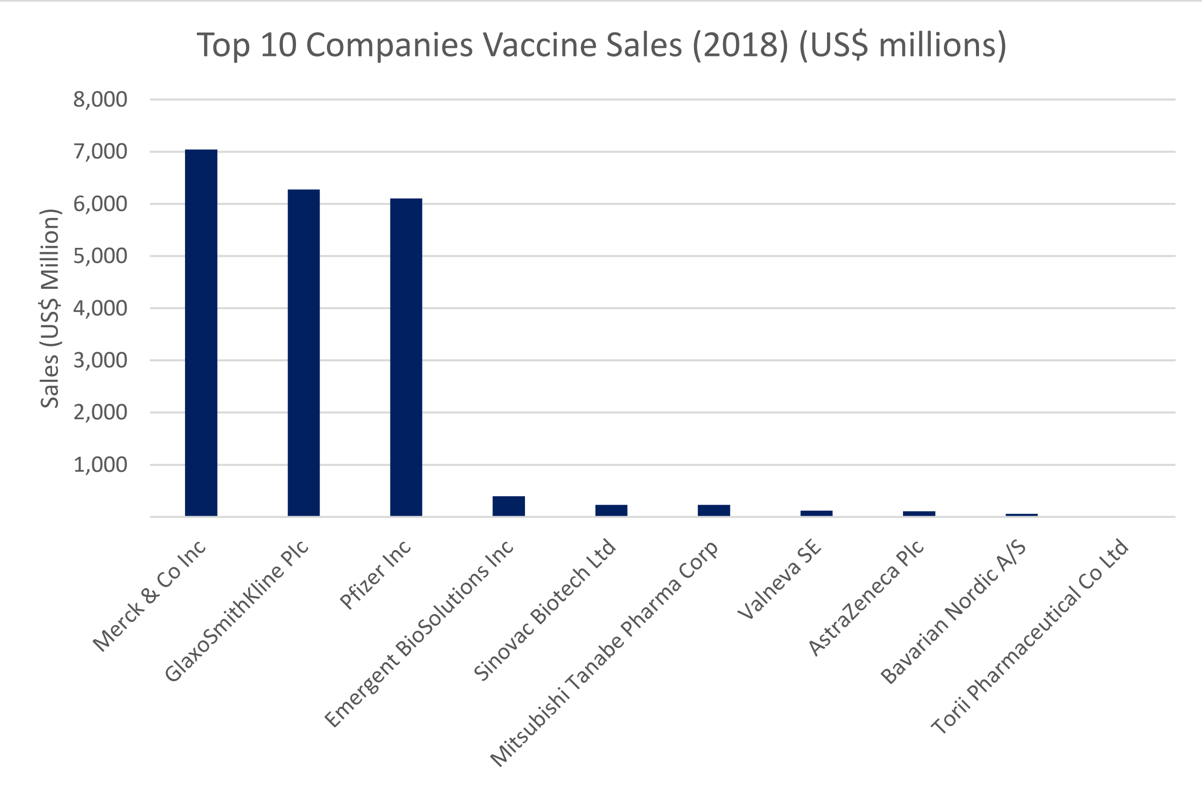

Figure 13. Top human health vaccine companies based on sales in 2018 (US $ Millions).

Merck & Co Inc

Merck & Co Inc (Merck) is a biopharmaceutical company that focuses on the discovery, development, manufacturing and commercialization of prescription medicines, biologic therapies, vaccines and animal health products. In 2018 Merck reported revenues of US $42.3 billion, an increase of 5.4% from 2017. Since 2015 Merck has had 231 deals with an estimated value of US $53.7 billion.

In October 2019 Merck entered into a research agreement with 4D Pharma, a pharmaceutical company engaged in the development of live biotherapeutics. The aim of this partnership was to discover and develop live biotherapeutics (LBPs) for vaccines. This agreement enabled 4D Pharma and Merck to advance the understanding of the microbiome space to develop a new class of vaccines in areas of high unmet need. This deal was estimated to be worth US $347.5 million[25].

In September 2019 Merck invested US $44 million in Themis Bioscience, to accelerate its pivotal Phase III clinical trial program for its Chikungunya vaccine and to support further expansion into oncology indications using its proprietary vaccine vector platform.

In August 2019 Merck announced a research collaboration with Themis Bioscience GmbH, a company developing immunomodulation therapies for infectious diseases and cancer. The collaboration was for the development of vaccine candidates against an undisclosed disease target, using Themis' measles virus vector-based platform.

GlaxoSmithKline Plc

GlaxoSmithKline Plc (GSK) is a healthcare company that focuses on the development, manufacture and commercialisation of pharmaceuticals, vaccines and consumer healthcare products. GSK's vaccine portfolio covers various diseases including: hepatitis, diphtheria, tetanus, whooping cough, rotavirus and HPV infections, measles and bacterial meningitis. In 2018 GSK reported revenues of £30.8 billion, a 2.1% increase from 2017. Since 2015 GSK has had 192 deals with an estimated value of US $60.4 billion.

In November 2019 GSK entered into a partnership with Viome, a mission-driven company aiming to improve people's health based on individual biology. The long-term goal was to improve understanding of chronic diseases and the potential role for vaccines[26].

In August 2019 The Sabin Vaccine Institute (Sabin) entered into an exclusive licensing agreement with GSK, with the aim of advancing development of prophylactic candidate vaccines against the deadly Ebola Zaire, Ebola Sudan and Marburg virus. Under the agreement, Sabin has exclusively licensed the technology for all three candidate vaccines and has acquired certain patent rights specific to these vaccines. The candidate vaccines, based on GSK's proprietary ChAd3 platform, were further developed by GSK, including the Phase II development for the Ebola Zaire vaccine[27].

Pfizer Inc

Pfizer is a biopharmaceutical company which works to discover, develop, manufacture and market healthcare products including: medicines, vaccines and consumer healthcare products. In 2018 Pfizer reported revenues of US $53.6 billion, an increase of 2.1% compared to 2017. Since 2015 Pfizer has been involved in 303 deals with a total value of US $385.5 billion.

In January 2020 Insilico Medicine, entered into a research collaboration with Pfizer, in order to utilize Insilico's machine learning technology and proprietary Pandomics Discovery Platform with the aim of identifying real-world evidence for potential therapeutic targets implicated in a variety of diseases.

In May 2019 Pfizer raised a total of US $4.5 billion by public offering of 14.3%, and intend to use these proceeds for general corporate purposes, including to refinance, redeem or repurchase existing debt and to repay a portion of its outstanding commercial paper[28].

Emergent Biosolutions

Emergent Biosolutions is a life science company that focuses on protecting and enhancing life by providing specialised products to governments and healthcare providers including vaccines and antibody therapies, with a focus on infectious diseases, autoimmune disease and cancer. Its marketed products include BioThrax (anthrax vaccine). In 2018 Emergent Biosolutions reported revenues of US $782.4 million, an increase of 39.5% compared to 2017. Since 2015 Emergent Biosolutions has been part of 45 deals, with an estimated value of US $3.4 billion[29].

In May 2018 the Coalition for Epidemic Preparedness Innovations (CEPI) entered into a collaboration with Profectus BioScience Inc and Emergent BioSolutions Inc, to advance the development and manufacture of a vaccine against Nipah virus (NiV). Under this collaboration CEPI will fund Profectus and Emergent up to US $25 million, and under a separate agreement Emergent, has an exclusive option to license and to assume control of development activities for the NiV vaccine from Profectus[30].

Emergent BioSolutions has also made a number of company acquisitions; it acquired PaxVax from Cerberus Capital Management in October 2018. PaxVax is a company primarily focused on specialty vaccines against both existing and emerging infectious disease. In the deal Emergent BioSolutions acquired Vivotif (Typhoid Vaccine Live Oral Ty21a), Vaxchora (Cholera Vaccine Live Oral), an adenovirus 4/7 vaccine candidate being developed for military personnel under contract with the US Department of Defence (DoD) and additional clinical-stage vaccine candidates targeting Chikungunya and other emerging infectious diseases, European-based cGMP biologics manufacturing facilities, approximately 250 employees including those in research and development (R&D), manufacturing, and commercial operations with a specialty salesforce. This deal had an approximate value if US $270 million, and enables Emergent BioSolutions to diversify its customer base and expand its portfolio[32].

In August 2018 Emergent BioSolutions Inc entered into another partnership with CEPI and Profectus BioScience Inc, in order to further advance the Lassa Virus Vaccine. Over the five-year agreement CEPI will invest up to a total of US $36 million. Through the separate agreement with Profectus, Emergent also has an exclusive option to license and to assume control of development activities for the Lassa-virus vaccine from Profectus[33].

Sinovac Biotech Ltd

Sinovac Biotech Ltd is a biopharmaceutical company that develops, manufactures and commercializes vaccines. In 2018 Sinovac Biotech reported revenue of US $229.7 million, a 31.7% increase on 2017. Since 2015 Sinovac Biotech Ltd has been involved in 3 deals, with a total value of US $944 million[34].

In July 2017 Sinovac Biotech was acquired by Shandong Sinobioway Biomedicine Co Ltd. This deal had an estimated worth of US $455.25 million[35].

In July 2018 Sinovac Biotech raised US $86.73 million through private investment with the proceeds being used to increase its capabilities in research to support the development and commercialisation of sIPV-based combination vaccine, as well as other new vaccine projects[36].

Other companies

Mitsubishi Tanabe Pharma Corp

Mitsubishi Tanabe is a subsidiary of Mitsubishi Chemical Holdings Corp. The company develops vaccines for preventing various infectious diseases, as well as drugs for autoimmune disease, diabetes, kidney diseases, and central nervous system disorders. In 2019 they had a reported revenue of 424.8 billion Japanese Yen, down 2.1% on 2018[37].

Valneva SE

Valneva SE is a biotechnology company that develops lifesaving vaccines against infectious diseases and cancer. The company's products include a vaccine indicated for the prevention of Japanese encephalitis; and a vaccine indicated for the prevention of cholera and diarrhoea. In 2018 Valneva reported revenue of €113 million, an increase of 7.4% on 2017[38].

AstraZeneca Plc

AstraZeneca Plc is a biopharmaceutical company that focuses on therapy areas including: respiratory, cardiovascular, renal, autoimmune, neurological and metabolic disorders, as well as cancer. Its portfolio includes prescription pharmaceuticals and vaccines. In 2018 the company reported revenue of US $22.1 billion, a decrease of 1.7% on 2017[39].

Bavarian Nordic A/S

Bavarian Nordic A/S is a biotechnology company that develops, manufactures and commercializes cancer immunotherapies and vaccines for infectious diseases. The company develops its products using poxvirus-based technology platforms including modified vaccinia ankara – bavarian nordic (MVA-BN). The reported company revenue for 2018 was 500.6 million Danish Krone, which was a decrease of 63.5% compared to 2017[40].

Torii Phamaceuticals Co

Torii Phamaceuticals Co, a subsidiary of Japan Tobacco Inc. They manufacture and market treatments for renal and skin diseases, as well as allergies. The company reported revenues of 62.5 billion Japanese Yen in 2018, which was a decrease of 2.5% compared to 2017[41].

4.2 ANIMAL VACCINES

In the global animal health market, there is a diverse range of competitors which offer both companion and livestock vaccines. In 2019 the animal vaccine markets revenue totalled US $7.8 billion with the top 3 companies accounting for 62%. Key competitors include Merck, Zoetis and Boehringer Ingelheim[42].

Company	Market Share (%)	Revenue (US $ billion)
Merck	23	1.76
Boehringer Ingelheim	20	1.54
Zoetis	19	1.5
Others	38	3
Total	100	7.8

Other leading companies in the animal vaccine market include: Virbac, Hipra, Ceva, Huvepharma, and Dechra.

The distribution of vaccines across species of the leading company portfolios was also assessed using the UK as an example. Merck and Boehringer Ingelheim had the largest animal vaccine portfolios with more livestock vaccines than companion animal vaccines, with the largest number of vaccines in poultry.

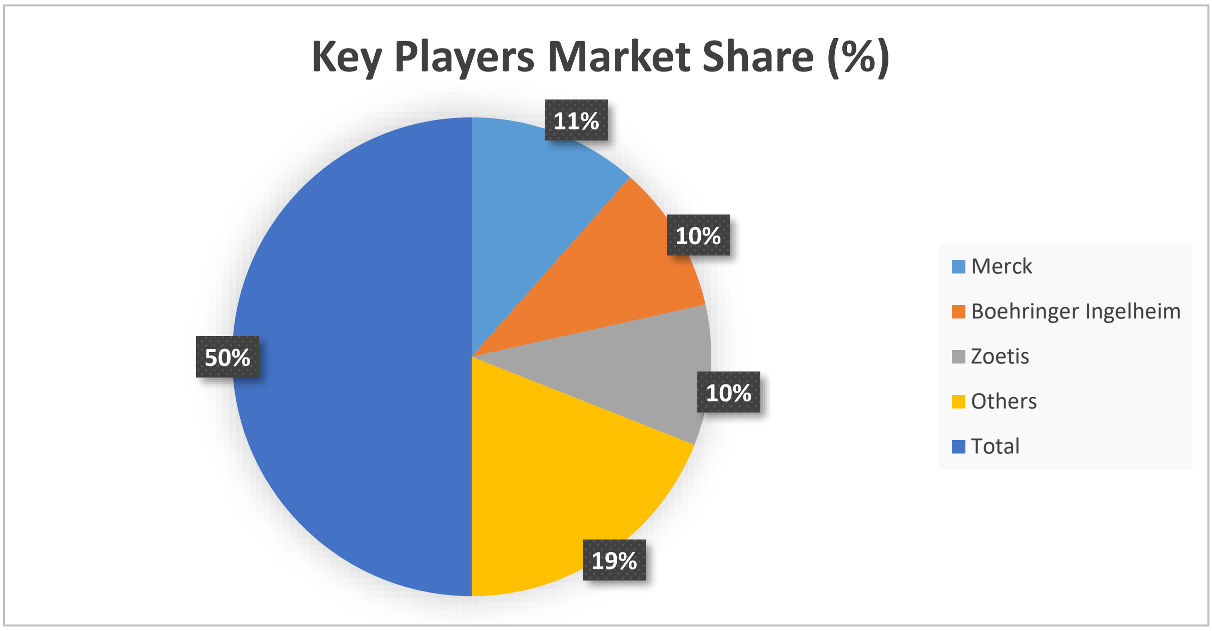

Figure 14. Market share of key players in Animal Health vaccines.

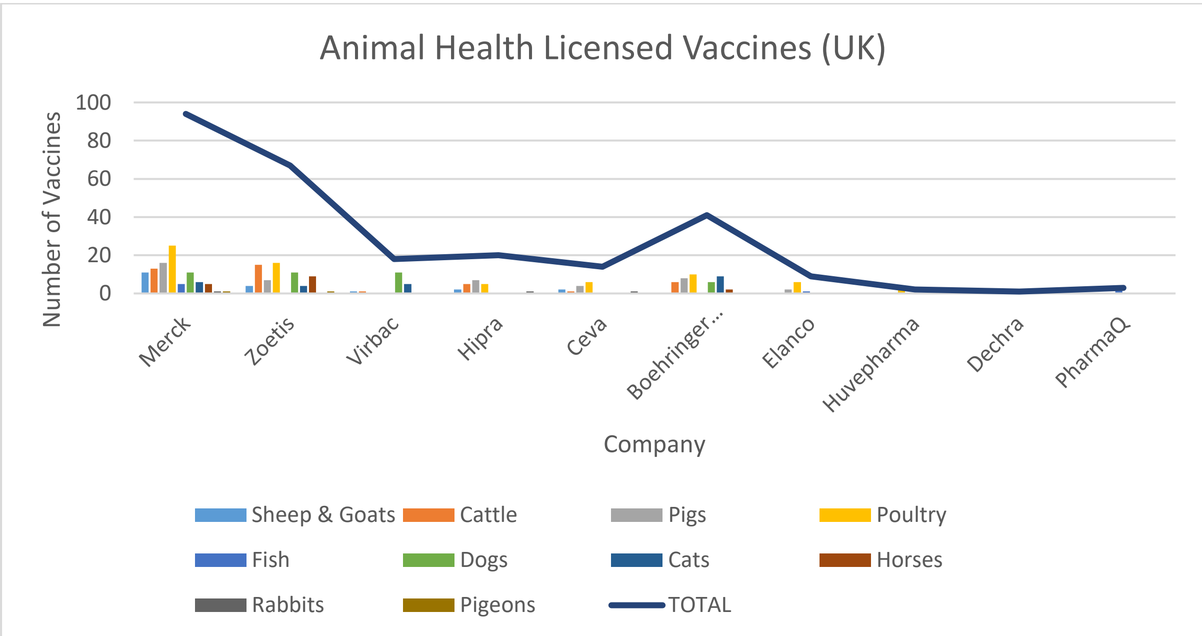

Figure 15. Distribution of animal health vaccines in key players portfolio, divided into species areas for each company.

When looking more closely at livestock vaccines, Merck has the largest number of licensed livestock vaccines followed by Zoetis and Boehringer Ingelheim. There are similar trends in companion animal vaccines, with Virbac also having a number of companion animal vaccines.

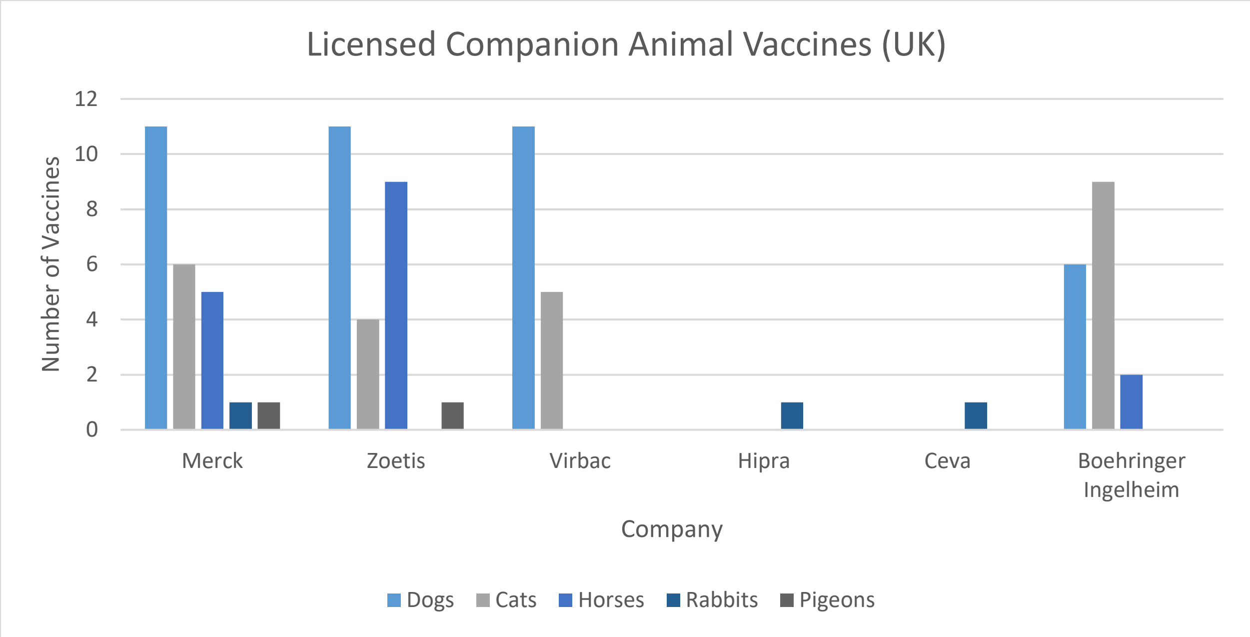

Figure 16. Licensed livestock vaccines in the UK for top 10 animal vaccine companies, split by species for each company.

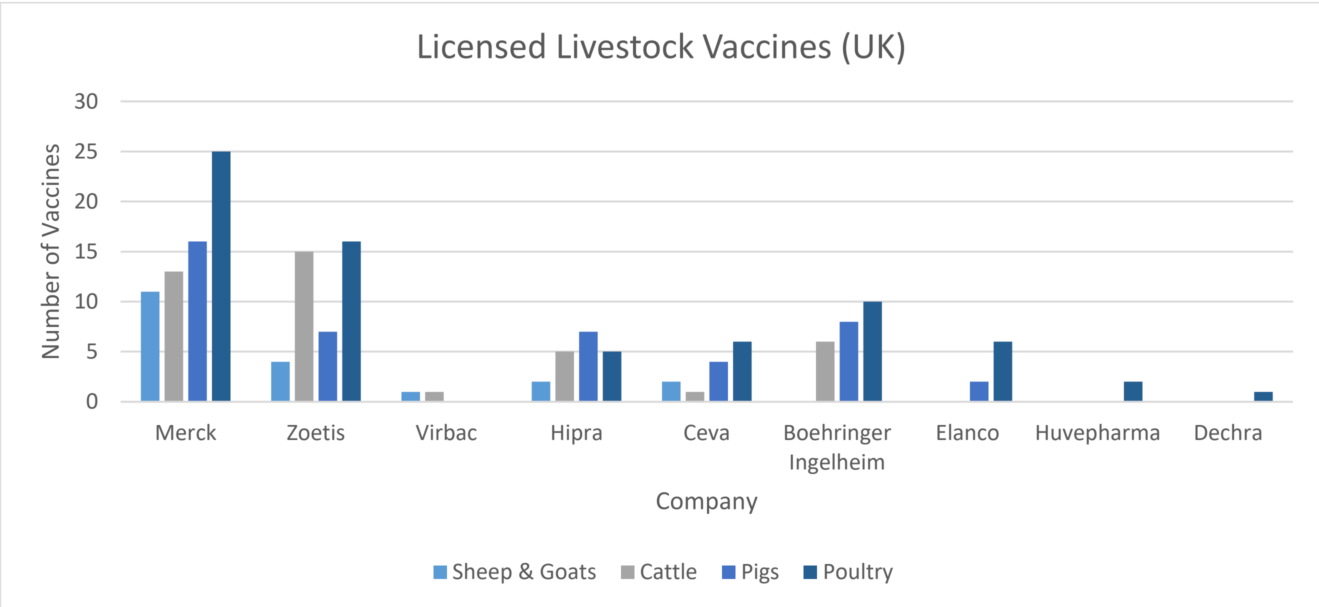

Figure 17. Licensed companion animal vaccines in the UK for top 10 animal vaccine companies, split by species for each company.

When looking at the product portfolio distribution for the leading companies in companion animals, canine vaccines occupy the largest segment for the leading companies. In the livestock market, the leading companies do not appear to have such a clear divide. However, the larger segments appear to be occupied by cattle and poultry.

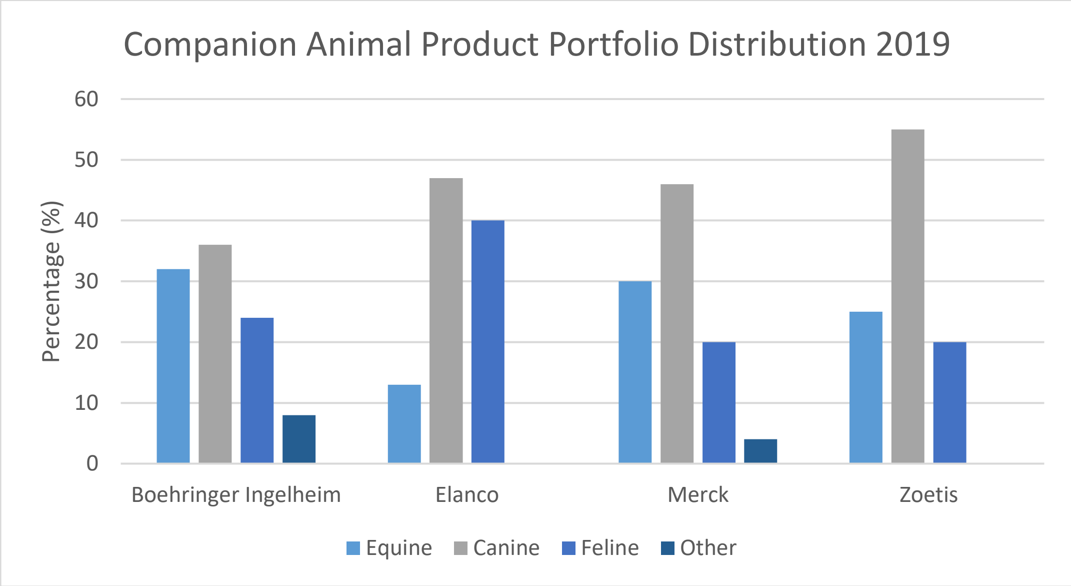

Figure 18. Companion animal vaccine portfolio distribution in 2019 for leading companies.

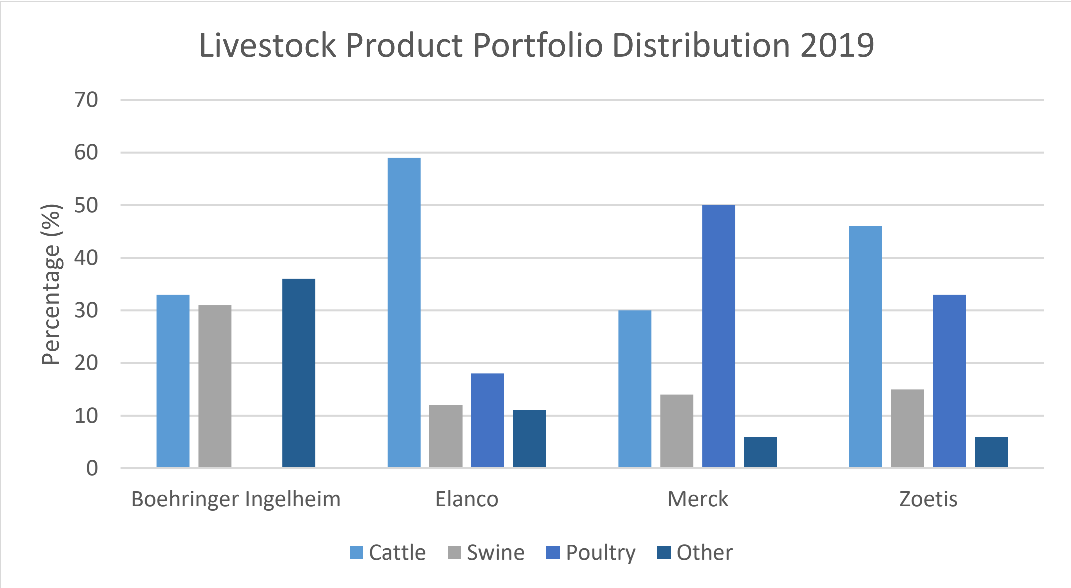

Figure 19. Livestock vaccine portfolio distribution in 2019 for leading companies.

Merck Animal Health

Merck Animal Health is the global animal health business unit of Merck. It is one of the leading global animal health companies that researches, develops, manufactures and sells veterinary medicines including: anti-infective and anti-parasitic drugs, pharmaceutical specialty products, vaccines, innovative delivery solutions, and more. Merck Animal Health is present in more than 50 countries, with its products available in around 150 markets. Merck covers all segments of the veterinary market including: companion animals, food producing animals and aquaculture. In 2018 Merck Animal Health reported a revenue of US $4.2 billion, and a CAGR of 10% between 2016 and 2018 accounting for 10% of Merck & Co.'s total income.

In August 2019 Merck Animal Health received approval from European Authorities for PORCILIS® Lawsonia Vaccine for Piglets, an intramuscular vaccine against *Lawsonia intracellularis*, and it will also be approved for mixing with PORSILIS® PCV M Hyo, providing the opportunity to protect against three major diseases in one single injection: *Lawsonia intracellularis*, porcine circovirus type 2 (PCV2) and *Mycoplasma hyopneumoniae* (M. hyo)[43].

In December 2019 Merck Animal Health announced its acquisition of Vaki, a leader in fish farming and wild fish conservation equipment. This further strengthens Merck Animal Health's position in this market, expanding into complementary fish farming and conservation areas to generate outcomes with precision farming and fish welfare solutions, which complement its existing portfolio of vaccines and pharmaceuticals[44].

Zoetis

Zoetis is a global animal health company which works on the discovery, development, manufacture and commercialisation of both vaccines and diagnostic products in the animal health market. Their products serve livestock and companion animals in over 100 countries. In 2018 Zoetis reported US $5.8 billion revenue, with 54% of this revenue from the livestock market, and the remaining 45% from the companion animal market[45].

In May 2017 Zoetis announced a five-year collaboration with a multidisciplinary team spanning the public and private sector for animal and human health. The programme named "Bac Vactory" will take a One Health approach to develop a new generation of vaccines to help control bacterial infections that pose a significant threat to both human and animal health. The Bac Vactory programme partners include the academic institutions Utrecht University, VU Amsterdam, VU Medical Centre, Eindhoven University of Technology, and Radboud University Medical Centre as well as corporate partners Zoetis, Wageningen Bioveterinary Research, Abera Biosciences, GlaxoSmithKline, Pulike Biological Engineering Inc., and Immuno Valley[46].

In July 2017 Zoetis acquired Nexvet Biopharma, an Irish biopharmaceutical company, allowing Zoetis to strengthen its monoclonal antibody pipeline and help sustain its position in chronic pain management for companion animals. This deal has an estimated worth of US $85 million[47].

Zoetis received the Best New Product for Companion Animals 2018 for their Core EQ Innovator™ vaccine. The Core EQ Innovator™ vaccine was the first equine vaccine to protect against all five core equine diseases: West Nile virus, Eastern and Western Equine encephalomyelitis, tetanus and rabies[46].

Boehringer Ingelheim

Boehringer Ingelheim is a research driven global pharmaceutical company, involved in the research, development manufacture and sale of pharmaceuticals for both human and animal health. In 2018 Boehringer Ingelheim had a reported revenues of €17.5 billion in 2018, with a net sales growth of 4%, although R&D expenses increased by 18.1% of net annual sales[48]. Boehringer Ingelheim is the second largest animal health business, with the Animal Health Business Unit's net sales for 2018 totalling approximately €4 billion, with a presence in over 150 markets globally[49]. Since 2015, Boehringer Ingelheim have completed 108 deals with a combined value of approximately US $25.4 billion[50].

In November 2016 the European Commission approved the acquisition of Sanofi's animal health business Merial by Boehringer Ingelheim. This merger resulted in the combination of two key competitors in the development, manufacturing, marketing and sale of animal health products across the European Economic Area (EEA)[51]. The transaction was officially completed in January 2017 when the acquisition of Merial made Boehringer Ingelheim the second largest animal health company globally[52].

In October 2018 Boehringer Ingelheim introduced its new global centre for veterinary vaccine R&D in Lyon, France. A €70 million investment reinforced the company's leading position in the veterinary vaccine market by providing a new R&D centre of 14,500 square meter high-tech facility employing more than 200 employees[54].

In January 2019 Boehringer Ingelheim launched the first veterinary vaccines produced in China. The Swine vaccine Ingelvac® PRRS MLV is now produced by their veterinary vaccine manufacturing in the China Medical City in Taizhou, Jiangsu Province to supply the Chinese market. The manufacture of Ingelvac® PRRS MLV at the Taizhou plant is expected to provide Chinese customers with most swine vaccines[55].

Elanco Animal Health Inc

Elanco Animal Health Inc (Elanco), previously a subsidiary of Eli Lilly and co, develops and manufactures animal health products. In 2018 Elanco reported revenues of approximately US $ 3.1 billion[50].

In August 2019 Elanco announced an agreement with Bayer AG to acquire its animal health business. The transaction is valued at around US $7.6 billion, and is thought to double Elanco's companion animal business. This acquisition will also expand innovation at Elanco through pipeline, delivery platforms, scale and access to Bayer R&D[56].

Elanco also announced the acquisition of Prevtec Microbia Swine Vaccine Company, a start-up that specialises in the development of vaccines to prevent bacterial diseases in food animals. Acquiring Prevtec expands Elanco's swine portfolio to include Coliprotec® line of vaccines designed to protect pigs against post-weaning diarrhoea (PWD) and associated clinical signs caused by *E. coli*. Along with the acquisition of Prevtec, Elanco has also strengthened its position in the swine industry with the launch of Prevacent™ PRRS vaccine[57].

Other companies

Ceva Sante Animale SA

Ceva Santé Animale is a global veterinary health company specialized in pharmaceutical products and vaccines for companion animals and livestock[58].

Virbac SA

Virbac is a veterinary pharmaceutical company, dedicated to animal health. Virbac's innovation offers a range of products and services to diagnose, prevent and treat the majority of pathologies, while improving the animals' quality of life[59].

Hipra

Laboratorios Hipra (Hipra) is an animal health company that manufactures and markets biologicals for veterinary application. Hipra develops vaccines, diagnostic kits and a range of pharmaceuticals[60].

Huvepharma

Huvephama is a subsidiary of Advance Properties OOD, developing, manufacturing and marketing human and animal health products that focus on animal health and nutrition[61].

Dechra Pharmaceuticals

Dechra Pharmaceuticals is a manufacturer and distributor of veterinary pharmaceutical products. Dechra manufactures product for both companion animals and livestock. In 2019 the company reported revenues of GBP £481.8 million[62].

5. MARKET DRIVERS AND TRENDS

The vaccine market for both the animal and human health is concentrated on supply as well as demand, and are both highly regulated. As a result of this, these markets share common market drivers, as well as threats to market growth. However, there are also some distinct differences between these two market segments. The market drivers are highlighted below:

Human Vaccine Market	Animal Vaccine Market
Government & Independent Funding	Government & Independent Funding
Increasing Risk of Endemics	Increasing risk of Zoonotic Diseases
Advances in Vaccine Technology	Rise in Pipeline Vaccines
Increasing risk of Zoonotic Diseases	Increasing demand for animal protein
Rise in Pipeline Vaccines	Increase in pet ownership

5.1 HUMAN VACCINES MARKET

Infectious disease epidemics pose a distinct threat to global health, security and economic prospects. It is estimated that the annual cost of a pandemic risk is approximately US $30 billion. The experiences of past epidemics such as the Ebola outbreak in 2015, the SARS outbreak in 2003, and now the current global COVID-19 pandemic, highlights the need for proactive and coordinated research and product development, to improve emergency preparedness. With an increase in international trading and travel, the risks of epidemic outbreaks will only increase. As a result of this the WHO has highlighted the infectious pathogens likely to cause severe outbreaks, these are detailed in the table below[63].

Disease	Description	Vaccine Availability
Crimean-Congo Hemorrhagic Fever (CCHF)	CCHF causes a severe viral haemorrhagic fever with a fatality rate of up to 40%. Transmission is to people from ticks and livestock, and human-to-human transmission can occur.	No human or animal vaccine available.[64]
Ebola Viral Disease (EVD)	EVD is a rare but often severe haemorrhagic fever with fatality rates around 50%, but can reach 90% in outbreak situations. Transmission is through human-to-human contact.	Experimental vaccine under development.[65]
Marburg Viral Disease (MVD)	MVD is a rare but often severe haemorrhagic fever with fatality rates around 50%, with rates reaching 88% in previous outbreaks. The Marburg virus is transmitted to people from fruit bats and spreads through human-to-human transmission.	There is as yet no licensed treatment proven to neutralize the virus. Some therapies under development.[66]
Middles East Respiratory Syndrome Coronavirus (MERS-CoV)	MERS is a viral respiratory disease caused by a novel coronavirus. Approximately 35% of reported patients with MERS-CoV have died. Most transmission is human-to-human but some transmission may be from camels to humans.	No vaccine or treatment available. Several vaccines and treatments are in development.[67]
Severe Acute Respiratory Syndrome (SARS)	SARS is another coronavirus, with transmission primarily from person-to-person, with a case fatality rate of 10%.	Experimental vaccines under development.[68]

Disease	Description	Vaccine Availability
Nipah and Henipaviral diseases	Nipah virus infection in humans causes a range of clinical presentations, from asymptomatic infection (subclinical) to acute respiratory infection and fatal encephalitis. Case fatality rates range from 40 to 75%. Transmission can be animal (bats and pigs) to human, human-to-human, or through contaminated food.	CEPI currently funding vaccine development.[69]
Rift Valley Fever (RVF)	RVF is a viral zoonosis that primarily affects animals but can also infect humans. Transmission can be animal to human, and also through infected mosquito bites.	Vaccines under development.[70]
Zika Virus	Zika virus infection is most severe in pregnant woman and can cause infants to be born with microcephaly and other congenital malformations, as well as cause complications with the pregnancy. Infection with Zika virus also carries an increased risk of neurologic complications. It is transmitted through mosquito bites.	No treatment available.[71]
Lassa Fever	Haemorrhagic fever caused by virus transmitted from items that have contacted rodent urine or faeces, with case-fatality rate of 15% in severe cases (1% overall). Human-to-human transmission is possible.	No vaccine available; Vaccine development funded by CEPI.[72]
Disease X	Disease X represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease	CEPI is funding the development of institutional and technical platforms that allow for rapid R&D in response to outbreaks of any number of pathogens for which vaccines do not yet exist.[73]

Following this a number of new initiatives were put in place to increase R&D preparedness in these areas, including:

- The Coalition for Epidemic Product Innovation (CEPI)
- The Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)
- The Chatham House project on data sharing in infectious disease surveillance[63]

These initiatives have seen a lot of backing by both public and private sector funding and as a result are a large driver of growth in the vaccine market. Independent funding in vaccine development R&D is also on the rise, which will be another key factor in market growth. This increase in funding for vaccine development has resulted in the advancements in vaccine technologies, including delivery platforms and routes or administration and technology. A further area of growth in the market is the use of adjuvants in vaccines[3].

Advances in vaccine technology are required in order to overcome the threats of upcoming pandemics, and combat unpredictable emerging pathogens. The average development time for traditional vaccines is around 10 years, with high costs associated, which highlights the need for novel technology. Many new vaccine technologies provide a promising solution to the problems associated with traditional vaccine development, and as a result of being cheaper and easier to develop are able to drive the market forward. This surge of new vaccine technologies has resulted in an increase in developmental pipeline drugs – expected to further increase market growth[74].

5.2 ANIMAL VACCINE MARKET

Funding

There has been an increased focus on funding vaccine development in both human and animal health. For example, in 2017 in the UK the BBSRC announced funding of £5 million to support a one health approach to accelerate vaccine development. The aim of which was to promote research to aid vaccine development for a range of viral and bacterial families that are known to have a significant impact on animal and human health in low and middle income countries[75]. In addition to this, the UK government committed to invest £120 million between 2016 and 2021 for the development of new vaccines, in line with expert advice provided by the UK Vaccines Network. The UK Vaccine Network is made up of experts from academia, industry and policy across both human and animal health[76].

Other funding initiatives include the Livestock Vaccine Innovation Fund (LVIF), a seven-year CA $57 million partnership that seeks to improve the health of livestock and to protect the livelihoods of smallholder farmers[77]. Another source of funding is the catalyst funding awarded by the International Veterinary Vaccinology Network[78].

Risk of Epidemics

As previously discussed, infectious disease epidemics pose a distinct threat to global health, security and economic prospects. Many of the pathogens likely to cause severe outbreaks are zoonotic, these include:

- Crimean-Congo Haemorrhagic Fever (CCHF)
- Ebola Virus (EVD)
- Marburg Viral Disease (MVD)
- Middle East Respiratory Virus (MERS)
- Severe Acute Respiratory Syndrome (SARS)
- Zika Virus
- Lassa Fever
- Nipah Virus
- Rift Valley Fever

In response to the increased risk of zoonotic outbreaks from these pathogens, there has been a drive to increase funding towards a One Health approach to vaccine development, resulting in a total of 80 pipeline vaccines in this area.

Virus	Pipeline Vaccines
Crimean-Congo Haemorrhagic Fever (CCHF)	6
Ebola Virus EVD	7
Marburg Viral Disease (MVD)	3
Middle East Respiratory Virus (MERS)	3
Severe Acute Respiratory Syndrome (SARS)	6
Zika Virus	38
Lassa Fever	10
Nipah Virus	4
Rift Valley Fever	3

Meat Production

Meat production, including: cattle, poultry, sheep/mutton, goat, pigs, and wild game has increased significantly over the last decade from 294 million tonnes in 2010 to 334 million tonnes in 2017. The distribution of meat production globally is outlined below[79].

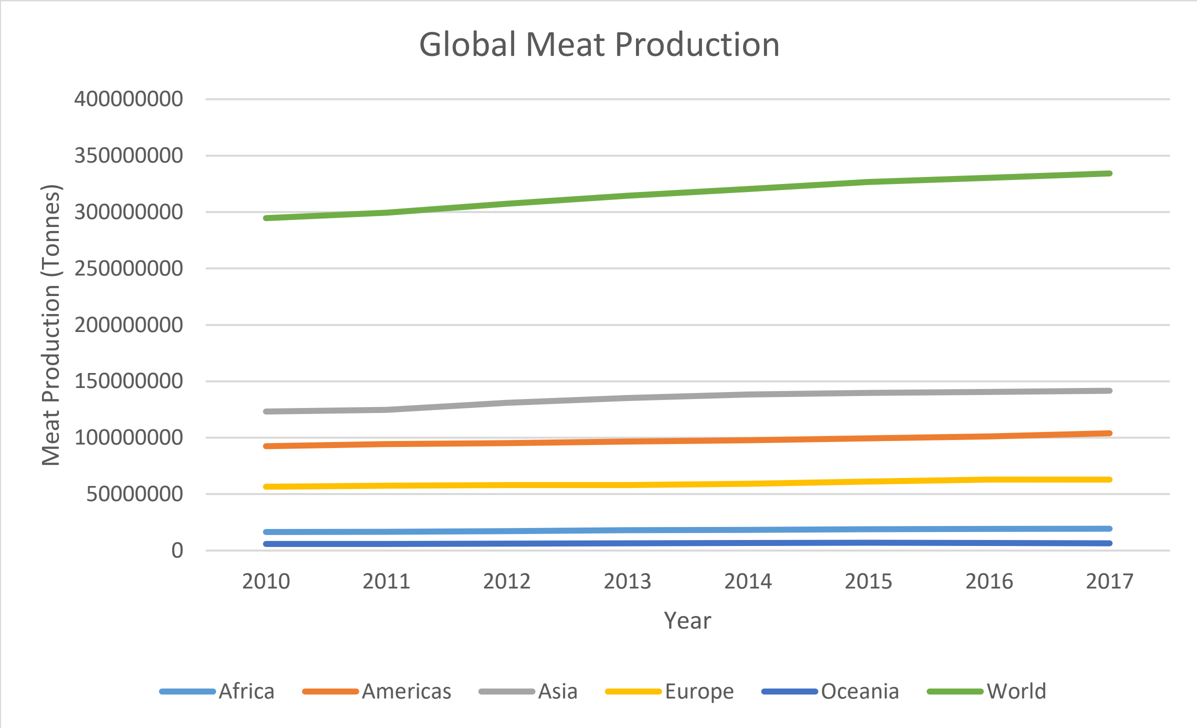

Figure 20. Global meat production trends by continent.

This increase in meat production is a potential driver for market growth, due to an increased demand for livestock vaccines.

Whilst not a particular focus in this white paper, it is also worth noting that as well as growing demands for meat, a rise in demand from aquaculture is driving growth in vaccines for these species.

Increase in companion animals

Growth in the companion animal market is due to an increase in pet ownership. For example, in the United States, overall pet ownership has increased by 25% from 115.5 million households owning a pet in 2011 to 144.2 million households in 2018.

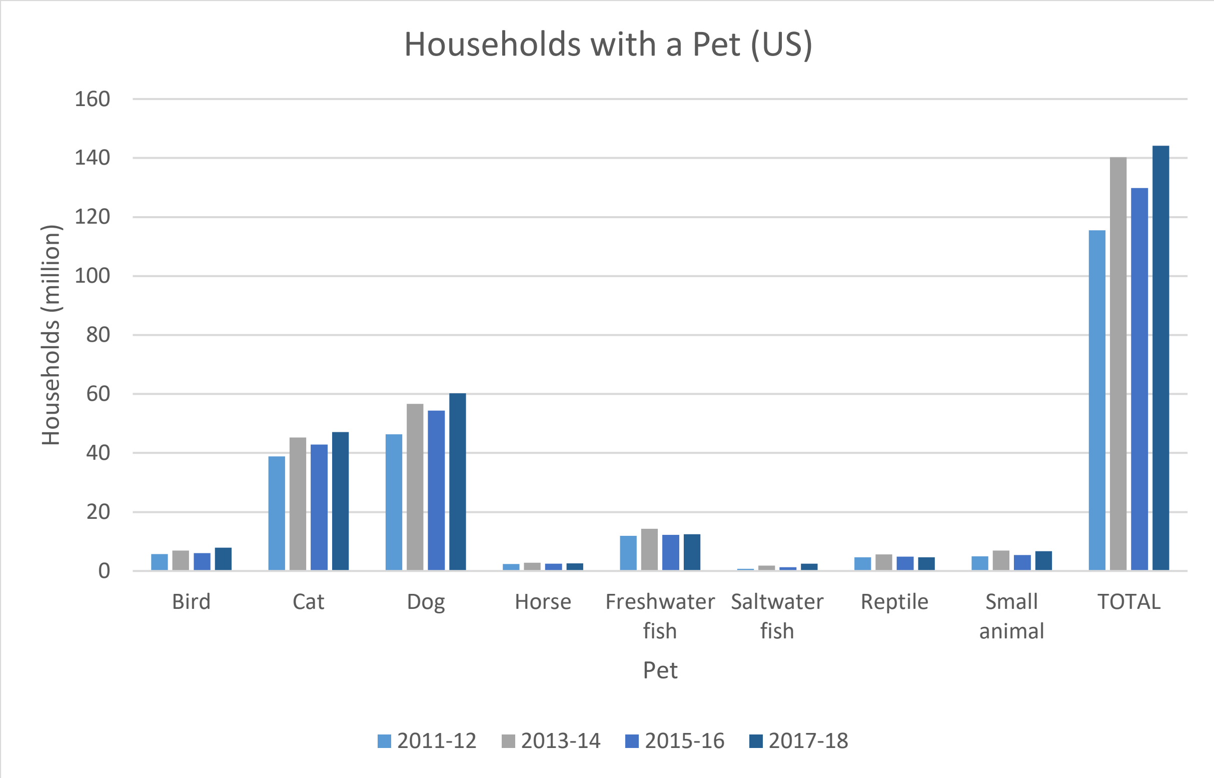

Figure 21. Number of US households with a pet from 2011-2018.

An increase in pet ownership increases demand for companion animal vaccines.

6. BARRIERS TO ENTRY

For both the human and animal vaccine markets the barriers to entry are very similar and are summarised in the following sections with an emphasis on human health where more data is available.

6.1 REGULATION OF VACCINE DEVELOPMENT

A drug regulatory authority (DRA) ensures all medicinal products are of acceptable quality, safety and efficacy, are manufactured and distributed in ways that ensure their quality until they reach the consumer and to certify accurate commercial promotion. The main functions of DRAs are to licence products, inspect and license manufactures and distributers, undertake post-marketing surveillance, regulate claims made for the commercial promotion of products, and authorise clinical trials[80]. Receiving marketing approval for new vaccines from these regulatory agencies is expensive and time consuming, the financial position of companies carrying out vaccine development are significantly influenced by their ability to obtain or retain regulatory approvals.

The risk of biological and physical variability makes R&D outcomes for vaccine development extremely uncertain and therefore makes manufacturing more challenging than other pharmaceuticals. For this reason a high proportion of vaccine manufacturing fails[81]. In addition, the high level of regulation surrounding vaccine development means human vaccine development typically takes between 10 to 15 years[82]. Animal health vaccine timelines are quicker, typically 5-7 years, but still significant given the lower market sizes.

6.2 RISING COST OF VACCINE DEVELOPMENT

With R&D taking an average of 10 years or more for the successful development of a human vaccine, followed by a further 12-18 months for the first regulatory approval, and another 24 months to manufacture the vaccines, vaccine development is a costly process. In the UK it is estimated that human vaccine development costs between £374 million to £1.5 billion, with a further cost of around £448 million of building a biological manufacturing site. Vaccine development for human health is also a risky process, with only 6% probability of market entry from preclinical testing[83]. Development and regulatory approval costs for veterinary vaccines are considerably lower than for human vaccines (a few £10s of millions), but this needs to be balanced by the much smaller markets. Few animal health vaccines generate more than £50 million in sales per year.

6.3 VACCINE MARKET COMPETITIVE LANDSCAPE

The competitive market of vaccine development is a major barrier to entry. The market is characterised by intense competition, evolving industry standards, and established business models. There is immense competition from both major drug discovery companies, as well as larger pharmaceutical and biotechnology companies, who have significant resources. In both human and animal health, much of the market is also driven by government or international (e.g. WHO) tenders, which drives down prices and increases the competitive nature of winning these contracts.

7. RESEARCH LANDSCAPE

7.1 HUMAN VACCINES

To give an indication of the academic institutions contributing to the field, a broad search of academic publications was carried out using Lens.org. A search of the title, abstract, keyword and field of study for (Vaccine*) NOT (Animal) NOT (Veterinary) NOT (livestock). For the search period of 2000-2019 there were 291,238 publications, of which 35,245 were cited by patents.

Analysis of publications of time from 2000 to 2019 show increasing number of publications in this area over time.

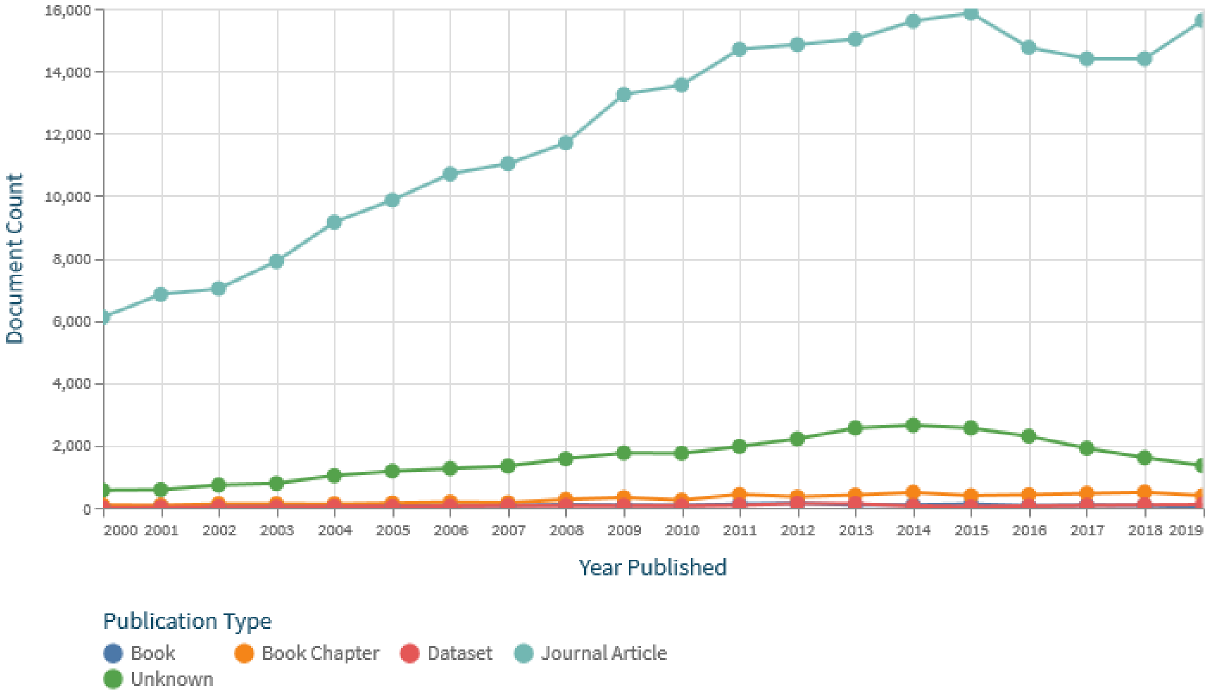

Figure 22. Publication of scholarly works from 2000-2019 relating to human vaccines (Lens.org).

The key organisations involved in publication of research relating to human vaccines include the Centers for Disease Control and Prevention, National Institutes of Health, Harvard University, Johns Hopkins University and the University of Oxford.

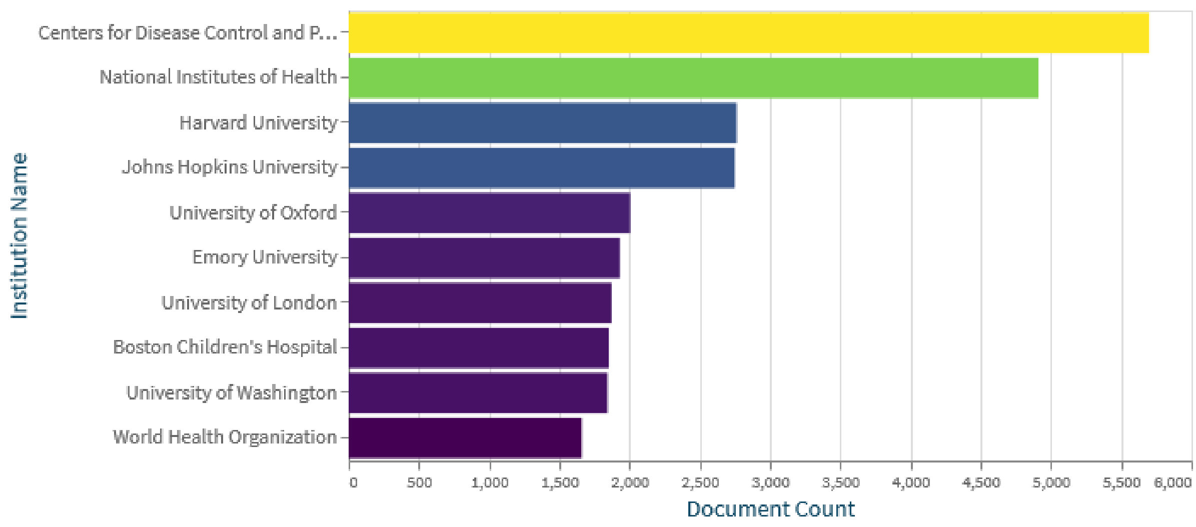

Figure 23. Top Institutions for publications relating to human vaccines (lens.org).

When split by the key countries or regions, the United States is significantly ahead which the most documents published, followed by the United Kingdom and China.

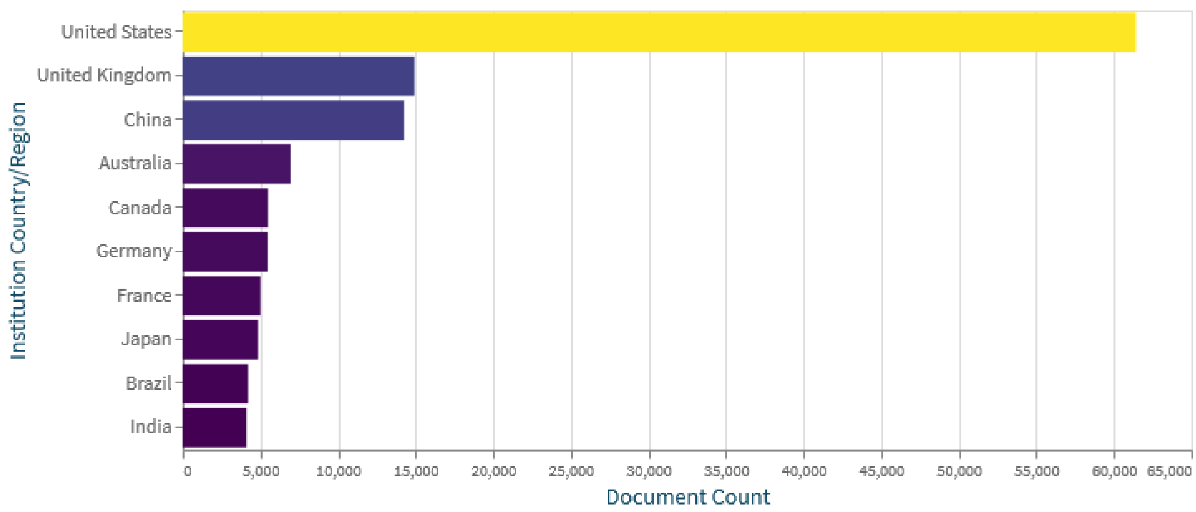

Figure 24. Top countries or regions for publications relating to human vaccines (lens.org).

For scholarly works cited in patents, the top organisations and main countries gives an indication of where the research is being carried out in a field that has more industrial application as opposed to fundamental science. In the human vaccine field, the top patent cited organisations include the National Institutes of Health, Harvard University, Johns Hopkins University, the Centers for Disease Control and Prevention and Pasteur Institute. The top countries include the United States, the United Kingdom, China, Germany and France.

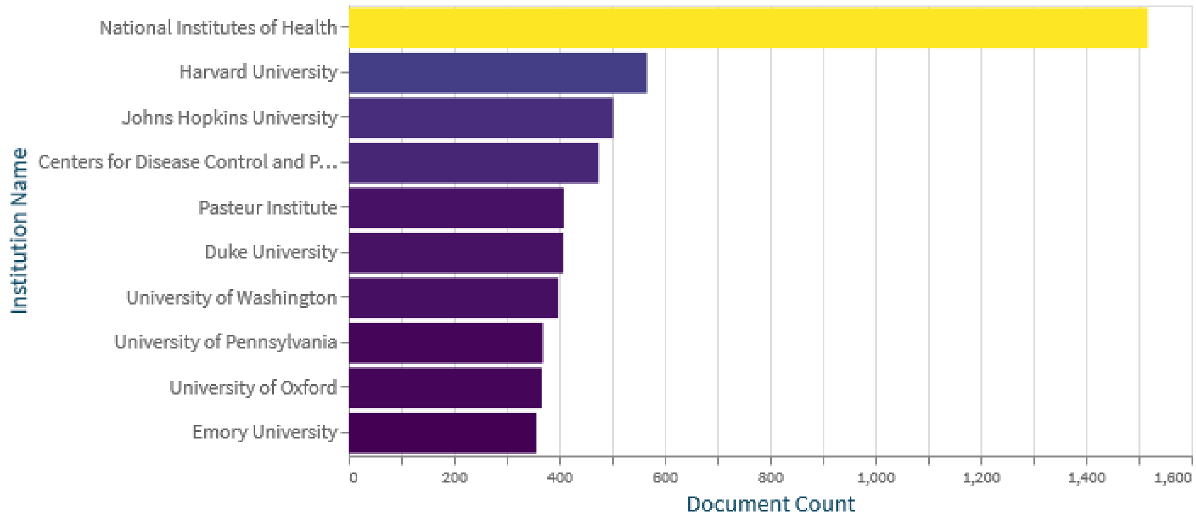

Figure 25. Top Institutions for publications cited in patents relating to human vaccines (lens.org).

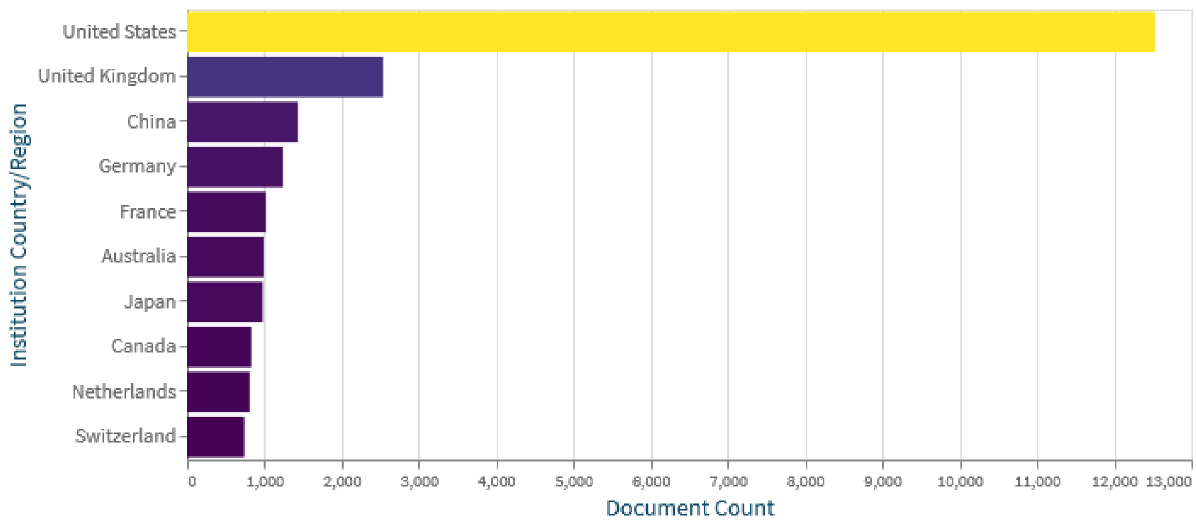

Figure 26. Top countries or regions for publications cited in patents relating to human vaccines (lens.org).

7.2 ANIMAL VACCINES

To give an indication of the academic institutions contributing to the animal vaccine field, a broad search of academic publications was carried out using Lens.org. A search of the title, abstract, keyword and field of study for (Vaccine*) and (Animal OR Veterinary OR Livestock), for the search period of 2000-2020 showed 39,267 publications, of which 7,902 were cited by patents.

Analysis of publications of time from 2000 to 2019 show a steady increase in the number of publications in this area over time, with a slight decrease from 2014-2017, although the number of publications then begin to increase again.

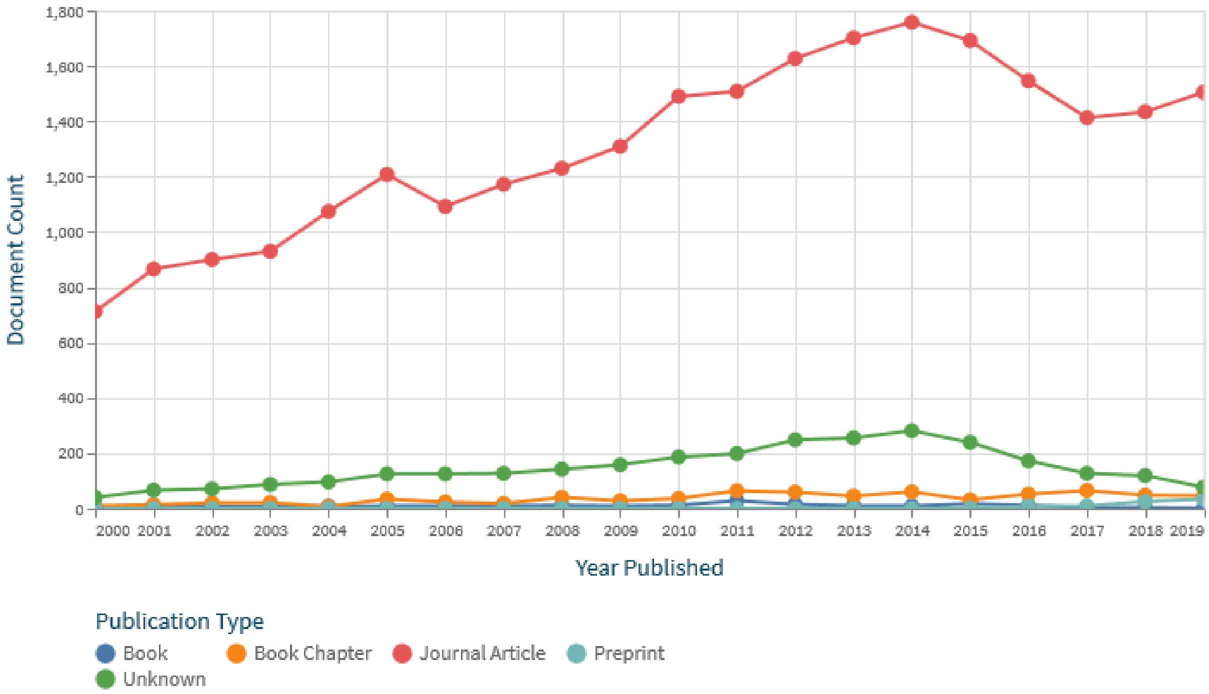

Figure 27. Publication of scholarly works from 2000-2019 relating to animal vaccines.

The key organisations involved in publication of research relating to animal vaccines include the National Institutes of Health, Centers for Disease Control and Prevention, United States Department of Agriculture, Harvard University and University of Texas Medical Branch.

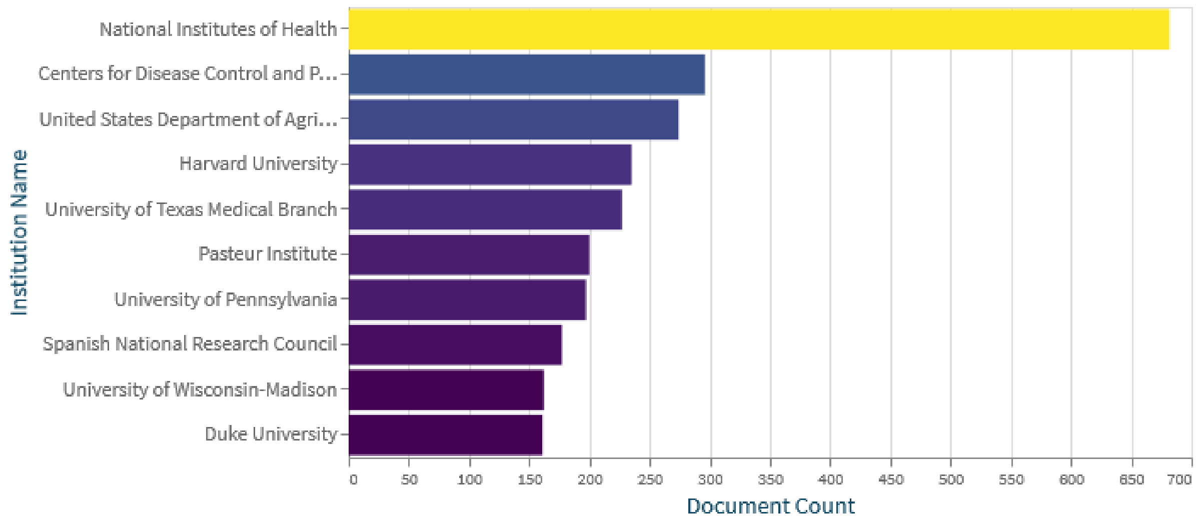

Figure 28. Top Institutions for publications relating to animal vaccines.

When split by the key countries or regions, the United States is significantly ahead with the most documents published, followed by the United Kingdom and China.

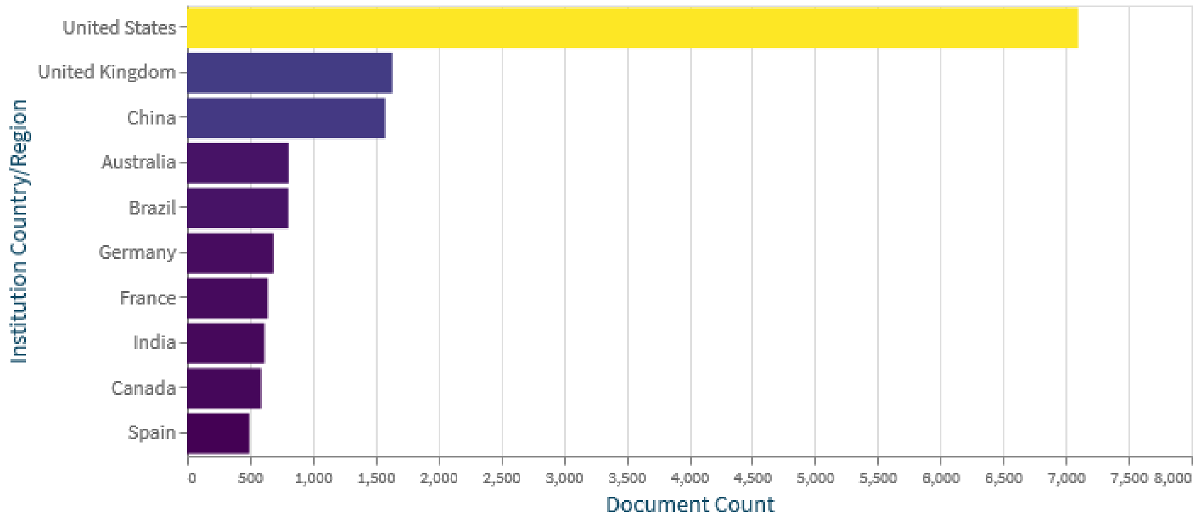

Figure 29. Top countries or regions for publications relating to animal vaccines.

For scholarly works cited in patents, the top organisations include the National Institutes of Health, Harvard University, Johns Hopkins University, the Centers for Disease Control and Prevention and University of Texas Medical Branch. The top countries include the United States, the United Kingdom, China, Germany and France.

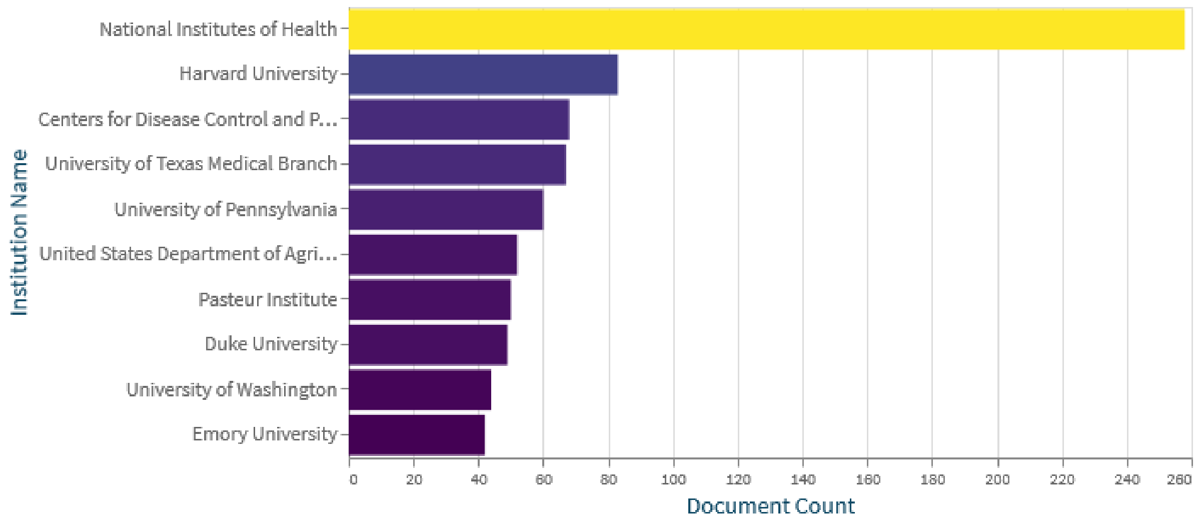

Figure 30. Top Institutions for publications cited in patents relating to animal vaccines.

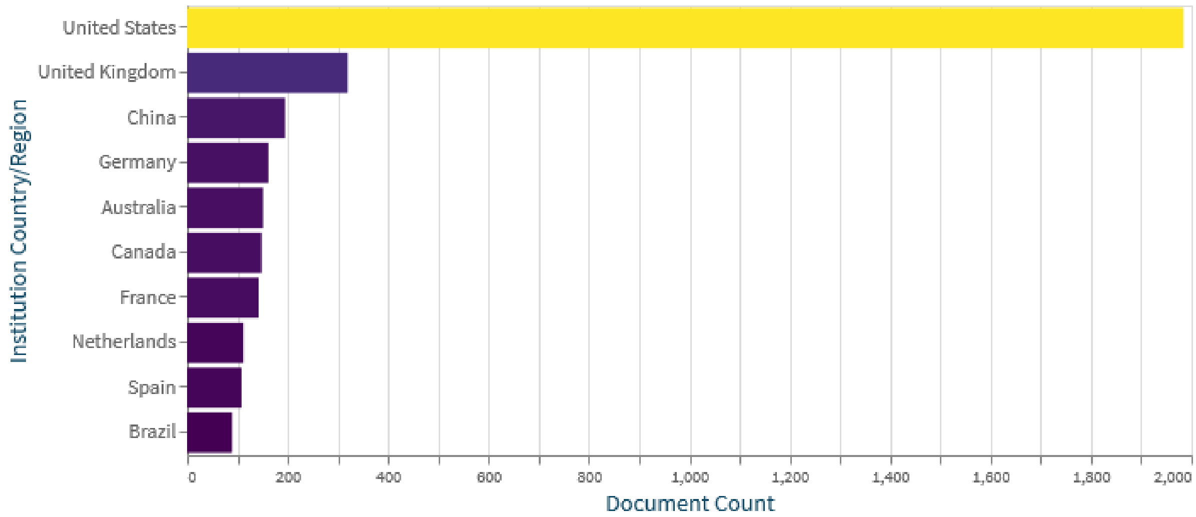

Figure 31. Top countries or regions for publications cited in patents relating to animal vaccines.

8. PATENT ANALYSIS

8.1 PATENT FILING TRENDS

A general patent search for patents claiming vaccines and either including or excluding animal health was conducted using Questel's Orbit IP to compare filing trends in both fields. Between 2000 and 2018 there is an increase in patents filed relating to both human and animal vaccines, aligning with the size of the market opportunity. However, there are significantly more patents filed, both pending and granted relating to human health compared to animal health. Data for 2019 and 2020 have not been included due to the delay between patent filing and publication.

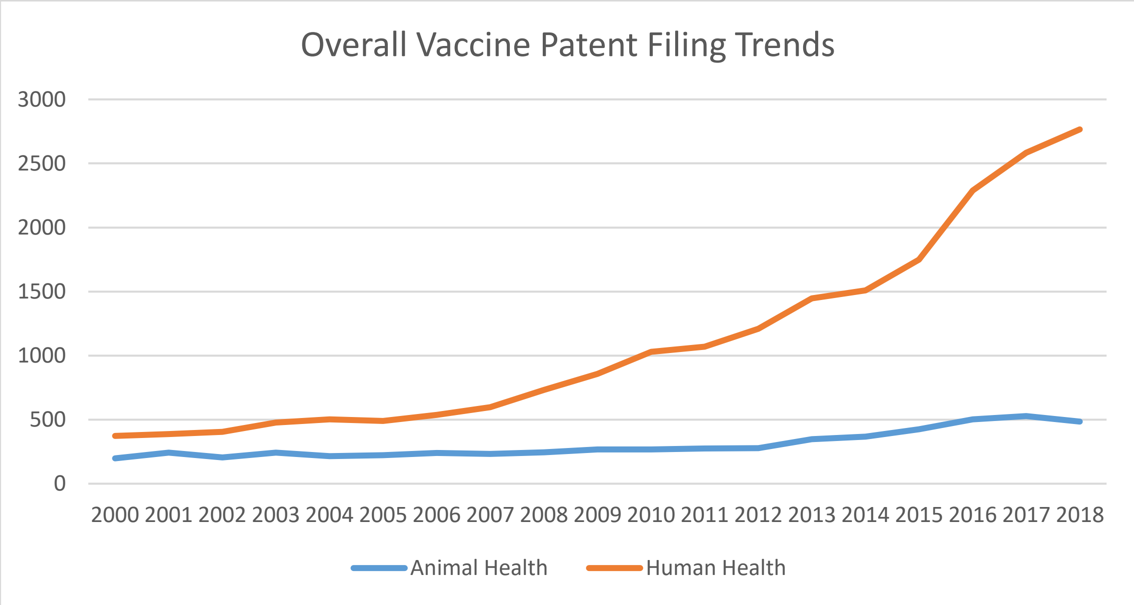

Figure 32. Vaccine patent filing trend between 2000-2018 in human and animal vaccines.

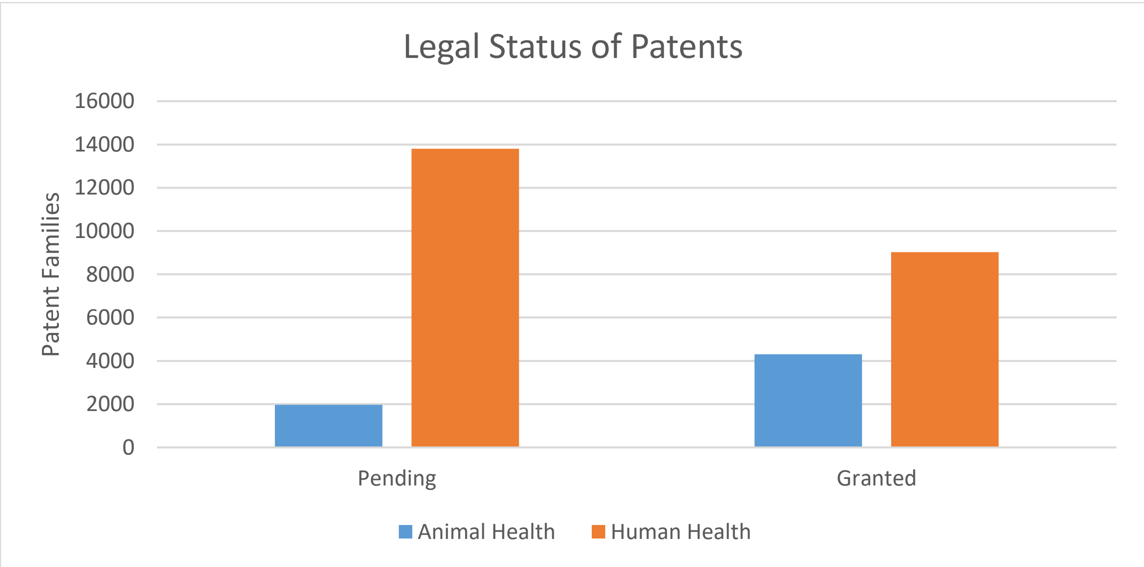

Figure 33. Legal status of patents in animal and human vaccines.

8.2 KEY PLAYERS

When looking at patent filing trends in animal and human vaccines the top assignees can identify the key players. In animal health, these key players include Boehringer Ingelheim Animal Health, Merck and Zoetis. In human health the top assignees include GlaxoSmithKline, Merck and the US Department of Health & Human Services.

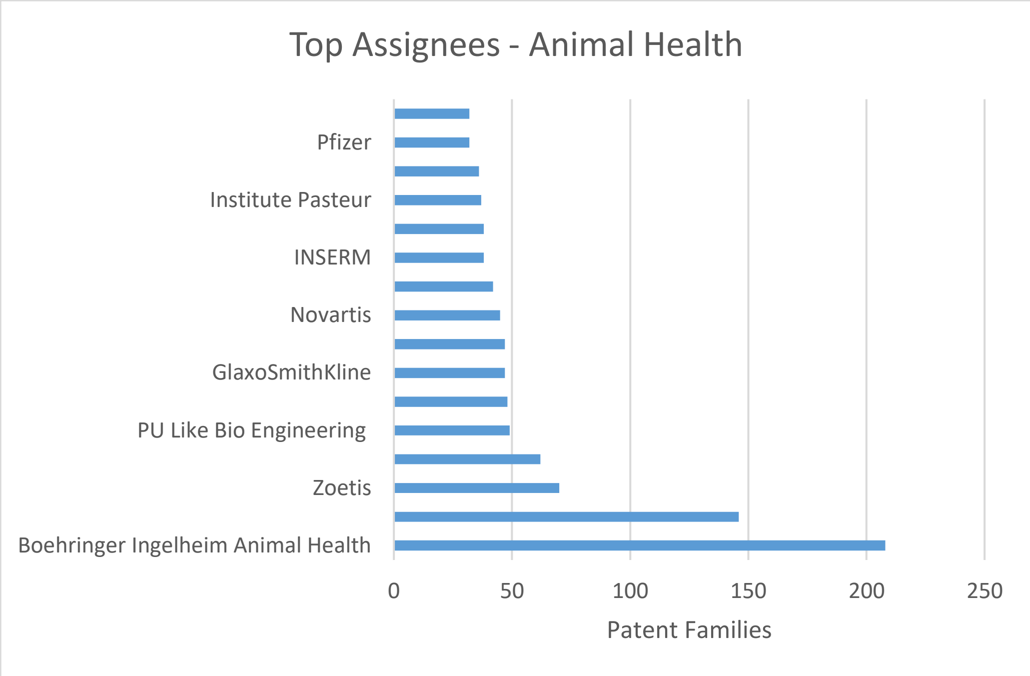

Figure 34. Top assignees for animal vaccine patents.

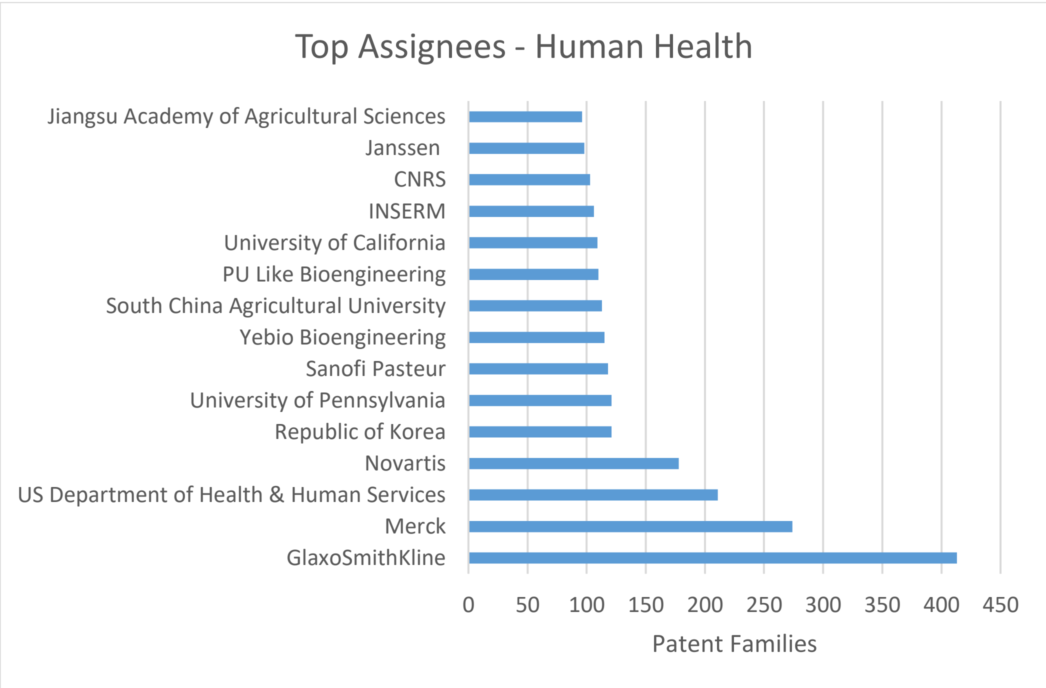

Figure 35. Top assignees for human vaccine patents.

8.3 GEOGRAPHICAL ANALYSIS

The global market coverage for patents for in both human and animal health has a similar pattern, with patents filed broadly in all key markets.

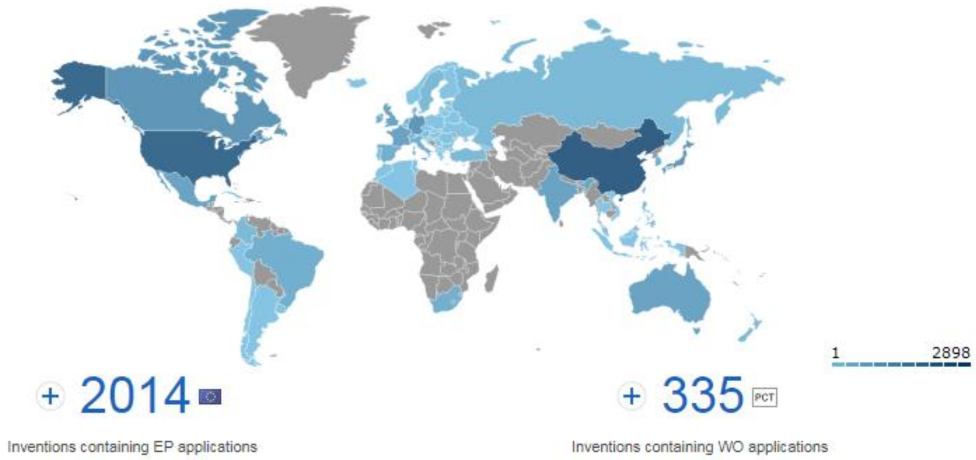

Figure 36. Animal vaccine market coverage of patents by protection country.

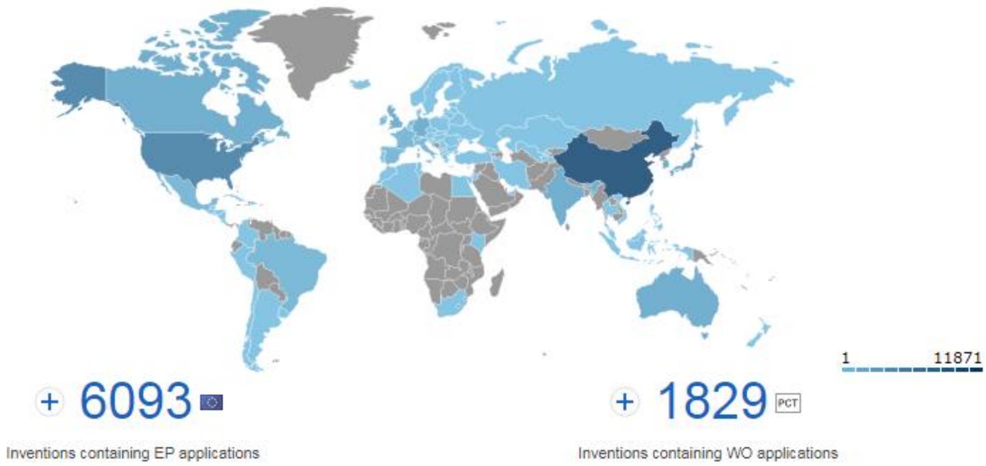

Figure 37. Human vaccine market coverage of patents by protection country.

In both human and animal health the top 5 patent markets are the same. These include: China, USA, Europe, Japan and Canada; although China has a larger percentage of patents filed in human health than animal health.

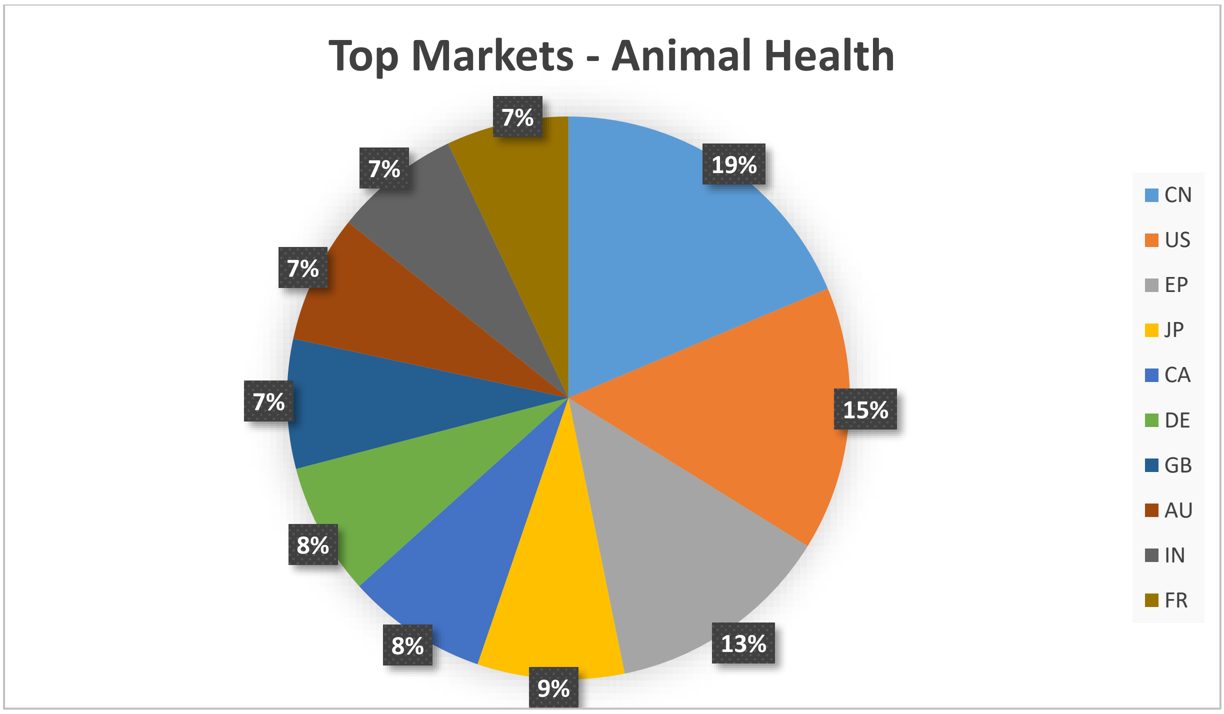

Figure 38. Top markets for animal vaccine patents.

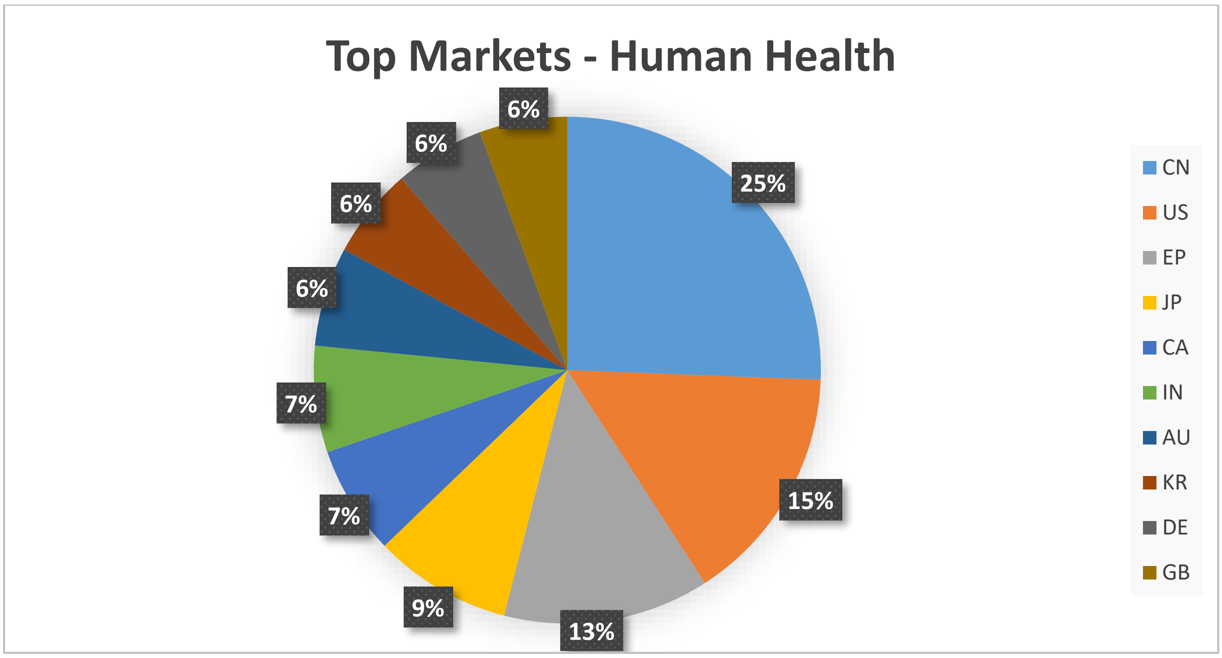

Figure 39. Top markets for human vaccine patents.

The top priority countries can be analysed to see where the patent applications are initially filed. This can be a good indication of the countries where the majority of research and innovation in a particular technology field is taking place since organisations generally file patent applications first in the local territories where their research bases are located. Likewise, for universities the priority country will usually tend to be the country in which they are based.

For animal health patents, the top priority countries/regions include the United States, China, Europe, and Australia. These are compared in the figure below to the top countries where patents are subsequently filed for protection.

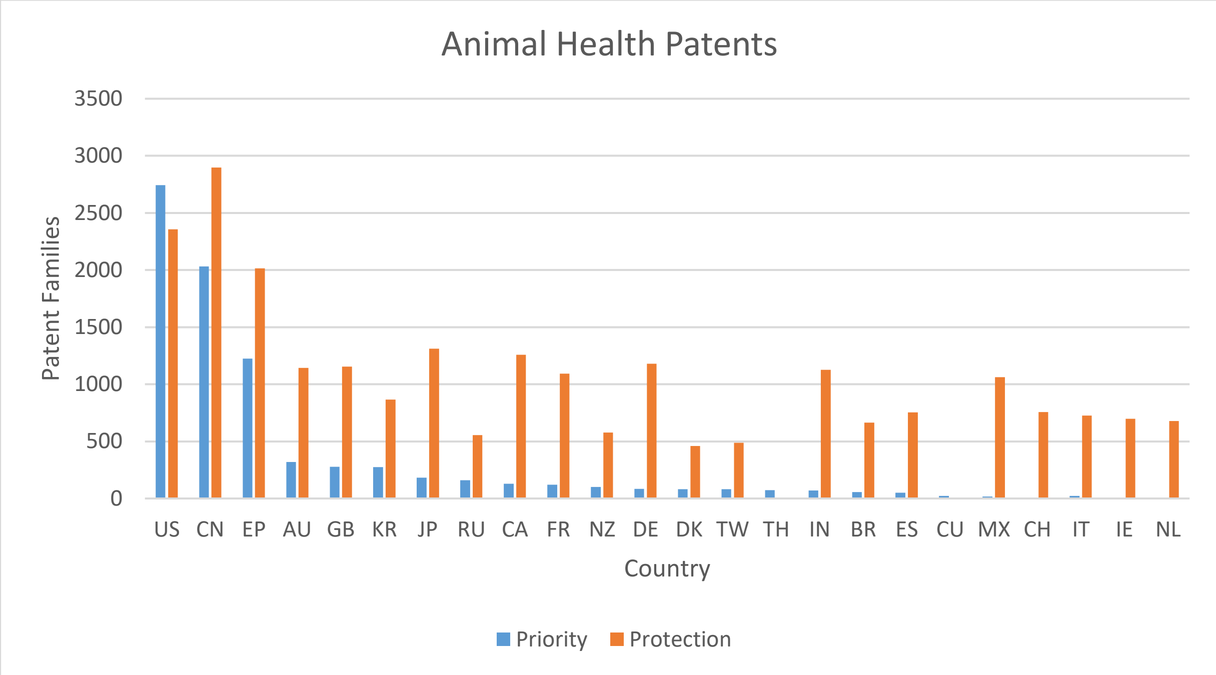

Figure 40. Animal vaccine patents comparing priority and protection countries.

In human health the top priority countries include China, the United States, Europe, Japan and Korea (see figure below).

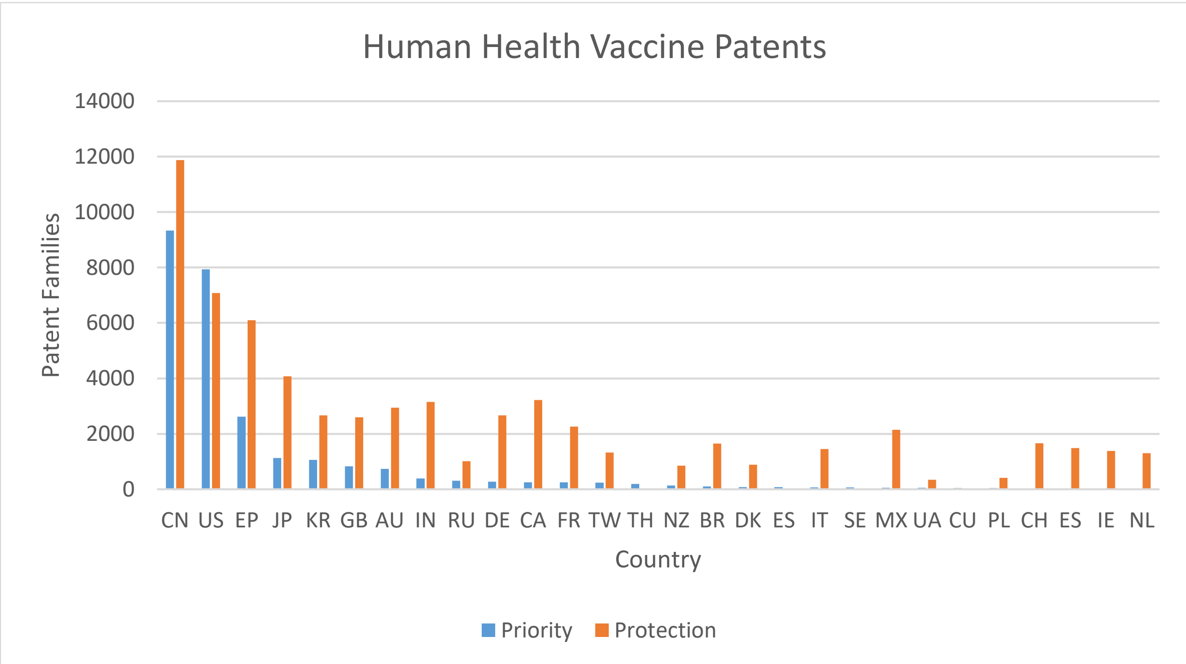

Figure 41. Human vaccine patents comparing priority and protection countries.

8.4 KEY TECHNOLOGY AREAS

Patents were analysed by technology area to understand where the focus is within both sectors in terms of the underlying vaccine technologies being developed. In both human and animal health the majority of patents mention nucleic acid, reflecting that this key term may also be mentioned in patents for other vaccine platforms. Next are patents that mention inactivated or attenuated vaccines followed by patents mentioning conjugate vaccines. In the coming years there is likely to be an increase in patents in areas such as subunit and VLP vaccines judging by research trends.

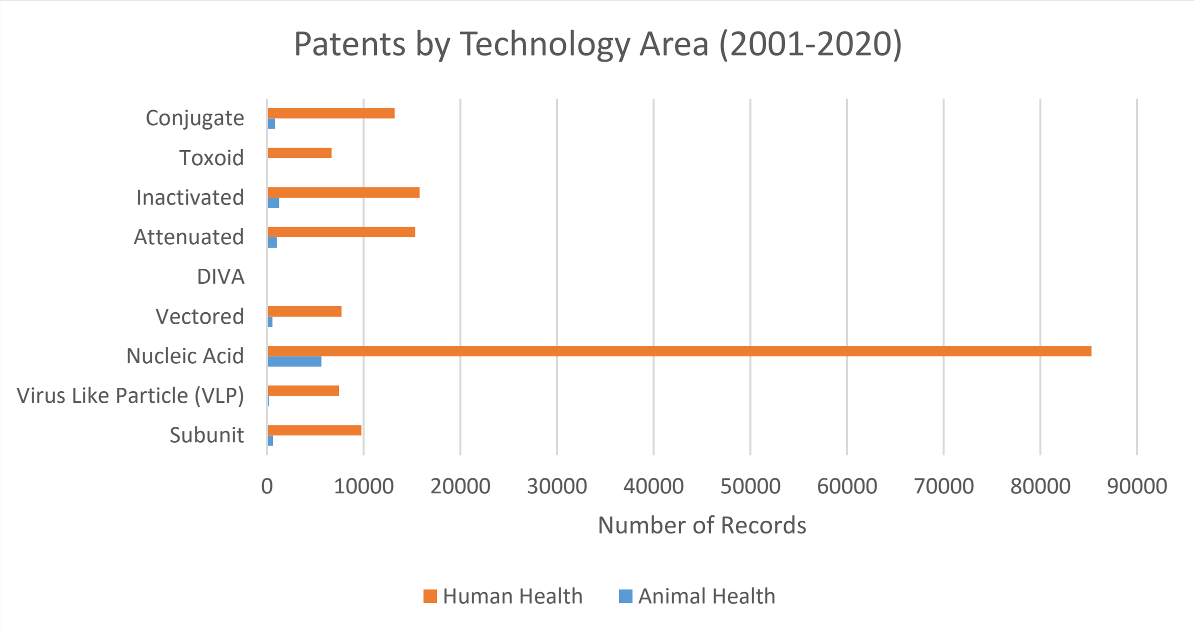

Figure 42. Comparison of patents by technology area for both human and animal vaccines.

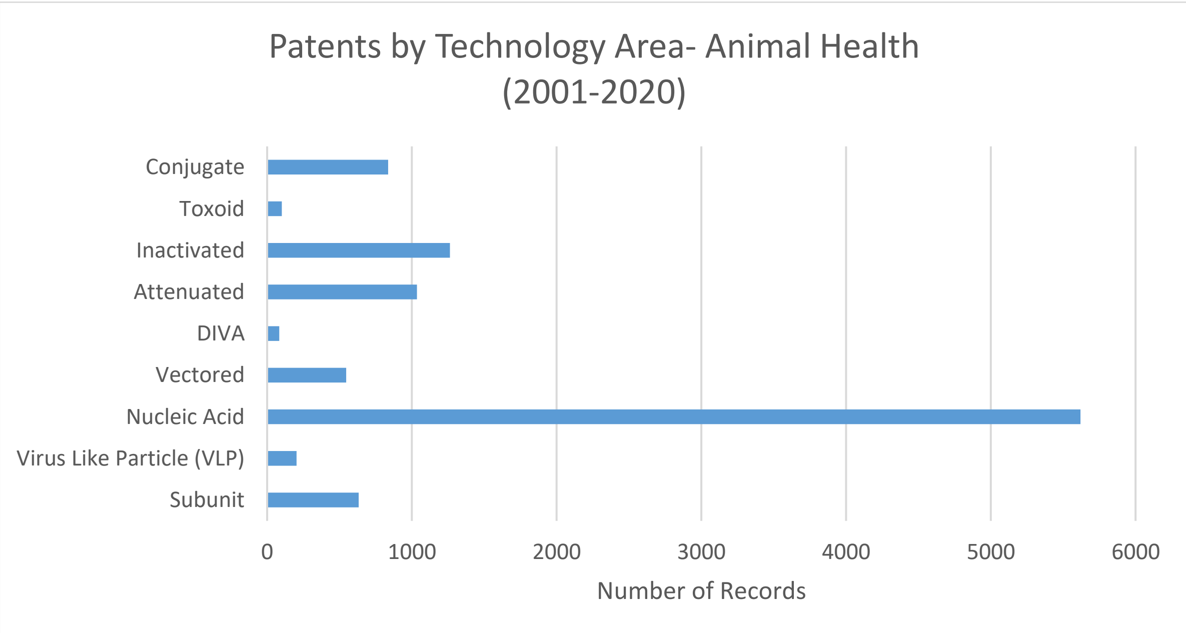

Figure 43. Animal vaccine patents by technology area.

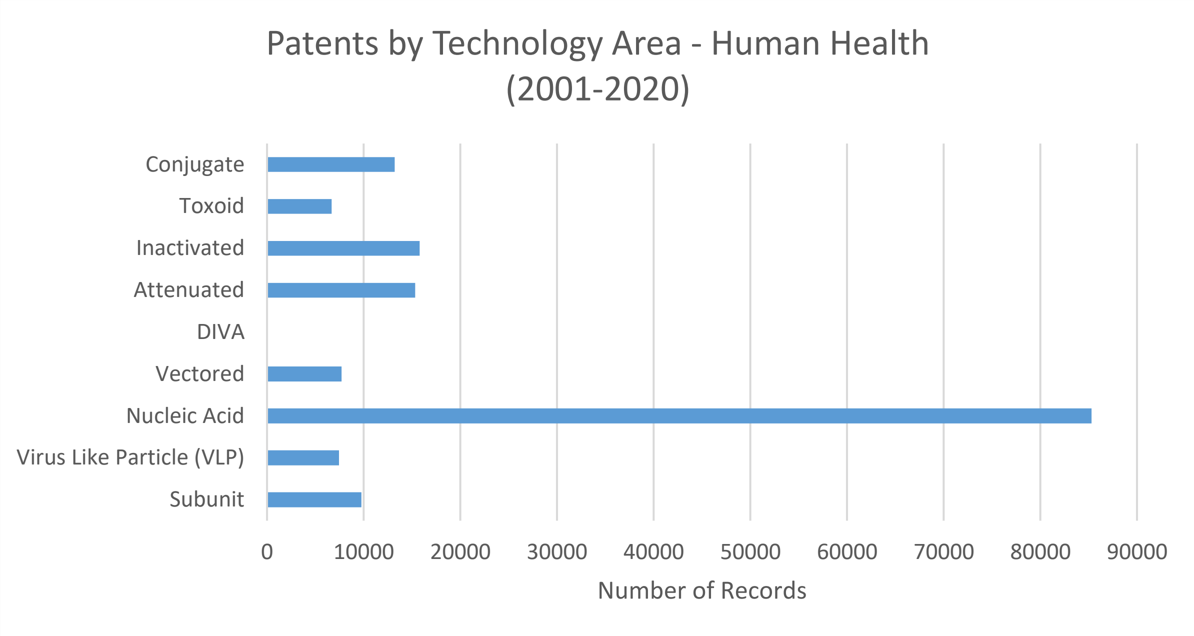

Figure 44. Human vaccine patents by technology area.

8.5 MARKET LEADERS PATENTS

The patents for each market leader were analysed based on different vaccine technology. With the acquisition of Merial, Boehringer Ingelheim is the clear leader in the animal vaccine market by patent number. Their patent portfolio covers a wide range of vaccine technologies including Subunit, VLP, Nucleic Acid, DIVA, Attenuated, Inactivated, Toxoid and Conjugated vaccines.

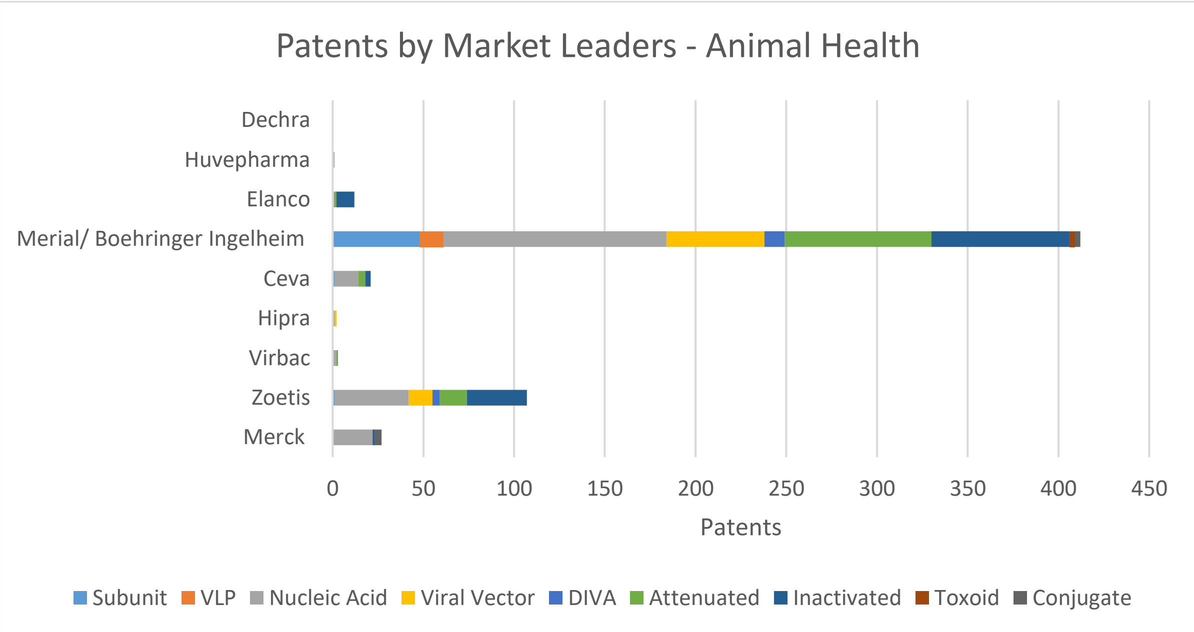

Figure 45. Patents by market leaders in animal vaccines split by vaccine type.

In human health, the top 3 players Merck, GlaxoSmithKline and Pfizer all have large vaccine patent portfolios spanning all vaccine technology areas.

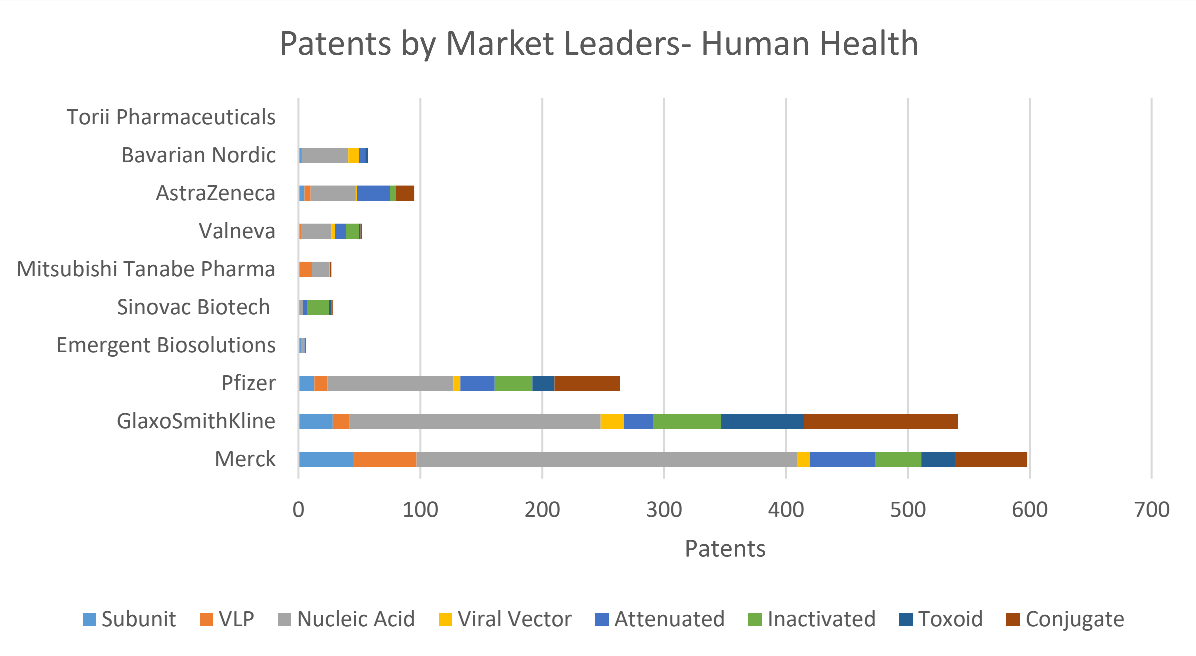

Figure 46. Patents by market leaders in human vaccines split by vaccine type.

There were a number of patents highlighted in the broad vaccine searches for both human and animal health that did not fall into any of the specific technology areas. For these patents the majority referenced vaccine composition, administration or formulation.

8.6 ASSIGNEE PATENT STRENGTH

In the following figure, the strength of an assignee's patent portfolio can be benchmarked by comparing the number of forward citations (vertical axis) (forward citations are where a patent is referred to by a later filed patent) relative to the average age of the portfolio (horizontal axis). Portfolios positioned further to the right side of this graph correspond to pioneers in the area studied. A position at the top right is indicative of a pioneer with a strong impact on the field studied (potential blocking player). The portfolios further to the left side of this chart are the portfolios of the newcomers. A position at the top left corresponds to a later entrant into the space who quickly became important in the field (strong impact). The size of the bubbles corresponds to the number of families that have at least one family member issued. The larger the bubble, the greater the crowd/competition potential within the sector

Using this analysis for animal vaccine patents highlights five companies (Novartis Animal Health (now part of Elanco), GlaxoSmithKline, Merck, Zoetis and Boehringer Ingelheim) as being influential players in this sector. Interestingly, there are no newer entrants who have become important in the field, highlighting the dominance of the established large global players.

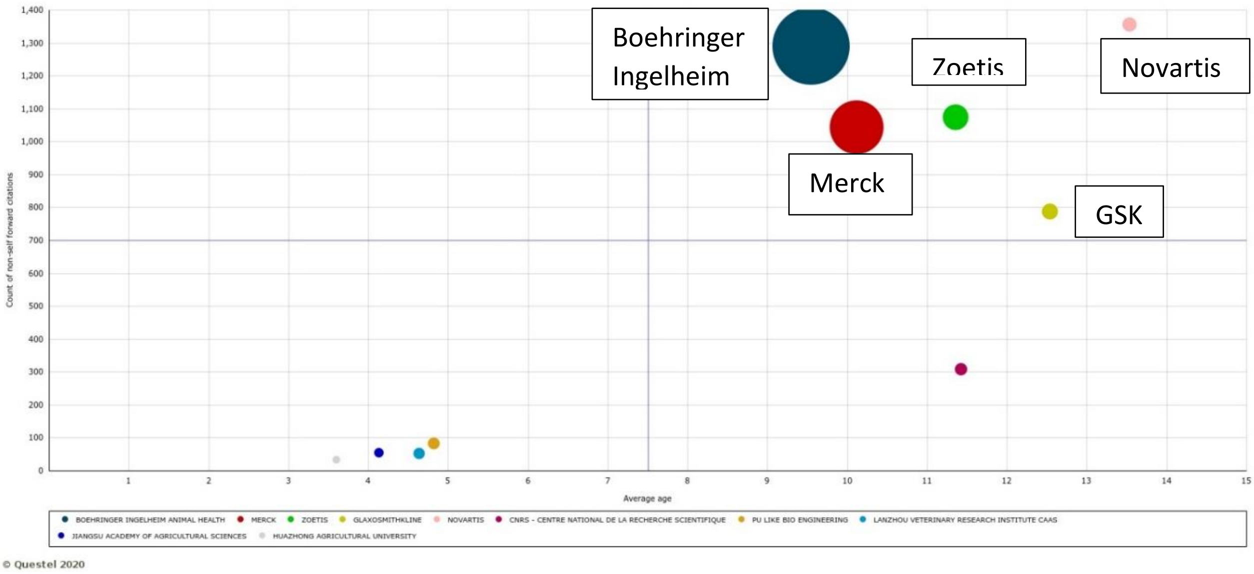

Figure 47. Animal vaccine assignee indicators.

In the human vaccine sector GlaxoSmithKline is the main company highlighted as influential by the assignee indictor.

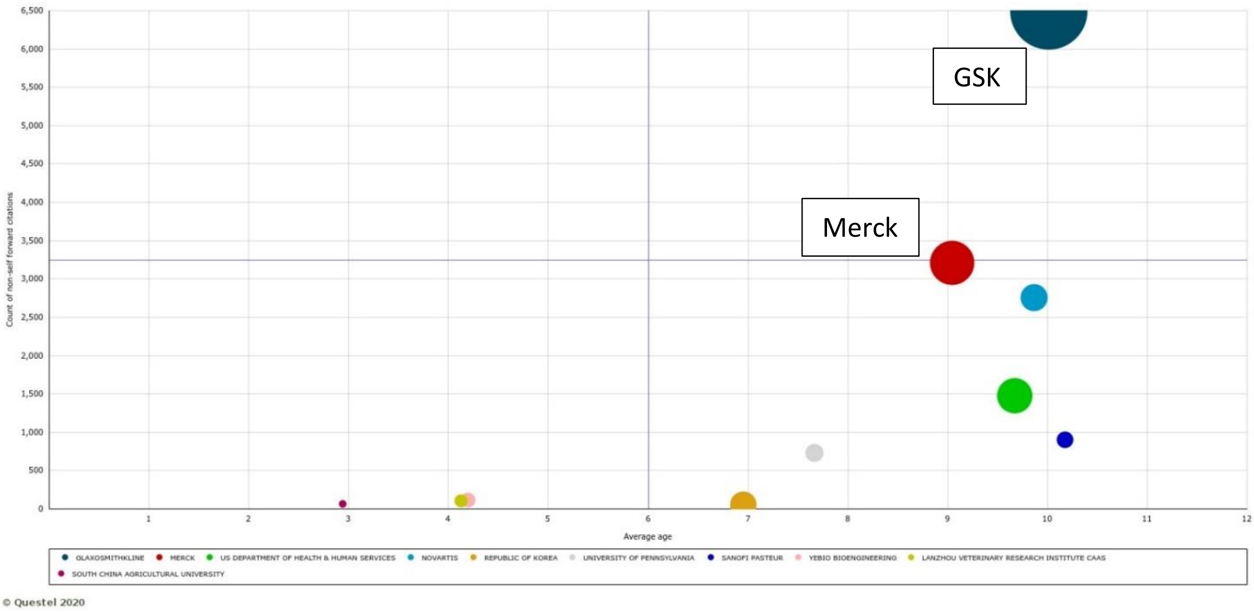

Figure 48. Human vaccine assignee indicators.

As with the animal vaccine market, there are **no newer entrants** who have become important in the human vaccine field.

9. CASE STUDIES

The rise of two deadly diseases COVID-19 in humans and African Swine Fever (ASF) in pigs illustrates the challenges and opportunities to develop vaccines to emerging threats.

9.1 COVID-19

In 2019, a novel coronavirus was identified in China that had not been seen in humans previously. The disease caused by the virus has been termed COVID-19 and has ranged from mild symptoms including fever, cough and shortness of breath to severe respiratory illness and death. It is known to be transmitted between people in close contact, via respiratory droplets when an infected individual coughs or sneezes. It is also possible that it could be spread by contact with infected surfaces or objects. There is currently no vaccine to COVID-19[84]. On 11th March 2020 the WHO characterised COVID-19 as a pandemic.

Global Responses

European Commission

- The Commission, with support from relevant EU agencies, is providing technical guidance related to: risk assessments; case definition for diagnosis and aligned reporting of suspected and confirmed cases; infection prevention and control in health care settings; advice for travellers; updated information on therapeutics and vaccines; contact tracing on aircrafts; management of points of entry and aviation sector recommendations.

- To boost global preparedness, prevention and containment of the virus, new funding worth €232 million will be allocated to different sectors, namely:
  - €114 million will support the World Health Organization (WHO), in particular the global preparedness and response global plan. This intends to boost public health emergency preparedness and response work in countries with weak health systems and limited resilience.
  - €15 million are planned to be allocated in Africa, including to the Institute Pasteur Dakar, Senegal to support measures such as rapid diagnosis and epidemiological surveillance.
  - €100 million will go to urgently needed research related to diagnostics, therapeutics and prevention, including €90 million through the Innovative Medicines Initiative, a partnership between the EU and the pharmaceutical industry.
  - €3 million allocated to the EU Civil Protection Mechanism for repatriation flights of EU citizens from Wuhan, China.

The Commission, with relevant EU agencies, is actively engaged in the arena of therapeutics and vaccine developments. At this stage, the Commission is focusing its funding efforts on research with a timely impact on the current public health emergency due to COVID-19, including on the development of diagnostics and therapeutics. This is in line with the Commission's emergency research funding of €10 million that was made available at the early stages of the outbreak.

Through the Horizon 2020 programme the European Commission has also increased the original €10 million to €47.5 million for COVID-19 research, in addition to public and private funding of €140 million for research on vaccines, diagnosis and treatment. Finally, the Commission offered up to €80 million to CureVac to scale up development and production of a coronavirus vaccine in Europe.

The Coalition for Epidemic Preparedness Innovations (CEPI)

- CureVac and CEPI extend their Cooperation to Develop a Vaccine against Coronavirus COVID-2019
- CEPI and GSK collaborate to strengthen the global effort to develop a vaccine for COVID-19
- UK Government supports CEPI with £20 million additional funding
- CEPI launches new call for proposals to develop vaccines against novel coronavirus COVID-19
- Norway provides NOK 36 million additional funding to CEPI in response to COVID-19
- Ethiopia funds Coalition for Epidemic Preparedness Innovations to combat spread of epidemics
- CEPI will invest a further $4.4 million through a partnering agreement with Novavax Inc and The University of Oxford.
- CEPI received a further €140 million funding from The German Government's Federal Ministry of Education and Research to accelerate the vaccine development against COVID-19
- CEPI partners with the University of Hong Kong to develop a COVID-19 vaccine, investing and initial $620,000, which brings CEPI's total investment in COVID-19 vaccine R&D to $24.3 million.

Other responses

- Clover and GSK announce research collaboration to evaluate coronavirus (COVID-19) vaccine candidate with pandemic adjuvant system
- Johnson & Johnson expands US partnership for coronavirus treatments
- GeoVax, a US-based pharmaceutical company, and BravoVax, a China-based pharmaceutical company, have announced plans to develop a coronavirus cure in the form of vaccine based on the former's MVA-VLP vaccine platform.
- iBio and CC-Pharming have formed a partnership to develop a plant-derived coronavirus vaccine based on the former's FastPharming System™, which has been previously used for producing antibody candidates for Ebola and Dengue fever viruses.
- Rome-based biotech companies, Takis and Evvivax have announced their plans to develop a vaccine against Covid-19. The companies will use genetic vaccination technologies that are capable of generating several antibodies to neutralise viruses and stronger immune response.
- Regeneron Pharmaceuticals signed an agreement with the U.S. Department of Health and Human Services (HHS) to develop new coronavirus drugs. The company will utilise its VelociSuite® technologies comprising of the VelocImmune® platform that uses a genetically-engineered mouse with a humanised immune system. The platform can be used to quickly identify, validate, and development antibody candidates.
- Sanofi Pasteur to develop COVID-19 vaccine with US government.

Research & Development for COVID-19

As a result of COVID-19 world experts and funders have set priorities for COVID-19 research and development. The WHO held a meeting in conjunction with the Global Research Collaboration for Infectious Disease Preparedness, to discuss all aspects of the outbreak and methods of controlling it, including:

- The natural history of the virus, its transmission and diagnosis
- Animal and environmental research on the origin of the virus, including management measures at the human-animal interface
- Epidemiological studies
- Clinical characterization and management of disease caused by the virus
- Infection prevention and control, including best ways to protect against the virus
- Research and development for candidate therapeutics and vaccines
- Ethical considerations for research
- Integration of social sciences into the outbreak response

R&D efforts to investigate potential vaccine candidates for COVID-19

COVID-19 is similar to that of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) in its pathogenicity, clinical spectrum and epidemiology. Ongoing research:

- Imperial College London, have started testing a vaccine against COVID-19
- Jenner Institute at the University of Oxford are testing a coronavirus vaccine in collaboration with Advent, which is based on their ChAdOx1 vector. ChAdOx1 nCoV-19 is currently being prepared for clinical testing

Clinical Trial analysis for COVID-19

A search of the GlobalData database showed as of Friday 20th March 2020, 308 clinical trials for COVID-19, 172 of these were ongoing, 127 planned, 2 completed and 7 suspended or withdrawn. These ranged from Phase 0 to Phase IV trials. The top 10 sponsors for these clinical trials are outlined below.

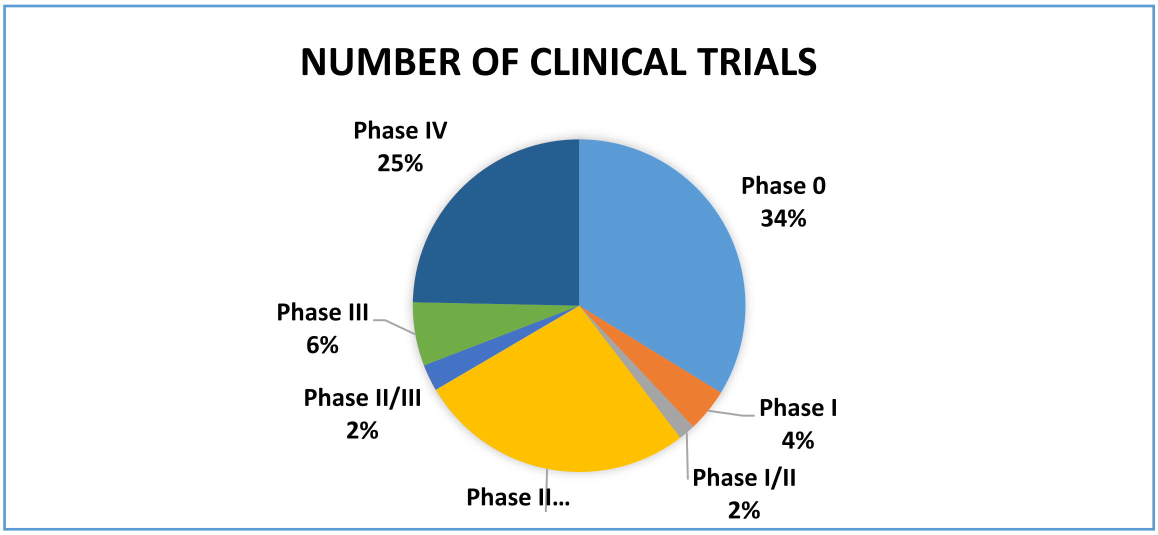

Figure 49. Number of clinical trials relating to COVID-19 by Phase

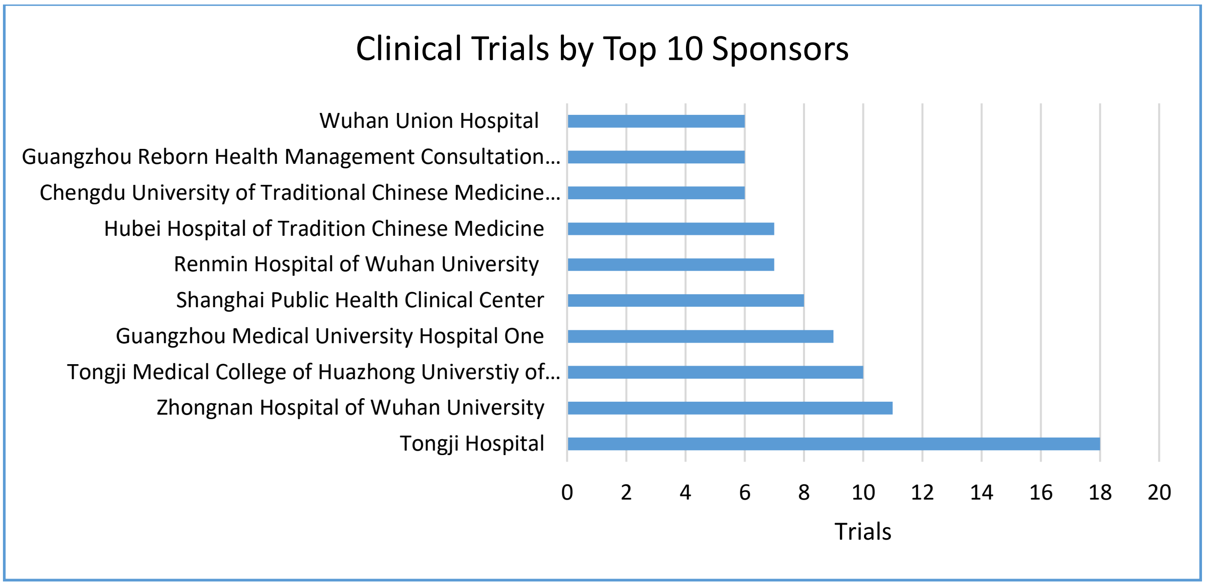

Figure 50. Top 10 sponsors of COVID-19 clinical trials

Of these 308 clinical trials there are 7 trials planned for prophylactic COVID-19 vaccines, with 5 Phase I trials, 1 Phase I/II and 1 Phase IV trial planned or ongoing. Of the phase I studies one is sponsored by Novavax Inc, which is estimated to start in May 2020. The vaccine candidate was created using its proprietary recombinant protein nanoparticle technology platform to generate antigens derived from coronavirus spike (S) protein, with the addition of their Matrix-M™ adjuvant, which is expected to boost immune responses. Three of the Phase I studies are sponsored by Inovio Pharmaceuticals Inc surrounding the DNA Vaccine INO-4800. The Phase I/II study is sponsored by Expres2ion Biotechnologies ApS assessing a COVID-19 vaccine being developed based on Drosophila S2 insect cell expression systems and virus-like particle technology, it is expected to start within the next 12 months.

Studies currently recruiting and ongoing include a safety and immunogenicity study of 2019-nCov Vaccine (mRNA-1273) sponsored by the National Institute of Allergy and Infectious Diseases. It is a phase I trial thought to continue through to June 2021. mRNA-1273 is an mRNA-based vaccine designed to express the coronavirus spike (S) protein, based on the genomic sequence of COVID-19. It has been developed based on messenger RNA based vaccine technology, and is administered through intramuscular route as lipid nanoparticle (LNP). The final trial ongoing currently is a Phase IV trial sponsored by Guangxi Medical University and the People's Hospital of Nanning 4. It will look at the basic and clinical study of inhalation of inactivated mycobacterium vaccine in the treatment of COVID-19.

9.2 AFRICAN SWINE FEVER (ASF)

African Swine Fever Virus (ASFV) is a severe viral disease affecting both domestic and wild pigs with no licensed vaccine, resulting in severe production and economic losses. Transmission is possible through both live and dead animals, via contaminated feed and fomites.

ASFV is endemic in Africa, and outbreaks have previously been reported in Europe, South America, the Caribbean and Asia. In August 2018 the Ministry of Agriculture and Rural Affairs (MARA) confirmed the first ASFV outbreak in China. There has since been 165 outbreaks detected in China, with up to 40% of China's approximate 400 million pigs being lost as a result[85,86,87,88]. **Vaccine**

- ASFV has up to 100% mortality rate in domestic pigs
- No treatment or licenced vaccines against ASFV
- ASFV endemic in Africa
- Outbreaks reported in Europe, South America, the Caribbean and Asia
- Losses in China equivalent to Europe's entire pig industry
- Novel vaccine development strategies are required to develop an effective vaccine

ASFV Timeline

1921:
ASFV first described in 1921 in Kenya and remained in Africa until 1957

1957
First reported in Lisbon, Portugal, the disease then became established in the Iberian peninsula. Outbreaks continued in these regions until it was eradicated in 1995, except in Sardinia where the disease remains endemic

2007:
ASFV outbreak occurs in Georgia and subsequently spreads across Russia, Ukraine and Belarus

2014
ASFV spread to the EU Baltic States and Poland

September 2016
ASFV outbreaks occur in Moldova

June-July 2017
ASFV outbreaks in Czech Republic, followed by Romania.

April 2018
Outbreak of ASFV in Hungary, followed by Bulgaria in August 2018

August 2018
ASFV entered China. This is of particular significance as China had around 45% of the world's pig population (~435 million pigs)

September 2018
Recurrence of ASFV in wild boar in Belgium

January - March 2019
Mongolia reported ASFV in January, followed by Vietnam in February and Cambodia in March.

May 2019
ASFV reported in Hong Kong

Development Strategies

With a pressing need to develop an effective vaccine against ASFV many approaches are being taken.

Understanding immune evasion & determinants of immune protection

In order to develop a successful vaccine against ASFV, it is paramount to understand the immune evasion mechanisms of ASFV, as well as the determinants of immune protection. ASFV has evolved multiple immune evasion mechanisms to establish infection in the host, and modulate the host immune response. A number of immune evasion mechanisms have been identified including the inhibition of type I interferon, apoptosis, NF-κB, lymphocyte proliferation, TLR signalling and modulation of MHC class I antigen expression.

To date research has shown the protective immune response to be both cell and antibody mediated, the limited understanding of the immunogenicity of ASFV proteins further hinders successful vaccine development.

ASF vaccine strategies

Inactivated vaccines

Although inactivated vaccines have been successful against other viral infections, inactivated ASFV vaccines have failed to induce protection, even in conjunction with a range of adjuvants. This is due to their inability to induce a sufficient cellular immune response.

Live/Naturally attenuated vaccines

The immunisation of animals with naturally attenuated ASFV conferred protection with related virulent strains. This research highlighted the potential for attenuated vaccine development against ASFV. Live attenuated vaccines have been developed through deletion of specific genes that have been identified as having potential roles in ASFV virulence and modulation of the immune response. Some of these experimental vaccines that have shown initial promise are outlined below.

Subunit vaccines

Subunit vaccines have been shown to confer partial protections against ASFV. Subunit vaccines are a safer, more specific vaccine approach. Several different subunit vaccines have been designed against ASFV. Proteins such as p54, p30, p72, pp62 and CD2v have been described as potentially immunogenic. DNA (nucleic acid) vaccines have been shown to be a potential alternative vaccine platform, due to the fact DNA vaccines have been shown to have greater immunogenicity through the important activation of CD8 T cells. In the case of ASF, subunit vaccines show great promise, although there is still the need for further development to provide a sufficient protective response.

Table 2 Experimental attenuated vaccines

Experimental Vaccine	Target Gene(s)	Outcome
NH/P68ΔA238L	A238L	Protection against homologous challenge
NH/P68ΔA224L	A224L	Protection against homologous challenge
NH/P68ΔEP153R	EP153R	Protection against homologous challenge

Experimental Vaccine	Target Gene(s)	Outcome
BeninΔMGF	MGF360/530/505	Protection against homologous challenge
BeninΔDP148R	DP148R	Protection against homologous challenge
BA71ΔCD2	CD2v (EP402R)	Protection against homologous & heterologous challenge
ASFV-G-Δ9GL/UK	9GL and UK	Protection against homologous challenge
Pret4Δ9GL	9GL	Protection against homologous challenge
ASFV-G-ΔMGF	MGF360/505	Protection against homologous challenge
ASFV-G-Δ9GLv	9GL	Protection against homologous challenge
OURT88/3	Naturally Attenuated	Protection against homologous challenge
NH/P68	Naturally Attenuated	Protection against homologous challenge
Lv17/WB/Rie 1	Low virulence	Protection against virulent challenge
E75CV1	Cell culture adapted	Protection against homologous challenge

<u>The future of vaccine development</u>

The ability to maintain ASF-free status is critical for the pork industry. With no known cure or vaccine, ASFV has historically been controlled by quarantine and culling of affected animals, at great cost to the industry. With the outbreak of ASFV in China putting 48% of the world's pork production at risk the need for a vaccine against ASFV is at an all-time high. One consideration of the future vaccines developed for ASFV needs to be the ability to differentiate infected from vaccinated animals (DIVA), in order to identify ASF free countries following vaccination programmes.

APPENDIX 1

Companion Animal Vaccines[42]

Product	Target Species	Indication	Manufacturer
Calvenza	Horses	Equine rhinopneumonitis, influenza	Boehringer Ingelheim
Rabisin	Dogs, Cats	Rabies	
Raboral V-RG	Raccoons, coyotes	Rabies	
Rhinomune	Horses	Equine rhinopneumonitis	
Strepvax II	Horses	Strangles (Streptococcus Equi)	
Tetguard	Horses	Tetanus	
Vetera	Horses	Equine Influenza	
RecombiTEK Lyme	Dogs	Borrelia Burgdorferi	
RecombiTEK	Dogs	Distemper, Adenovirus Type 2, Coronavirus, parainfluenza, parvovirus, leptospira	
Imrab	Dogs, Horses	Rabies	
PureVax	Cats	Feline Leukemia, Feline Panleukopenia, Respiratory disease, Rabies	
Potomavac	Horses	Potomac horse fever	
RecombiTEK Equine	Horses	West Nile virus, eastern equine encephalitis, western equine encephalitis, tetanus, rabies	
Equine Coli Endotox	Horses	*E.coli*	Elanco
Fel-O-Guard	Cats	Feline panleukopania virus, feline leukemia viru, feline calicivirus, herpesvirus, rabies, chlamydia felis	
Rabvac 3	Dogs, Cats, Horses	Rabies	
Duramune	Dogs	Distemper, adenovirus, parvovirus, coronavirus, *L.canicola*, *L.grippo, L.icetero, L.pomona,* Lyme, leptospirosis	
Brinchi-Shield	Dogs	Bordetalla bronchiseptica	
Encevac	Horses	Eastern, Western and Venezuelan equine influenza, encephalomyelitis and tetanus	Merck
Equirab	Horses	Rabies	
Flu-Avert	Horses	Equine Influenza	
EquineNile	Horses	West Nile Virus	
Nobivac	Canine	Rabies, Lyme disease, distemper, parvovirus, canine respiratory infections	
Nobivac	Cats	Rabies, feline bordetalla, feline rhinotracheitis, calicivirus, and panleukpenia	
Nobivac	Rabbits	Myxomatosis, rabbit haemorrhagic disease	
Prestige	Horses	Encephalomyelitis, equine herpes virus, equine influenza and tetanus.	
Prodigy	Horses	Equine herpesvirus EHV-1	
Super-Tet	Horses	Tetanus	
Equilis Prequenza	Horses	Equine influenza	
Canvac	Dogs	Bordetella, distemper, adenovirus, parvovirus, parainfluenza	Zoetis
Core EQ Innovator	Horses	Rabies, tetanus, West Nile, eastern and western equine encephalitis	
Defensor	Cats, Dogs	Rabies	
Duvaxyn EHV1, 4	Horses	Equine Herpes Virus	

Product	Target Species	Indication	Manufacturer
Duvaxyn R	Horses	Equine Rotavirus	
Equivac HeV	Horses	Hendra Virus	
Felocell	Cats	Feline panleukopenia, feline viral rhinotracheitis, feline calicivirus and/or Chlamydia psittaci	
Fevac 4	Cats	Feline panieucopenia, feline rhinotracheitis, feline calcivirus, Chlamydophila psittaci	
Fevac 5	Cats	Feline panieucopenia, feline rhinotracheitis, feline calcivirus, Chlamydophila psittaci, feline leukemia	
FluVac Innovator	Horses	Respiratory disease	
Leukocell 2	Cats	Feline Leukaemia	
LymeVax	Dogs	Lyme disease	
Pinnacle I.N.	Horses	Stangles caused by S.equi	
Vanguard/Vanguard Plus	Dogs	Canine influenza virus, bordatella, coronavirus, canine respiratory disease, lyme disease, distemper, adenovirus, parainfluenza, leptospirosis	
West Nile Innovator/Equip WNV	Horses	West Nile Virus	

Livestock vaccines:

Product	Target Species	Indication	Manufacturer
Alpha	Cattle	Clostridial diseases	Boehringer Ingelheim
Aftopro, Aftovaxpur, Aftovax, Afrobov Oleosa, Aftovaxpur DOE	Livestock	Foot and mouth disease (FMD)	
Bar-Guard	Cattle	*E.coli*	
Bar-vac	Cattle, Sheep, Goats	Tetanus, enterotoxemia, BVD, IBR, BRSV	
BO-BAC-2X	Cattle	Arcanobacterium pyogenes, *E.coli* pasteurella multocida, salmonella typhimurium	
Bovela	Cattle	Bovine viral diarrhea virus (BVDV) types 1 and 2	
Caliber	Cattle	Clostridial diseases	
Citadel	Cattle	Leptospiosis	
Enterisol Ileitis	Swine	Ileitis	
Enterisol Salmonella	Swine	Salmonella	
Express	Cattle	BVDV, Bovine RSV, Infectious Bovine rhinotracheitis, para influenza	
Flex family	Swine	Respiratory diseases	
Ingelvac (Mycoflex, Provenza, Circoflex, PRRS, PRRSFLEX, ReprocycPRRS)	Swine	Bordetella, pseudorabies virus pneumonia, progressive atrophic rhinitis (PAR), mycoplasma hyopneumoniae, and respiratory and reproductive form of porcine reproductive and respiratory syndrome (PRRS) virus, porcine circovirus disease (PCVD)	

Product	Target Species	Indication	Manufacturer
Gallimune/Gallivac/Volvac	Poultry	Avian influenza, Newcastle disease, avian coryza, egg drop syndrome, infectious bronchitis, infectious bursal disease, gallibacterium anatis	
Pyramid/Presponse	Cattle	Respiratory Disease	
Prevexcion RN	Poultry	Marek's Disease	
ReproCyc	Swine	Erysipelothrix rhusiopathiae, leptospira canicola, grippotyphosa, hardjo, icterochaemorrhagiae, pomona bacterin, parvovirus, PRRS	
Reprocyc ParvoFLEX	Swine	Porcine parvovirus	
BTVPUR AlSap 8	Cattle	Bluetongue virus	
Vaxxitek	Poultry	Infectious bursal disease (IBD) virus, Marek's disease	
Avinew/Avinew NeO	Poultry	Newcastle disease virus (NDV)	
Newxxitek HVT+ND	Poultry	Newcastle disease virus (NDV), Marek's disease	
AviPro	Poultry	Salmonella typhimurium, salmonella enteritidis, salmonella heidelberg, Newcastle disease, infectious bronchitis, fowl cholera, mycoplasma gallisepticum	Elanco
Denagard	Swine	Dysentery	
Master Guard	Cattle	Reproductive and respiratory diseases	
Scour Bos	Cattle	Rotavirus, coronavirus	
Titanium	Cattle	BVD, IBR, BRSV, PI3, Leptospira	
Vira Shield	Cattle	BVD, BRSV, IBR, PI3	
Vira Shield 6	Cattle	BVD, broad spectrum vaccine for respiratory and reproductive diseases	
Clynav	Aquaculture	Atlantic salmon protection for disease associated with salmonid alphavirus subtype 3 (SAV3)	
Prevacent PRRS	Swine	PRRS	
20/20 Vision 7	Cattle	Pinkeye	Merck
2177	Poultry	Reovirus	
89/03	Poultry	Bursal disease virus	
Aquavac-Col / Aquavac - ESC	Aquaculture	Flavobacterium columnare vaccine	
ART VAX	Poultry	Bordetella avium diseases	
Ava-Pox-CE	Poultry	Fowl Pox	
Bovilis	Cattle	Bovine coronavirus, *E.coli*	
Breedervac	Poultry	Inactivated bursal and REO combination vaccines plus Newcastle disease and respiratory diseases	
Bron-Newcavac-SE	Poultry	Salmonella Enteritidis	
Busa-Vac	Poultry	Infectious bursal disease	
Cavalry 9	Cattle	Diseases in cattle caused by: Clostridium chauvoei, C. septicum, C. novyi type B, C. haemolyticum, C. sordellii, C. tetani, and C. perfringens types C and D.	
Cav-Vac	Poultry	Anemia virus	
Circumvent PCV	Swine	Porcine circovirus type 2	
Circumvent PCV M	Swine	Porcine circovirus type 2 and Mycoplasma hyopneumoniae	
Clonevac	Poultry	Infectious bursal disease	

Product	Target Species	Indication	Manufacturer
Coccivac	Poultry	Live coccidiosis vaccine	
ComboVac	Poultry	Newcastle disease, Massachusetts and Connecticut types infectious bronchitis	
Compact PD	Aquaculture	Salmonid Alphavirus	
Covexin 8	Cattle, sheep	Diseases caused by C. chauvoei, C. septicum, C. novyi type B, C. haemolyticum, C. tetani, and C. perfringens types C and D.	
EnteroVax	Poultry	Avian reovirus	
Guardian	Cattle	Scours	
Innovax	Poultry	Marek's disease, Newcastle disease (ND) and infectious laryngotracheitis (ILT)	
L5 SQ	Cattle	Leptospirosis	
LT-IVAX	Poultry	Laryngotracheitis	
M-Ninevax	Poultry	Fowl cholera	
Magestic 7	Swine	Arvovirus, E. rhusiopathiae and five major Leptospira serovars	
Prime PAC PRRS RR	Swine	PRRS	
Mildvac	Poultry	Bronchitis viruses	
Nasalgen IP	Cattle	Bovine rhinotracheitis-parainfluenza	
Once PMH	Cattle	Respiratory disease	
Oralvax	Poultry	Hemorrhagic enteritis	
Piliguard product line	Cattle	Pinkeye	
Porcilis Ileitis	Swine	Ileitis caused by Lawsonia intracellularis	
ProSystem product line	Swine	Rotaviral diarrhea and TGE	
Super-Tet	Cattle	Tetanus	
Tremvac	Poultry	Infectious anemia	
Univax	Poultry	Bursal disease viruses	
Vision product line	Cattle	Clostridium chauvoei (blackleg), C. septicum (malignant edema), C. sordellii, C. perfringens types C and D (enterotoxemia), C. haemolyticum, C. novyl (Black disease), Haemophilus somnus	
Vista product line	Cattle	IBR virus; BVD virus (type 2); BRSV and as an aid in the control of disease caused by BVD virus (type 1), parainfluenza-3 virus (PI-3), Mannheimia haemolytica and Pasteurella multocida	
VL5 SQ	Cattle	Reproductive diseases	
AE-Poxine	Poultry	Avian encephalomyelitis, fowl pox	Zoetis
Bovi-Shield and Bovi-Shield Gold product lines	Cattle	Prevention of respiratory and reproductive diseases	
Bursaplex	Poultry	Infectious bursal disease	
Bursine-2/Bursine Plus		Infectious bursal disease	
Calfguard	Cattle	Prevention of scours caused by bovine rotavirus and bovine coronavirus infections	
CattleMaster and CattleMaster Gold product line		Prevention of respiratory diseases caused by IBR, persistent infection (PI), BRSV, BVD and/or other infections	
Defensor	Cattle, sheep	Rabies	

Product	Target Species	Indication	Manufacturer
ER Bac Plus/ER BAC L5 Gold	Swine	Prevention of erysipelas and other related diseases	
FarrowSure Gold/FarrowSure Gold B	Swine	Prevention of reproductive failure caused by porcine parvovirus (PPV); erysipelas caused by Erysipelothrix rhusiopathiae; and leptospirosis caused by Leptospira canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae, and L. pomona. FarrowSure GOLD B helps protect against L. bratislava.	
FluSure product line	Swine	Swine influenza	
Fostera		PCV2 / PRRS	
Inforce 3	Cattle	Respiratory disease caused by BRSV, aid in preventing respiratory disease	
Laryngo-Vac	Poultry	Infectious laryngotracheitis	
Litterguard product line	Swine	Scours	
One Shot/One Shot Ultra	Cattle	Prevention of respiratory diseases and clostridial diseases	
Porcine Epidemic Diarrhea Vaccine*	Swine	Porcine epidemic diarrhea virus (PEDv)	
Poulvac product line	Poultry	Infectious bronchitis virus (IBV), infectious burasal disease, Marek's disease, Newcastle disease, E. coli, mycoplasma, salmonella	
PregGuard Gold FP	Cattle	Prevention of respiratory and reproductive diseases	
RespiSure/RepiSure-ONE	Swine	Chronic pneumonia caused by Mycoplasma hyopneumoniae	
Resvac	Cattle	Prevention of respiratory disease	
Scourguard product line		Prevention of scours	
Spirovac		Hardjo-bovis	
Staybred VL5		Prevention of reproductive diseases	
Suvaxyn PCV/Fostera PCV	Swine	Viremia	
TSV-2	Cattle	Prevention of respiratory diseases	
Ultrabac product line	Cattle, sheep	Prevention of clostridial diseases	
Ultrachoice product line		Prevention of clostridial diseases	
Vibrin	Cattle	Prevention of reproductive disease	

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