March 2010



European Vaccine Manufacturers



#### 1. Innovating for public health

- 2. Boosting Europe's competitiveness
- 3. Sustaining Europe's lead in the vaccines field

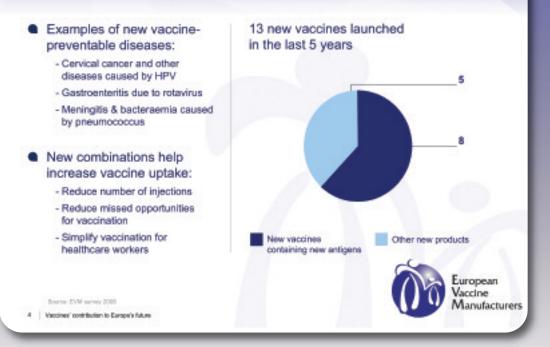


Vaccines' contribution to Europe's future

Vaccines make an invaluable contribution to Europe's public health. Since their introduction two centuries ago, vaccines have eradicated smallpox worldwide, eliminated endemic polio in Europe, and many other once common infectious diseases are now rare.

While vaccines' medical importance is clear, the broader strategic value offered by the vaccine industry is not always recognised. EVM's research into the sector provides an insight into its broader contribution to Europe. The research also reveals trends that may be relevant for sustaining Europe's leadership position in the vaccines field. Discovering, developing and introducing new vaccines involves major risk and requires significant investment over long periods of time. Major manufacturers are committed to innovating to enhance public health, and have launched a number of new vaccines in recent years. This innovation, as well as resulting in new products, boosts scientific research and supports high quality employment. This is particularly true for Europe, where much of the vaccine industry's research and development is based.

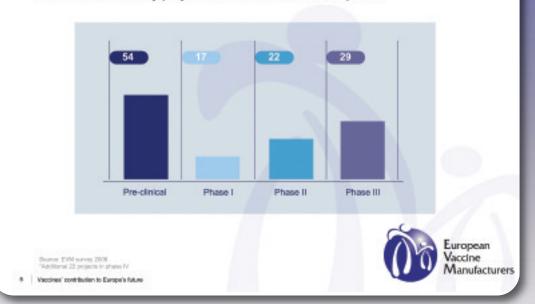




As a result of decades of industry innovation, a wide range of vaccines is now available. In recent years, producers have added to this and have introduced new vaccines, with a number targeting diseases for which none previously existed. In addition, several new combination vaccines offer practical advantages that can boost vaccine uptake, thereby further improving public health.

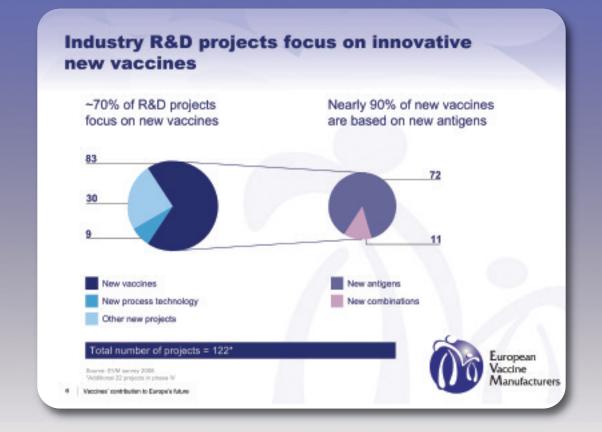
- Of the new vaccines introduced since 2003, over 60% are based on new antigens. Of these:
  - Two target human papilloma virus strains that are responsible for causing approximately 70% of cervical cancers.
  - Two protect against rotavirus infection, which can cause severe gastroenteritis, hospitalisation and even death, particularly in young children.
  - Two target invasive pneumococcal disease caused by Streptococcus pneumoniae bacteria; infections such as meningitis and bacteraemia caused by these bacteria are potentially life-threatening.

# Industry is developing a wide range of new vaccines with a strong pipeline of R&D projects

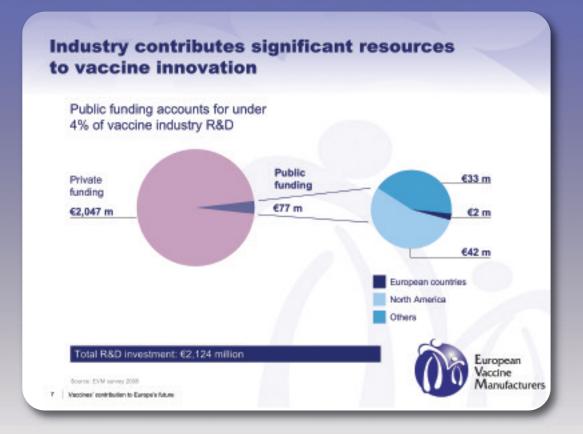


122 vaccine industry projects in research and development\*

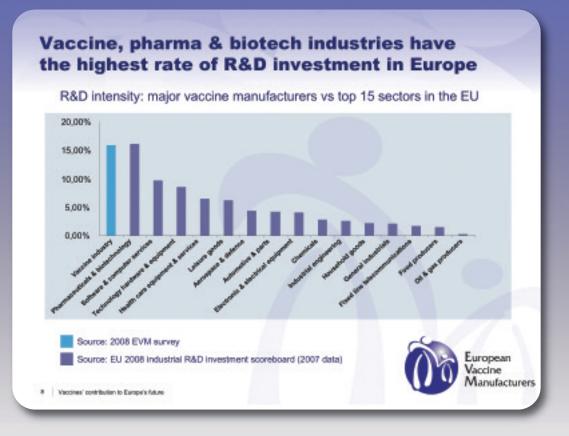
- Vaccine development is a lengthy process taking many years and requiring significant resources and expertise. The process to develop and introduce a new medicine takes on average 12 -13 years, with the cost of R&D estimated at over €1 billion in 2006 [source: EFPIA, 'The Pharmaceutical Industry in Figures, 2009 update'].
- Given the extensive requirements of research and development, manufacturers make a long-term commitment to the process of vaccine innovation. This dedication is borne out by the results of the EVM survey. In 2008, major producers had 122 ongoing R&D projects spread throughout the key stages of development. Of the ongoing studies, 29 were in the final phase of development (phase III), meaning many new vaccines targeting a range of diseases may become available in the relatively near future.
- A further 22 projects were in phase IV clinical studies. Phase IV studies provide further information on vaccine performance post-licensure, such as in special populations who may not have been included in earlier trials.



Manufacturers concentrate their R&D on highly innovative new vaccines. While a small number of projects address technological improvements and other advances, approximately 70% focus on the development on new vaccines. The EVM survey demonstrates that vaccine industry development efforts are focused on new vaccines, and of these nearly 90% are based on new antigens (new active ingredients). These could lead to innovative vaccines that result in new medical breakthroughs.

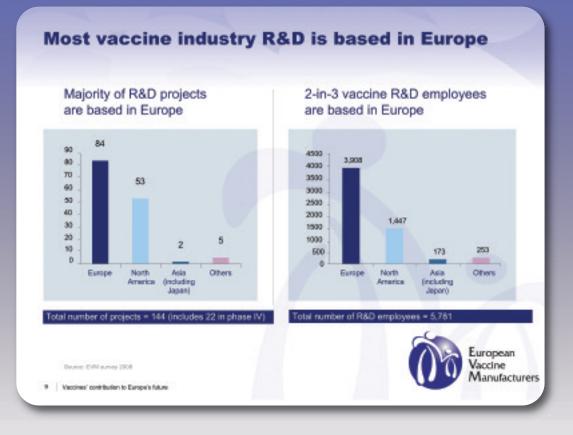


Vaccine R&D consumes significant amounts of capital, the vast majority of which is provided by private industry. In 2008, major manufacturers committed over €2 billion to the development of new vaccines. This has increased by nearly 40% since 2002, when industry investment amounted to approximately €1.5 billion. Given the importance of vaccines for public health, the public sector plays a key partnership role through investment in fundamental scientific research. However, of the total invested in 2008 in vaccine R&D, under 4% came from public sources. Throughout the EVM survey period (2002 – 2008), public funds have consistently accounted for only a small proportion (approximately 2 – 4%) of vaccine industry R&D investment.



■ Research and development forms the foundations on which the vaccine industry is based. Discovering and developing new vaccines is highly resource intensive, with producers investing over €2 billion in R&D during 2008.

To maintain this significant level of investment, manufacturers commit a major portion of their revenues to research and development activities. Within Europe, this high rate of investment is matched only by pharmaceutical and biotechnology companies. With investment amounting to over 15% of revenues these life science industries have an "R&D intensity" that is 50% greater than the next closest European industrial sector (software and computer services). Research and development investment plays a strategically important role in boosting Europe's economy, enhancing competitiveness and providing high quality jobs. The vaccine industry makes a major a contribution to each of these areas.



- While major vaccine manufacturers are global in nature, many of their operations are based in Europe. This is the case for much of the vaccine industry's research and development, which is concentrated in the region.
- Of the 144 R&D projects ongoing in 2008 (including 22 in phase IV development), nearly 60% (84) were based in Europe. This is nearly 60% greater than the number based in North America (53), with other territories home to under 5% of the total.
- Research and development employment is also highly concentrated in Europe. Of the nearly 6,000 R&D specialists employed by major manufacturers, 68% (approximately 4,000) are based in the region. This employment supports Europe's science base, providing high quality work in a broad range of technological and scientific disciplines.



Since their first introduction over two centuries ago, vaccines have greatly enhanced public health, and now save the lives of 3 million people each year [source: WHO Europe]. Thanks to vaccines, smallpox, which used to kill 5 million people annually, has been eradicated, and by 2002 endemic polio was eliminated from Europe [source: WHO Europe].

Although vaccines are now available against a range of infections, many disease targets still exist. Equally, the emergence of SARS in 2003 and H1N1 pandemic influenza in 2009 demonstrates that new threats can arise at any time. As a consequence, it is imperative that R&D efforts are sustained to combat future health challenges. The vaccine industry is committed to the development of new vaccines to further enhance public health. Europe is at the centre of this global effort, with the majority of the industry's 122 R&D projects and 6,000 R&D employees based in the region. With investment rates substantially higher than any other European sector outside the field of life sciences, Europe's vaccine industry is a strategic asset.

#### 1. Innovating for public health

## 2. Boosting Europe's competitiveness

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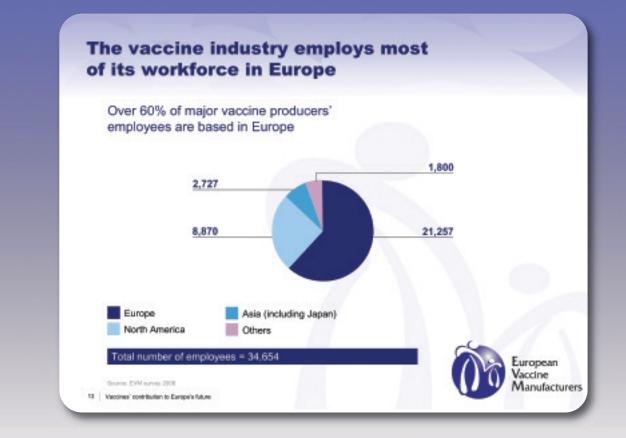
11 Vaccines' contribution to Europe's future

As well as concentrating its R&D activities in Europe, the global vaccine industry bases many of its other operations in the region. This is particularly true of vaccine manufacturing. Major manufacturers produce nearly all of their vaccines in Europe and export the majority of these important products worldwide. This export success story is in sharp contrast with recent industrial trends, in which a number of sectors have moved production outside of the European Union. As a research-based, high-technology, high-growth industrial sector, vaccines are an important contributor to Europe's global competitiveness. This largely European-based industry provides high quality employment, boosts the region's economy and contributes to social and economic development.

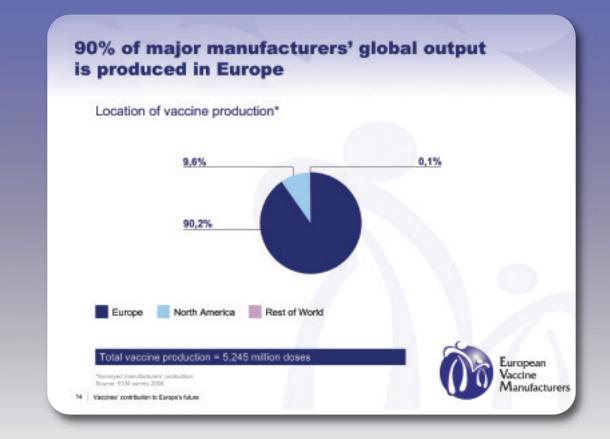
## Major vaccine producers concentrate manufacturing in Europe



Europe has a long history of vaccine manufacturing, and benefits from a strong industrial infrastructure. Of major producers' 32 production facilities around the world, over 60% are in Europe. Thirteen European countries are home to these vaccine manufacturing sites. In contrast only 5 countries across the rest of the world have plants operated by major producers, and of these the vast majority are in North America. Throughout the EVM survey period (2002 – 2008), the total number of production facilities in the continent has increased slightly, emphasising manufacturers' commitment to the region.

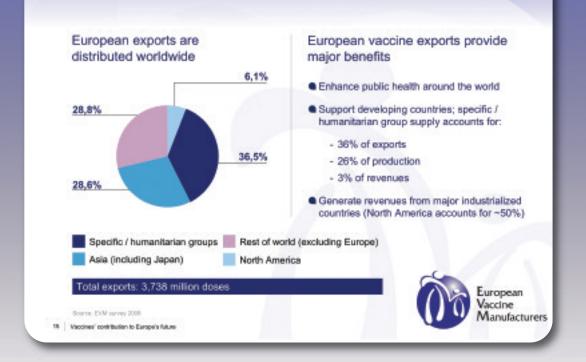


With Europe home to much of the world's vaccine R&D activities and most of its production facilities, it follows that the majority of the industry's employees are based in the region also. The EVM survey shows that Europe accounts for over 60% of industry's total employment, with the region's more than 20,000 workers amounting to nearly two-and-a-half times the number based in North America. Vaccine industry employment is important as it offers many of the qualities required to maintain successful economies. Many of the jobs are highly skilled and involve a range of high technology and scientific disciplines. These positions offer the prospect of long-term career and skills development in an expanding and successful sector. Consequently, the vaccine industry helps contribute to social as well as economic development.



- From their 20 production sites located in Europe, the world's major vaccine manufacturers produced more than 4.7 billion doses in 2008. This amounted to over 90% of their global output, and was nine times more than the number of doses they manufactured in North America.
- Throughout the EVM survey period both the overall volume of vaccine industry production has grown, as well as the proportion manufactured in European plants. In 2002, major manufacturers produced 3.9 billion doses, which grew by approximately 34% to reach 5.2 billion in 2008. During this period European production increased slightly more rapidly than the overall upward trend, with the 3.5 billion doses manufactured in 2002 increasing 36% to 4.7 billion in 2008.
- European manufacturing success stories on this scale may appear rare in recent times. However, in the case of vaccines, production by major manufacturers has continued to be concentrated in Europe.

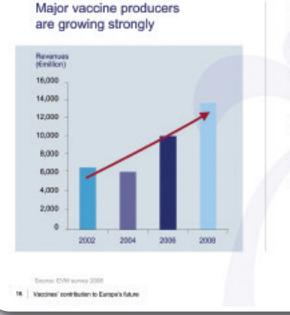
## European manufacturers export vaccines globally



- Of the 4.7 billion doses of vaccines produced in Europe in 2008, approximately 80% were exported around the world. Of these a small proportion were destined for North America (227 million doses), while over a third (approximately 1.4 billion doses) were distributed to developing countries via specific agencies and international organisations such as UNICEF: Europe plays a particularly important role in supplying large quantities of vaccines for the global initiative to eradicate polio.
- For many years producers have provided vaccines at reduced prices for use in the developing world. As a result, the 1.4 billion doses supplied to lower-income countries account for 36% of exports and 26% of total production, but less than 3% of revenues.

The success of Europe's vaccine exports has a dual importance. As well as supporting public health initiatives around the world, it demonstrates the competitiveness of a European industry sector that contributes positively to the region's economy.

## Europe's vaccine industry is a high-growth high-technology sector

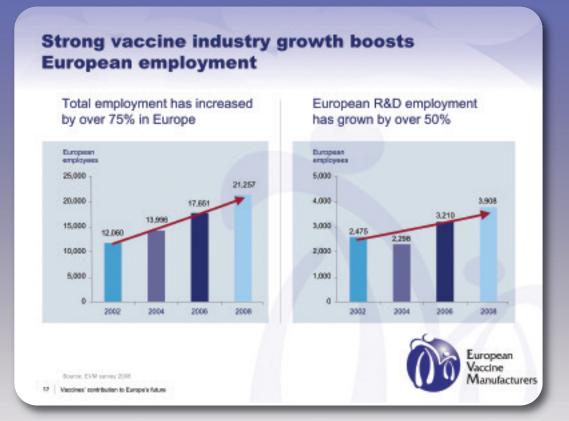


Vaccine industry is a major contributor to Europe's knowledge-based economy

- Provides high quality employment
- Boosts competitiveness
- Contributes to Europe's economy
- Supports Europe's science base
- Invests profits in future innovation



Throughout the EVM survey period major manufacturers have introduced new vaccines and substantially increased production. Similarly European manufacturing has grown significantly, along with exports from the region which rose by over 30% (increasing from 2.8 billion doses in 2002 to 3.7 billion in 2008). In parallel with this growth, vaccine industry revenues have also increased. As a result, manufacturers can continue to invest heavily in R&D activities, which in turn support Europe's knowledge-based economy and science base. As a rapidly growing sector, the European vaccine industry also contributes to the continent's broader economy, provides quality jobs and enhances the region's competitiveness. Overall, vaccines represent a strategically important industry for Europe.



- Mirroring its growing product range, production output, exports and revenues, Europe's vaccine industry has also increased its workforce dramatically in recent years.
- While the EVM survey completed in 2008 may not capture the full impact of the ongoing global recession, the long-term upward trend in vaccine industry employment is clear. Each biennial survey has shown a consistent increase in European employment from 2002 through to 2008. The total growth during this period stands at over 75%, outstripping the corresponding increase in North America where employment grew by 69% to reach 8,870 workers in 2008 (vs 21,257 in Europe).
- This general upward trend is largely mirrored in R&D employment also. Throughout the survey period, employment of research and development workers based in Europe has grown at each time point except 2004, with a total increase of 58% between 2002 and 2008.



- Vaccines have been developed in Europe for centuries, and EVM surveys show that the continent continues its long tradition in the field:
  - The global vaccine industry employs over 60% of its workers in Europe, and over 2/3rds of its R&D specialists.
  - Major manufacturers produce over 90% of their vaccines in the region, of which 80% are exported around the world.
  - European R&D and vaccine production enhances public health in all regions of the globe, including in the developing world, provides high quality employment, supports Europe's knowledge economy and boosts the region's competitiveness.

Unlike some other major industrial sectors, including pharmaceuticals, Europe's vaccine producers remain at the heart of the global industry. This regional concentration of operations provides a range of important economic and social benefits.

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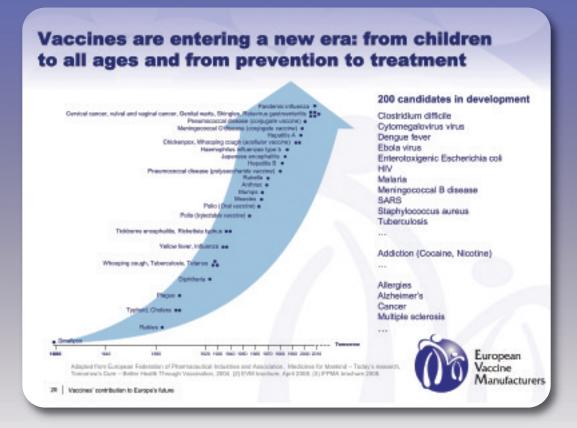
19 Vaccines' contribution to Europe's future

Over a period of time, the pharmaceutical industry has undergone a shift in its centre of gravity. For many years Europe enjoyed its position as a leading centre of pharmaceutical development and production. However, with more rapid growth. greater R&D spending and increased relative competitiveness North America has increased in importance, and the region now eclipses Europe on a number of kev measures. This situation is again in flux, with a number of experts believing Asia will be the future centre of the global market for the pharmaceutical sector.

[Sources: DG Enterprise and Industry: Pharmaceutical Industry Policy - Introduction (13/8/08); Commission staff working document 'European industry in a changing world updated sectoral overview 2009'; PricewaterhouseCoopers: Gearing up for a global gravity shift (2007).]

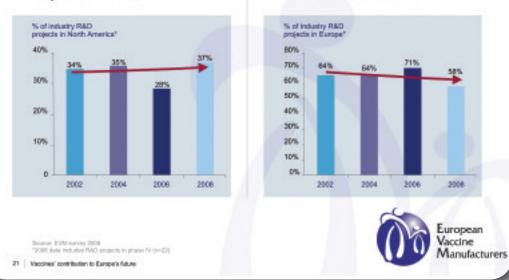
In recent years, the vaccines industry has experienced significant growth and reinvigoration. Europe has benefited from this success, and the region continues to enjoy its place at the heart of the global industry. However, analysis of EVM surveys over the last six years reveals an increase in opportunities in other regions of the world, particularly North America. The early signs of a potential future trend are perhaps most noticeable in R&D, which is at the beginning of the cycle of new vaccine creation and commercialisation.

Given the importance of vaccine innovation, experts from the European Academies Science Advisory Council (EASAC), a highlevel advisory group composed of members from EU Member States' scientific academies, have proposed a number of supportive policies. These may help sustain the region's global lead in the field, and the industry's important contribution to Europe's social and economic development.



- During the 20th Century, the development of vaccines progressed steadily for many years, and important public health improvements were made when they were introduced. In particular, the second half of the century witnessed a rapid acceleration in research and development, and many new vaccines became available during this period.
- In recent years vaccines have entered an exciting new era. Dramatic advances in immunology, genetics, molecular biology and bioinformatics are enabling scientists to target a wide range of diseases for which vaccines were previously unavailable. Vaccines have become important players in the 'biotechnology revolution', and the pace of new product introductions has increased substantially in the last 10 years.
- Currently 28 diseases are vaccine preventable; in the relatively near future this number is likely to expand considerably.
- By harnessing the power of a range of new technologies, vaccine development continues to accelerate. A large number of candidates are in development, targeting nosocomial infections, malaria, dengue fever, tuberculosis and other health threats (such as SARS and bioterrorism). In future, vaccines may address not only infectious diseases but Alzheimer's, various cancers and addictions.

## This new era offers new R&D opportunities



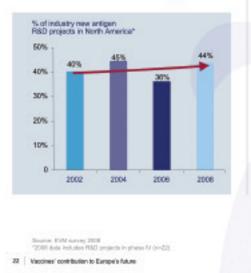
#### North American R&D may be on the rise

EVM surveys over the period 2002 – 2008 show that the current era of technological advance and accelerating vaccine development is creating many new R&D opportunities. The surveys demonstrate that at each biennial checkpoint Europe consistently remains home to the majority of vaccine industry R&D projects. Indeed, in 2006 it appeared Europe may be consolidating its R&D lead. However, the most recent research from 2008 paints a different picture. A rapid shift of power during the two-year period from 2006 has seen the gap between Europe and North America narrow. The difference between the proportion of total R&D projects located in Europe vs North America decreased from 43% in 2006 to just 21% in 2008. This move means that the two regions are now more evenly matched, and the trend over the entire survey period reveals a potential decline in Europe's dominance, with a corresponding rise in North America's importance.

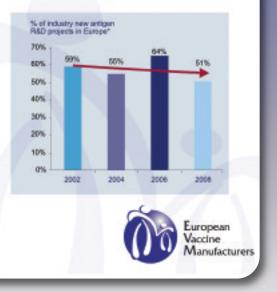
Europe's R&D dominance may

have started to decline

## R&D growth in innovative new vaccines appears stronger in North America

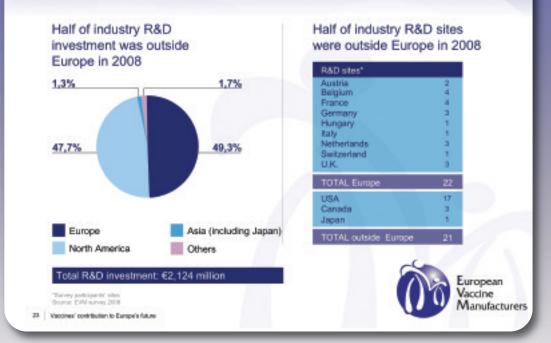


North American R&D growth has focused on new antigens New antigen R&D has fallen back in Europe



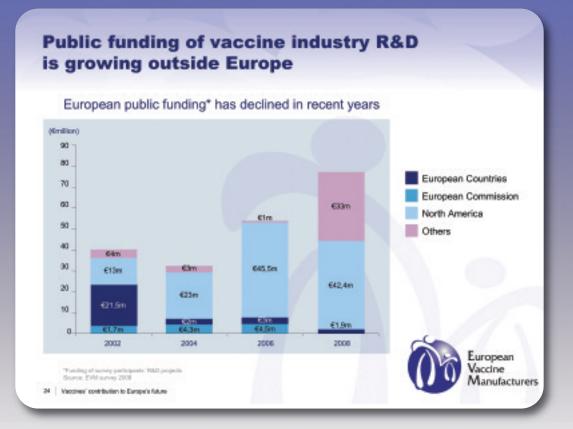
Deeper analysis of the EVM survey data shows that the recent trend in the movement of R&D projects appears to be mirrored in those projects based on new antigens (active ingredients). As these antigens have the potential to form the basis of innovative new vaccines they may represent a fundamental measure of R&D quality and overall commercial potential, giving trends in their development an added poignancy. From 2002 - 2006, Europe maintained its position as the leading centre for new antigen development programmes, and while the location of these projects changed repeatedly this did not follow a clear trend. However, the addition of the 2008 EVM data reveals an early trend of movement away from Europe towards North America. The difference between the proportion of new antigen R&D projects located in Europe vs North America decreased from 28% in 2006 to just 7% in 2008. This narrowing of the gap between the regions is similar to the changes seen in overall R&D projects during the same two-year period.

# Additional indicators demonstrate R&D opportunities outside Europe

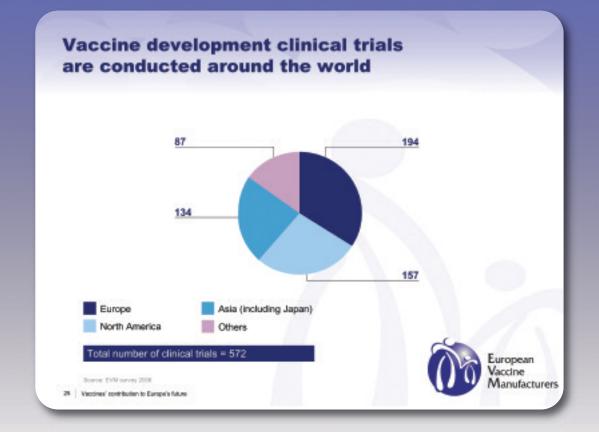


The 2008 EVM survey results highlight further objective measures that demonstrate the strength of R&D opportunities outside Europe. Analysis of R&D investment and the location of research and development sites shows the importance of North America, mirroring the new emphasis on the region in both overall R&D and projects based on new antigens.

- Of the €2 billion committed to vaccine R&D by the industry in 2008, slightly over €1 billion was invested in Europe and a similar sum in North America: Europe received just €34 million greater investment than North America.
- This even investment split between the two regions is mirrored in the location of research and development sites. While Europe was home to 22 such facilities, a similar number were based in North America (20).



- Although public funding accounts for a very small percentage of total vaccine industry R&D investment (under 4%), it may be seen as an indicator of the environment and support offered by the contributing region.
- In this regard, analysis of the EVM surveys is informative, showing steadily growing support from North America. In the last two years, contributions from other regions have increased dramatically to a level approaching those from North America.
- This is in sharp contrast with European funding. Throughout the survey period, and most notably during the last three surveys, very limited funding was taken up by major manufacturers from European governments or the Commission. In 2008, major producers did not receive any funding from the Commission at all.



- Clinical trials play an essential role in the development of new vaccines. Reflecting this importance, the most recent EVM survey shows that in 2008 major manufacturers were conducting 572 such studies.
- Conducting clinical trials is a complex undertaking, requiring skilled local personnel, consistently high quality standards and robust regulatory oversight. As a result, many factors influence the location of clinical studies. These include the necessity to conduct clinical trials in specific regions when targeting regionspecific diseases (e.g. malaria and dengue in Africa). Furthermore, regulatory authorities tend to request companies conduct additional clinical trials in local populations prior to authorisation.
- While the factors supporting the location of clinical trials may be complex, the EVM survey of such a large number of studies can provide an insight into the relative importance of different regions. In 2008, Europe accounted for almost exactly 1/3rd of vaccine clinical studies undertaken by major producers, while North America was home to a similar number (over 1/4 of the total). This fairly even split between the two regions is in line with the now more evenly balanced location of R&D projects, as well as research and development investment and R&D sites.



- Europe has much to benefit from its position at the heart of the global vaccine industry. In recognition of the importance of supporting new vaccine innovation in the EU, the European Academies Science Advisory Council (EASAC) 2006 report, 'Vaccines: innovation and human health', made a series of recommendations to incentivise and facilitate R&D and promote vaccine uptake.
- The report identifies 'a series of matters that have to be tackled at European level to exploit the potential of vaccines in the fight against infectious diseases'. Its comprehensive recommendations focus on strengthening support for vaccine R&D, reducing impediments and increasing vaccine usage to further enhance public health.
- The Commission in its 2009 update on European industrial sectors identified several issues for the wider pharmaceutical industry that demonstrate the impact of structural change. Of particular note is the relative decline of EU competitiveness and R&D investment in comparison with the US.
- By learning from the experience of the broader pharmaceutical industry in recent decades, concerted efforts by all stakeholders, including policy makers and industry, can help sustain Europe's lead in the vaccine field.

Europe's vaccine industry is a strategically important asset:

- Major public health partner in Europe and around the world
- Leading innovator, investing for the future
- Key contributor to social and economic development in Europe
- Successful European sector with strong growth opportunities
- Consequently, it is important that Europe fosters a positive environment and supportive policies to sustain its lead in the vaccines field



27 Vaccines' contribution to Europe's future

In conclusion, EVM surveys conducted over the last 6 years clearly demonstrate the strategic value of Europe's vaccine industry.

- Vaccines are of great importance for public health, and Europe leads the world in their research, development and production. As a result, the European industry is a global partner in the fight against infectious disease and the improvement of public health around the world.
- Vaccine producers are leading innovators, committing a greater proportion of revenues to R&D than any other major industrial sector in Europe outside the life sciences field. This investment is reaping rewards with several new vaccines introduced recently and many others in

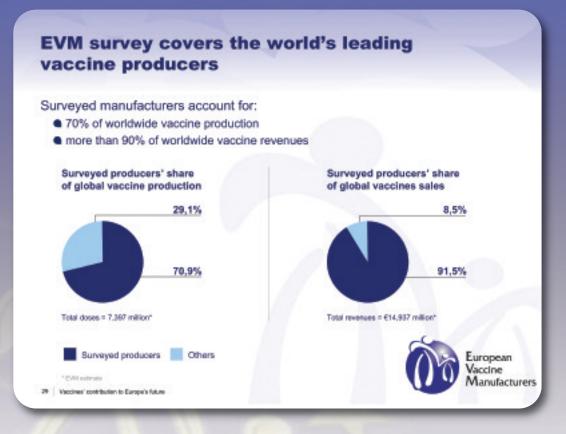
development, against existing infections, emerging health threats, cancers and addictions.

With the majority of the global vaccine industry's R&D, employment and manufacturing based in Europe, the region's competitiveness, science base and knowledge economy all gain. The ongoing success and growth of the vaccine sector is important for both public health and Europe's social and economic development. However, early trends suggest that Europe's R&D dominance may be lessening, with the gap between the region and North America narrowing. Consequently, it is important that Europe fosters a positive environment and supportive policies to sustain its lead in the vaccines field.



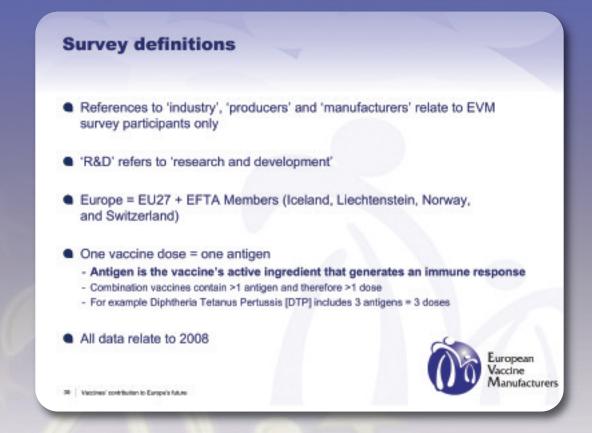
# Notes

Immunisation's key role in improving public health in Europe and around the world is well recognised. However, the contributions vaccine producers make to Europe's knowledge economy, science base, export performance and skills development are perhaps less well understood. To promote broader understanding of this strategically important industry, the European Vaccine Manufacturers (EVM) group conducts biennial surveys to capture a range of objective social and economic data. EVM's research, now conducted four times over the last six years, provides an insight into the innovation, research and development, employment and manufacturing undertaken by the industry in Europe. With information collected every two years over the period 2002 – 2008, the EVM database reveals industrial trends that can assist policy makers and other stakeholders concerned with Europe's social and economic development.



# Notes

- The EVM research includes information from all the major vaccine companies operating in Europe to ensure the data is as complete as possible.
- The vaccine producers covered by the survey are not only major regional manufacturers. Due to the dominance of Europe within the global vaccine industry, these companies are also leading producers on a worldwide basis.
- The global role of the manufacturers included in the research is clearly demonstrated by the survey results: surveyed producers account for the vast majority of worldwide vaccine production and revenues.



# **Notes**

- To ensure consistency the survey uses a number of standard definitions.
  - Based on the worldwide significance of the companies included in the research, they are taken as representing on a global scale the vaccine 'industry', vaccine 'producers' and vaccine 'manufacturers'. Consequently, these terms are used interchangeably when referring to the survey respondents.
  - The EVM surveys define Europe on a political rather than geographic basis. As a result, the survey includes the 27 European Union countries and four EFTA members.
- For the purposes of quantifying vaccine production and distribution, one dose is defined as targeting one disease. Consequently, a combination vaccine targeting several diseases will account for several doses. Similarly, the active ingredients in vaccines, termed 'antigens', differ for each targeted disease. Therefore, for the purposes of the survey, one dose = one antigen.

#### VACCINES' CONTRIBUTION TO EUROPE'S FUTURE



#### For further information please contact

European Vaccine Manufacturers (EVM) a specialised group of EFPIA Rue du Trône 108/Troonstraat 108, B-1050 Brussels, Belgium

> nfo@evm-vaccines.org www.evm-vaccines.org

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