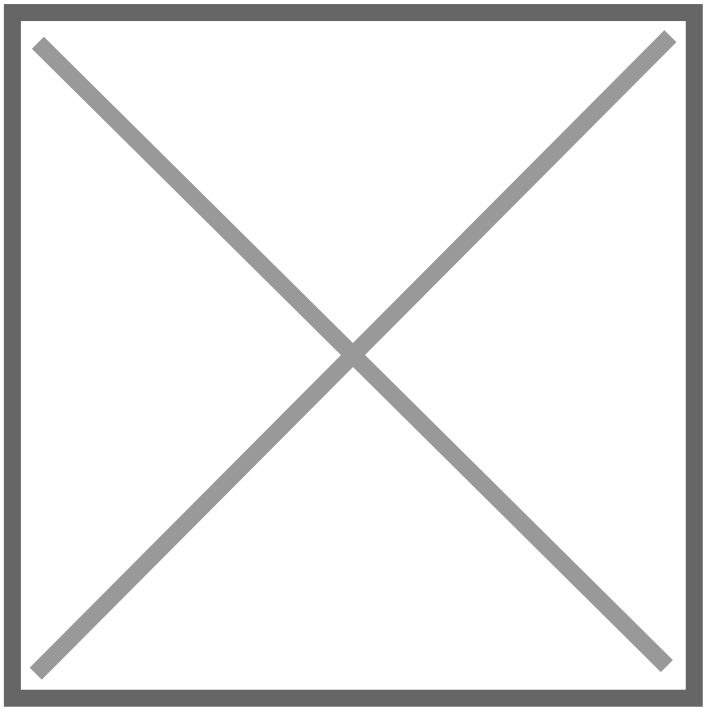
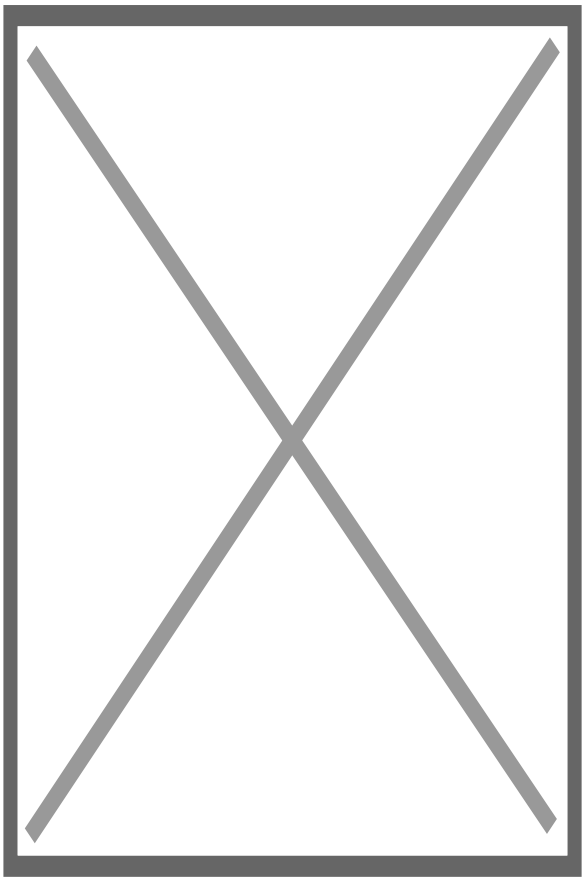
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Vaccine business to see uptake

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The driving factor for the vaccine industry will not only be innovative technology, but addressing unmet needs in the area of infectious disease. A majority of philanthropic organizations like the Bill and Melinda Gates Foundation and the Wellcome Trust, are investing in vaccines for the developing countries-in the areas of malaria, tuberculosis, rotavirus and cancer. Research is already being conducted for a number of major infectious diseases, including HIV, HPV and hepatitis.
While preventive vaccines have been the industry's focus, there is an increasing interest in therapeutic vaccines.

Ã¢â?¬Å?The growth in the industry depends on a breakthrough in therapeutic vaccines. The sale of therapeutic vaccines in developed markets and basic vaccines in emerging markets are likely to driveglobal vaccine sales in the near future,Ã¢â?¬? says Rajesh Jain, MD, Panacea Biotec.

Vaccines in the making
Unlike pharma products, new undifferentiated vaccines do not struggle to compete with established market-leading brands, the market is such that if a new vaccine is able to become a second or third alternative, it can capture a good share in the market and earn good revenues. Ultimately, the challenge for pipeline developers is innovation in terms of safety, efficacy and compliance. This stimulates a lot of companies to enter into common disease segments like hepatitis, Japanese encephalitis, dengue, rota virus, rabies and swine flu.

There is an extensive range of vaccines in the development pipeline undergoing various stages of testing and clinical evaluation in India. These include vaccines against bacterial diseases (tuberculosis, staphylococcus), parasitic infections like malaria, and viral diseases (HIV, rota virus, dengue). Most pose minimal risk in industrialized settings yet are prominent concerns in developing countries, stimulating private industry to engage in these markets.

Rotavirus is responsible for hundreds of thousands of deaths annually in the developing world. Two live oral rotavirus vaccines-116E and I321 are in various stages of development in conjunction with vaccine manufacturers in India.

Bharat has filed an IND for its rota virus vaccine. The product is currently in phase-III after successfully completing phase-I and phase-IIB studies. The company has invested Rs 179-224 crore ($40-50 mn) in the clinical trials, with funding assistance from Gates Foundation. The vaccine will hit the market in 2011.

The other company working in this area, Shantha Biotechnics, has started the phase-II clinical trial for rotavirus vaccine at Christian Medical College (CMC), Vellore. The company plans to start the phase-III in August 2010. Ã¢â?¬Å?By 2012 first or second quarter we will launch our rota virus vaccine,Ã¢â?¬? says Varaprasad
Reddy, MD, Shantha Biotechnics.

The company is progressing with its plans to start the phase-I study of typhoid polysaccharide vaccine. Simultaneously, it is working on conjugated typhoid vaccine that is more effective with less side reactions. The vaccine is getting ready for trials. The other products in development include the pneumococcol vaccine and a HPV vaccine which is being developed in collaboration with John Hopkins University, is very close to entering the preclinical trials. The company hopes to finish all studies in four years and launch it in 2014. Shantha will get two vaccines from Sanofi-a hepatitis A vaccine and an acellular pertusis vaccine.

Reddy says, Ã¢â?¬Å?If we get the IPV vaccine from Sanofi we will combine it with our pentavalent vaccine and make a hexavalent vaccine.Ã¢â?¬? Bharat Biotech too has a strong pipeline of vaccines to combat malaria, typhoid and Japanese encephalitis infections. The malaria vaccine in development in partnership with International Center for Genetic Engineering and Biotechnology (ICGEB), is entering phase-I trials.

Ã¢â?¬Å?Bharat Biotech is the only company working with four malaria vaccine candidates. We are also moving to specialized vaccines like rabies, Japanese encephalitis vaccine, chickungunya and staphylococcus aureas vaccine,Ã¢â?¬? says Suchitra Ella, co-founder and joint MD, Bharat Biotech. Its conjugated typhoid vaccine is entering phase-III, is anticipated to reach licensure by end of this year.

The most advanced product in Biological E's pipeline is a novel vaccine for Japanese encephalitis. Panacea Biotec's advanced pipeline include-Japanese encephalitis vaccine, dengue vaccine and the HINI vaccine for swine flu.

Pune-based Serum Institute of India Limited (SIIL) will soon bring out India's first indigenously developed meningitis vaccine for meningitis. The vaccine, which has completed phase-I and phase-II/III testing in Africa and India, will be first introduced in Africa in this year after DCGI approval and WHO pre-qualification. The company has invested about Rs 80 crore in this project. The meningococcal conjugate vaccine will be better than the currently available polysaccharide vaccines and at Rs 22.48 ($0.50) per dose, will be about half or third of the cost of the polysaccharide vaccines currently available. The company is also working on Novel Drug Delivery System (NDDS) initiatives. At present several other vaccines are under development like the rotavirus vaccines and monoclonal antibodies for rabies. The other interesting products that Serum Institute intends to manufacture in the near future are bladder cancer vaccine and pneumococcal polysaccharide and conjugate vaccine.

In addition to new vaccine development, research is ongoing in novel technologies to improve the delivery of vaccines so that administration can be faster, safer and more effective. This includes efforts to establish proof-of-principle in areas such as needle-free delivery (nasal, oral or transdermal) or heat stabilization. For example, preclinical studies have been successfully completed for aerosol delivery of measles vaccine, and phase-I-II trials are currently planned in India.
H1N1 vaccine race hotting up The race for the locally made H1N1 vaccine is hotting up, as Indian swine flu vaccine makers are preparing to enter the final phase of trials before launching them. The final commercial roll out would depend on regulatory approvals.

About one-third of novel vaccines in development by Indian companies are targeted at the H1N1 virus. Ã¢â?¬Å?Currently there are about 14 vaccines at various phases of development in India. Of these, 10 vaccines are innovative products while remaining are improved versions of available vaccines. About one-third of the new vaccines in development are targeted at the H1N1 virus,Ã¢â?¬? says Gunnam.

Ã¢â?¬Å?All the companies are gearing up for the launch of the H1N1 vaccine in India in mid-2010. Some players like Zydus Cadila and Biological E have entered into agreement with overseas players like Novavax and VaxInnate for the development technology, while Panacea Biotec has bagged a supply agreement from the Government of India. Apart from the Indian players, MNC players like GSK, Sanofi-aventis and Baxter, have conducted some bridge studies in India with their developmental swine flu vaccine, he adds. The government has already approved the use of Sanofi Pasteur's H1N1 influenza vaccine in India.

Serum Institute's Fluvac will soon be ready for commercial use. The company is likely to receive regulatory clearances by the end of April. Serum has sought permission from the Drugs Controller General of India (DCGI) for the phase-III trials of the

inactivate version of the vaccine. After Ahmedabad-based Zydus Cadila, Serum Institute becomes the second Indian company to have started phase-II/III trials, pushing it closer to the finishing line.

Other vaccine makers, including Bharat Biotech, have completed phase-I clinical trials of their cell culture-based H1N1 vaccine candidate. HN-VAC is awaiting approval for the DCGI to go in for phase-II/III clinical trials. The report has been submitted to the DCGI and is currently awaiting the approval from the regulator to go for phase-III clinical trials.

Zydus Cadila is currently in the middle of phase-II and phase-III trials. Panacea Biotec is developing PandyFlu (H1N1 vaccine) split virus vaccine using egg-based technology. It has also set up a BSL2 level manufacturing unit with BSL3 practices on its sprawling campus spread over 75-acre at Lalru, Punjab for manufacturing Pandyflu. The facility has a capacity to manufacture 4.5 crore doses of vaccine.

Panacea Biotec, has been recently awarded financial assistance of Rs 10 crore under the Biotechnology Industry Partnership Programme (BIPP), initiative of the Department of Biotechnology (DBT) for the development of pandemic influenza vaccine. The firm had earlier also been given a grant of Rs 10 crore by the Ministry of Health & Family Welfare (MoHFW) for development and manufacture of the same vaccine. Commenting on the development Soshil Kumar Jain, chairman, Panacea Biotec says, Ã¢â?¬Å?The award of assistance by DBT for development of Pandyflu is a positive development for Panacea closely following the grant by
MoHFW in connection with supply of Pandyflu vaccine.Ã¢â?¬?

Biological E is working closely with VaxInnate to rapidly develop and manufacture an innovative vaccine in India. The recombinant H1N1 vaccine is based on the novel Toll-Like Receptor (TLR) technology platform, which improves vaccine immunogenicity and efficacy. Using the TLR technology, vaccines can be produced by simple, low-cost, highly-scalable recombinant DNA techniques, avoiding many of the challenges and pitfalls of egg-based or cell-culture influenza vaccine production.

Vaccine Industry Trends

- Exports presently account for around 65 percent of the country's vaccine market.
- The driver of vaccine industry's growth is new product development. Increasingly, vaccines are being aimed at adults, in addition to infants.
- Influenza vaccines and Hepatitis vaccines, with an estimated growth rate of over eight percent, are the fastest growing segments.
- Flu vaccines have huge demand at present and all major vaccine manufacturers are to develop the vaccine.
- While preventive vaccines have been the industry's focus, there's increasing interest in therapeutic vaccines.
- The use of a combination of vaccines is becoming more common. Vaccines comprising five or more ingredients are being developed.
- New ways of administering vaccines are under development including skin patches, inhalation, etc.
- M&A activity in the vaccine segment is likely to occur at a rapid pace.

Vaccines being developed by Indian players

Vaccine	Company	Status of Development
Rotavirus vaccine	Bharat Biotech	Bharat Biotech, in collaboration with the Indo-American vaccine action programme, is developing a rotavirus vaccine for the prevention of diarrhoea. The vaccine will be entering phase III shortly.
Rotavirus vaccine	Shantha Biotechnics	Has entered phase II trials.
Cadi-05	Cadila Pharmaceuticals	Cadi-05 is a Mycobacterium cancer vaccine for the treatment of hormone-refractory prostate cancer.
Influenza vaccine	Cadila Pharmaceuticals; Bharat Biotech	Bharat Biotech and Cadila entered into a licensing agreement with Novavax in 2006 and 2009 respectively for the development of prophylactic influenza vaccine containing recombinant, functional influenza virus-like particles.

Malaria vaccine	Bharat Biotech; ICGEB	Bharat Biotech, in collaboration with the Malaria Vaccine Initiative (MVI) at Program for Appropriate Technology in Health (PATH), the US, and the International Centre for Genetic Engineering and Biotechnology, India, is developing a malaria vaccine.
H1N1 influenza (Swine flu) vaccine	Bharat Biotech	Bharat Biotech is developing a cell culture-based influenza vaccine. Will be entering phase-III.
H1N1 influenza (Swine flu) vaccine	Panacea Biotec	It is an inactivated, split virion monovalent vaccine.
H1N1 influenza (Swine flu) vaccine	Zydus Cadila	Zydus Cadila is developing an egg-based, inactivated vaccine against the H1N1 strain of influenza. It is the first Indian company to get DCGI approval for conducting clinical trials of H1N1 vaccine in January 2010. Plans to launch the vaccine mid-April.
H1N1 influenza (Swine flu) vaccine	Serum Institute of India	It is an indigenous live attenuated H1N1 virus intranasal vaccine for the prophylaxis of pandemic H1N1 influenza. Has started phase II/III.
H1N1 influenza (Swine flu) vaccine	Biological E	Biological E entered into a licensing agreement with VaxInnate Inc for clinical development and commercialization of its swineflu vaccine in India in January 2010.
H5 N1 (Avian flu) vaccine	Serum Institute of India	The company received the contract for developing the avian flu vaccine in 2006 and later in August 2009, Serum has prioritized the development of swine flu vaccine.
Malaria vaccine	Bharat Biotech; ICGEB	Entering phase-I.
Conjugated typhoid vaccine	Bharat Biotech	Conjugated typhoid vaccine is entering phase-III, will be ready by end of this year.

Jahanara Parveen in Bangalore