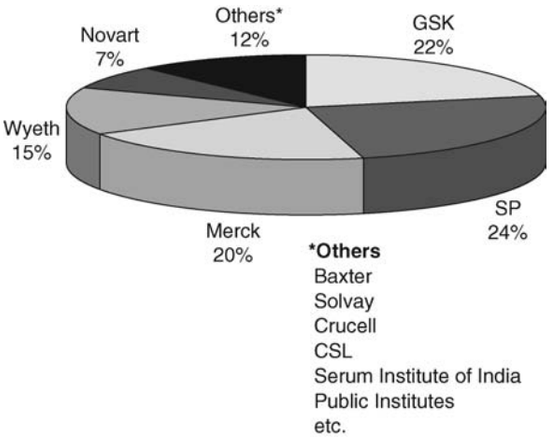

Figure 7 Manufacturers' estimated market shares 2008. (The sales of Sanofi Pasteur, a European joint venture between Merck and Sanofi Pasteur are split 50/50 between the two companies.)

Limited. Initially, a subsidiary of the Rhône-Poulenc Group, Pasteur Mérieux Connaught, changed its name to Aventis Pasteur (following the merger of Rhône-Poulenc and Hoechst) and more recently to Sanofi Pasteur following the acquisition of Aventis by Sanofi (2003).

GlaxoSmithKline (GSK) Biologicals originated in a small Belgian operation called RIT, which was acquired by SmithKline and French and, subsequently, through mergers, became SmithKline Beecham (SB) Biologicals and GSK Biologicals. A small operation until the mid-1980s, the company grew extensively on the basis of its Hepatitis vaccine franchise (recombinant Hepatitis B and Hepatitis A). It then broadened its product range to include infant combination vaccines, expanded international distribution, and development of a broad range of new vaccines, including varicella, rotavirus, HPV, pneumococcal and meningococcal conjugate, and candidate vaccines against malaria and tuberculosis. It is also becoming a major player in influenza vaccine with the extension of its current production facilities in Germany, investments in the United States, and the acquisition of ID Biomedical in Canada, as well as R&D investments in cell culture and adjuvant technologies that have already borne fruit.

Merck Vaccines is a specialized division of Merck & Co. that has long been the U.S. market leader. It expanded operations in Europe through a joint venture with Sanofi Pasteur MSD and is entering the international markets with a series of new vaccines against varicella, zoster, rotavirus, and HPV.

These 3 players represent each between 20 and 25% of the world commercial vaccine market.

A fourth company, Wyeth Vaccines, long a market leader in the United States, actually stopped distributing some basic pediatric vaccines before staging a resurgence at the end of the last century with licensure of a seven-valent pneumococcal conjugate vaccine (Prevnar®), as well as a meningococcal C conjugate vaccine (in Europe). From a market perspective, Prevnar was the first ''blockbuster vaccine.''

The fifth company, Novartis Vaccines, resulted from successive mergers between national companies in Italy (Sclavo), Germany (Behring), and the United Kingdom (Evans-Medeva/PowderJect) within Chiron vaccines in the United States. Chiron vaccines was in turn acquired in 2007 by Novartis, which is strengthening its position in influenza and polysaccharide conjugate vaccines.

Other less prominent actors have resulted from the concentration of several smaller companies, such as Baxter Vaccines (Immuno, Nava, etc.), Crucell acquiring Berna Biotech and SBL. The remaining smaller manufacturers in developed countries are mostly dependent on major manufacturers for supplying their needs and are generally meaningful only in their home markets (Australia, Netherlands, etc.).

One can expect the future to bring even more amalgamation of vaccine manufacturers, the emergence of new players, and the likelihood that the relative positions may well change again linked to the pace of innovation in the various companies and the success of the development projects that they have chosen to support. This is clearly illustrated by the recent involvement of Novartis, AstraZeneca (which acquired MedImmune), and Pfizer (acquiring Powdermed) in the vaccine business.

Yet other new actors are likely to appear. Some pharmaceutical companies may become involved in a selective manner, limiting their focus to a few highly innovative, high revenue–generating products. Biotech companies are increasingly becoming involved in the innovation process as major companies outsource an increasing share of their R&D budgets. Some new vaccine companies (e.g., Intercell in Austria) will mature and begin to manufacture multiple products, and some will try to progress to fully integrated operations, but this will remain a major challenge.

Also, producers from major less developed countries (such as Serum Institute of India and other Indian producers, Biopharma in Indonesia, Chinese producers, Brazilian companies, etc.) will become more prominent, especially as developed-country manufacturers rationalize their product ranges, particularly with respect to older traditional vaccines such as measles, Bacillus Calmette-Guérin (BCG), and diphtheria, tetanus, and pertussis (DTP) (32,33). Over time, the developing-country manufacturers will increasingly gain expertise and become more competitive with the main multinational actors. This is already the case for traditional, low-priced vaccines, for which the Developing Countries Vaccines Manufacturers Network (DCVMN) has become the largest supplier of UNICEF with respect to the number of doses needed for many monovalent and some multivalent vaccines. For more innovative and costly new vaccines, it will take more time. The above will also lead to increased cooperation either on specific programs or more globally between developing- and industrialized-country manufacturers and to a broader globalization of the vaccine market.

DEVELOPMENT AND SUPPLY OF VACCINES: MAJOR ISSUES FACING INDUSTRY

A large demand—present and future—and a limited number of existing or potential suppliers combine to pose a challenge for meeting and facing a complex process of researching, developing, manufacturing, and supplying the vaccines needed for the world at large. Without elaborating on each step of the process, some of the key issues or hurdles for industry will be discussed below.

The Research and Development Process

Although the different stages of the R&D process (Fig. 8) may look quite similar for vaccines, as for pharmaceuticals, they are