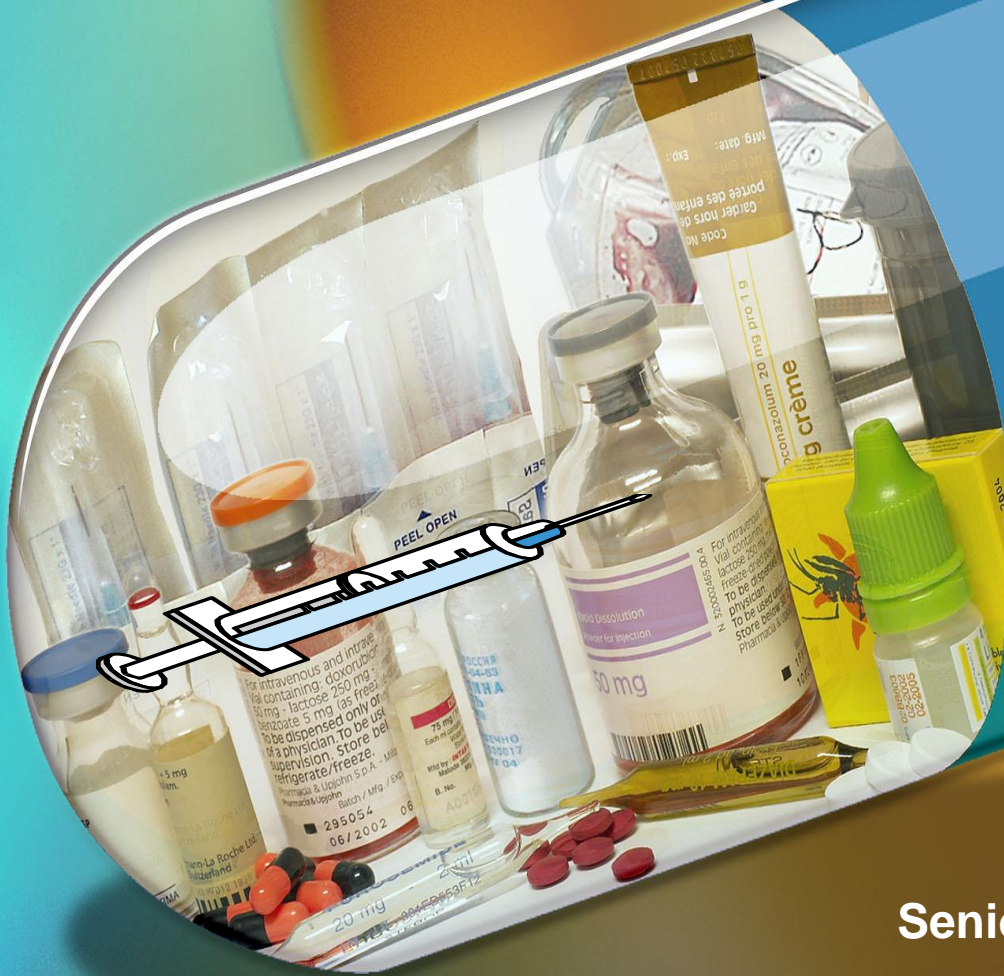


Global Vaccine Market Features and Trends



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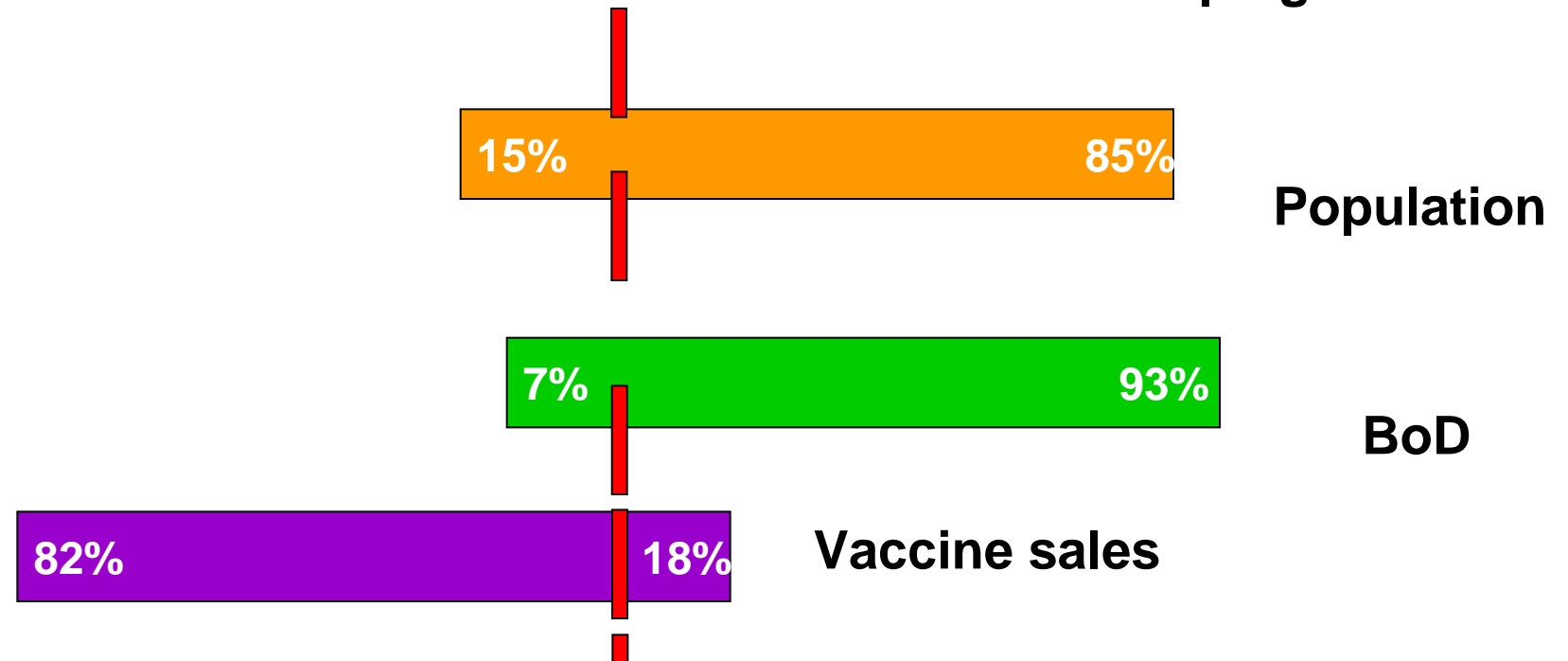
GLOBAL VACCINE MARKET

- MAIN FEATURES OF THE VACCINE MARKET ?
- NEW TRENDS SINCE 2000 ?
- IMPLICATIONS ?

Vaccine Market North – South GAP

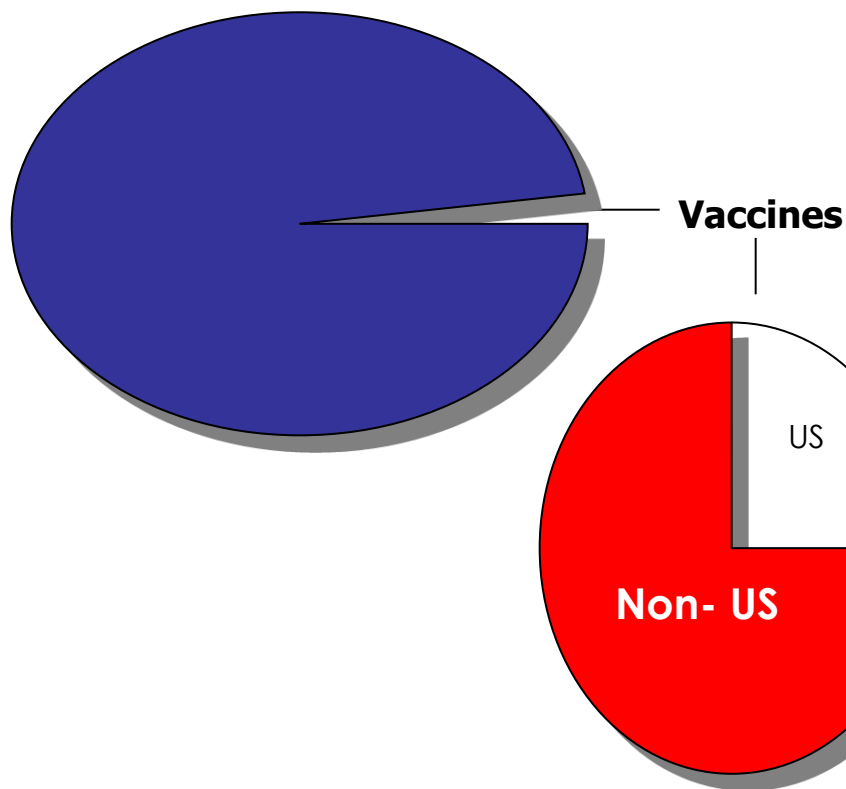
Industrialised countries

Developing countries



VACCINE MARKET STRUCTURE 2010

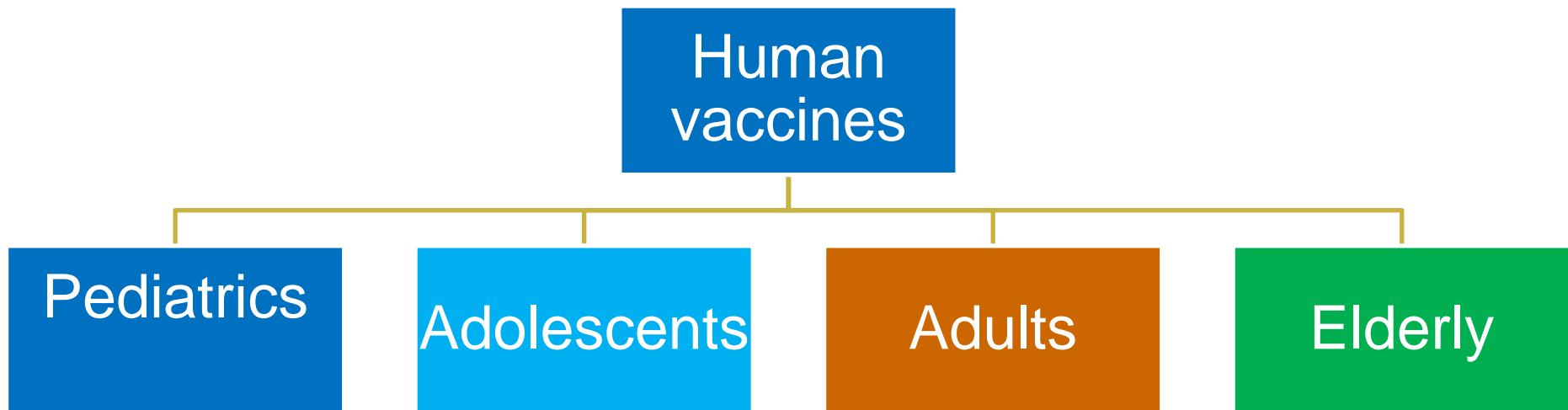
World sales for drugs



Small size market : 2/3% of the global pharmaceutical market but ...

Spectacular growth rate : 10 - 15% per year versus 5-7 % for Pharmaceuticals

Vaccine segments



GLOBAL VACCINE MARKET: RAPID GROWTH and CHANGING STATUS

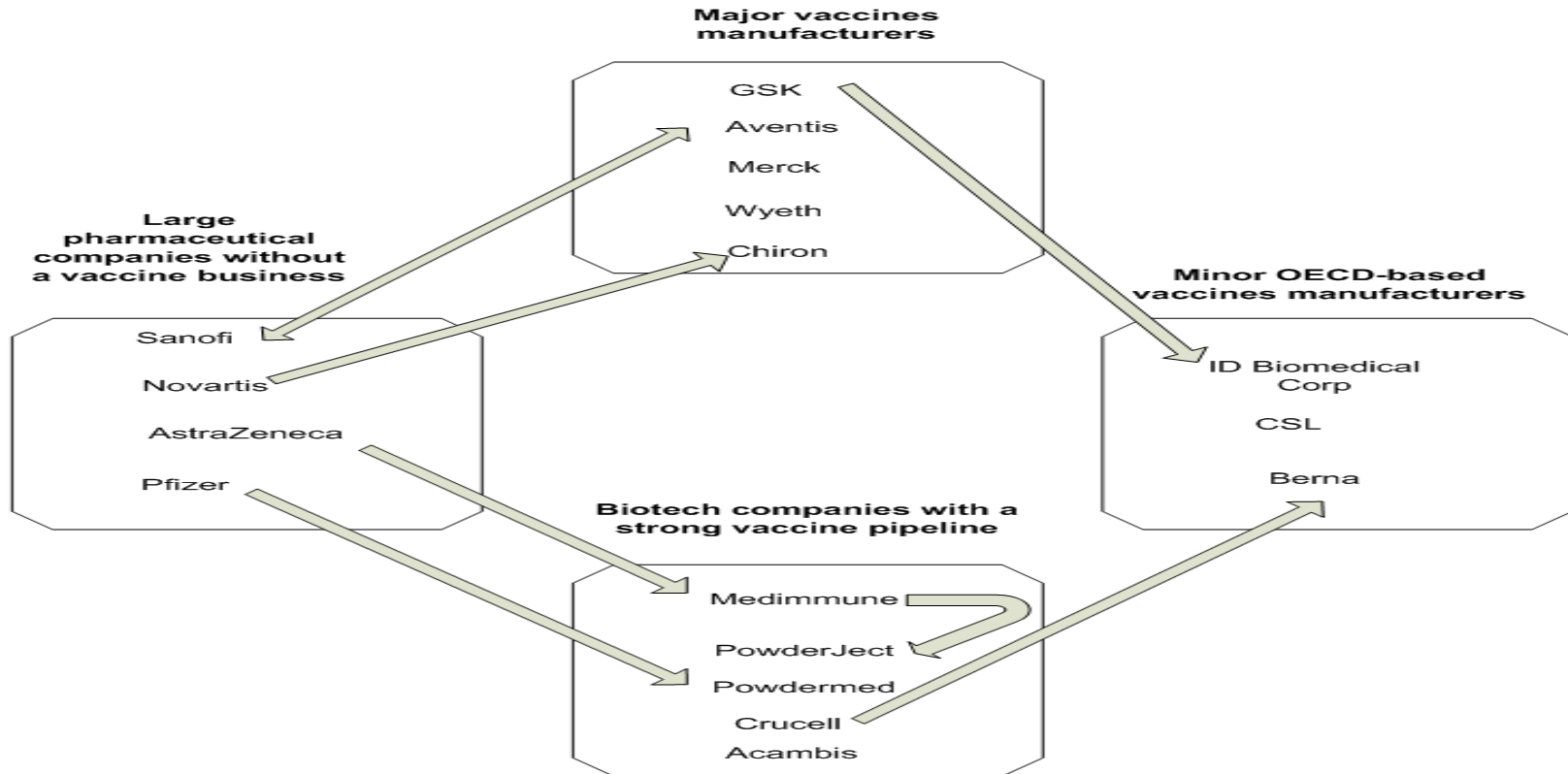
- Tripled in value from USD 5B in 2000 to almost USD 24 B in 2013
 - Influenza vaccine market: estimated at \$2.9 billion in 2011 to \$3.8 billion by 2018
 - US : \$1.6 billion in 2011 to \$2.2 billion in 2018
- Global market projected to rise to USD 100 B by 2025
- More than 120 new products in the development pipeline
- 60 are of importance for developing countries
- Vaccines: becoming an engine for the pharmaceutical industry
- Changing status of the vaccines within the pharmaceutical industry
- New business model for vaccines is emerging?

Main features of Vaccine market (2)

- **Newer and more expensive vaccines are coming into the market faster than ever before**
- **Growing concentration in OECD countries but also newcomers (Pfizer, J&J,...)**
- **Vaccine development: increasing investment**

MERGERS AND ACQUISITIONS 2002-2007: Illustration

Mergers and acquisitions in the vaccine industry, 2002-2007



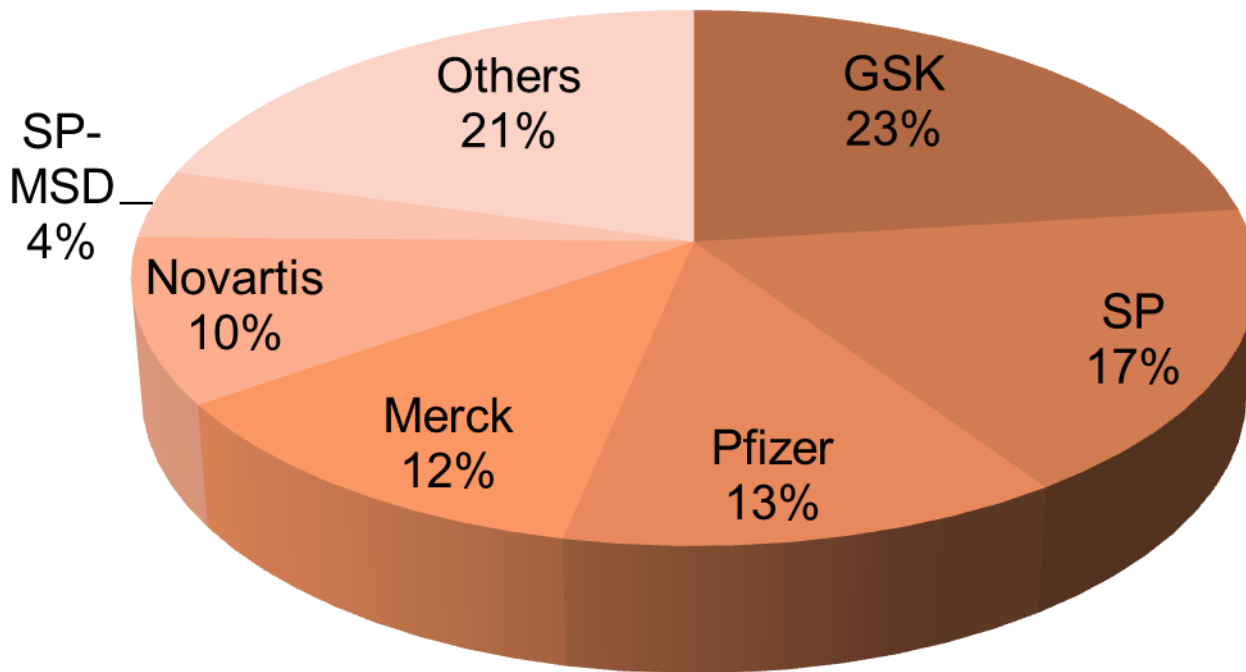
Note. Double arrows denote mergers, single arrows denote acquisitions where the origin of the arrow is the buyer. Headings (such as 'large pharmaceutical companies without a vaccine business') and company names refer to the situation in 2002.

Overview of major vaccine related acquisitions (2005-2012)

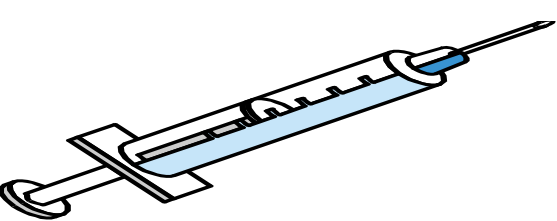
| Target Company | Acquiring Company | Investment Made | Date Announced |
|--------------------------------|------------------------------|-----------------|----------------|
| 1.Bilthoven Bio of Netherlands | Serum Institute of India Ltd | Euros 80M | July 2012 |
| 2.Zhejiang Tianyuan Bio | Novartis | \$ 125 M? | March 2011 |
| 3.Wyeth | Pfizer | \$68 bn | Jan 2009 |
| 4.MedImmune | AstraZeneca | \$15.6 bn | April 2007 |
| 5.Chiron | Novartis | \$5.1 bn | Oct 2005 |
| 6.Crucell | Johnson & Johnson | \$2.6 bn | Sep 2009 |
| 7. ID Biomedical | GSK | \$1.4 bn | Sep 2005 |
| 8.Santha Bio | Sanofi Aventis | \$781 mn | July 2009 |
| 9.Acambis | Sanofi Aventis | \$549 mn | July 2008 |
| 10. Intercell | Novartis | \$363 mn | July 2007 |
| 11. Corixa | GSK | \$300 mn | May 2005 |
| 12. PowderMed | Pfizer | \$230 mn | Oct 2006 |
| 13. Coley | Pfizer | \$214 mn | Nov 2007 |

Source: VacZine Analytics + Fierce vaccine

Global vaccine leaders



- 5 large multi-national corporations make up 80% of the global market
- Major focus on new vaccine development for industrialised country markets



Top product sales in 2010



| Brand name (producer) | Type/composition | 2010 sales (US\$) |
|--------------------------------|--|-------------------|
| Pevnar-13 (Pfizer) | 13-valent pneumococcal conjugate vaccine | \$2.4 billion |
| Proquad (Merck/Sanofi-Aventis) | Measles-mumps-rubella and varicella combination vaccine (MMR-V) | \$1.4 billion |
| Gardasil (Merck) | HPV | \$1.35 billion |
| Pevnar (Pfizer) | 7-valent pneumococcal conjugate vaccine | \$1.2 billion |
| Fluzone (Sanofi Pasteur) | Influenza (seasonal and H1N1 strains) | \$1.2 billion |
| Infanrix and Pediarix) (GSK) | Infanrix = DTaP Pediarix = DTaP-HepB-IPV (combination DPT-based vaccines with acellular pertussis) | \$1.2 billion |

Source: Krishan Maggon knoll (<http://knol.google.com/k/krishan-maggon/global-vaccine-market-2010/3fy5eowy8sug3/152....>)

Total sales First half 2012



| | <i>Vaccine</i> | <i>Company</i> | <i>H1 Sales</i> | <i>Use</i> |
|----|-----------------------------|-----------------|----------------------|--|
| 1 | Prevnar 13 | Pfizer | \$1.847 billion | Pneumococcal infection |
| 2 | PENTAct-HIB | Sanofi | \$672 million | Diphtheria, Pertussis/whooping cough; Tetanus; Polio; Haemophilus influenza type b |
| 3 | Gardasil | Merck & Co | \$608 million | human papillomavirus (HPV) |
| 4 | Pediarix | GlaxoSmithKline | \$535 million | Diphtheria; Tetanus; Pertussis/whooping cough; Hepatitis B; Polio |
| 5 | Hepatitis Vaccine Franchise | GlaxoSmithKline | \$500 million | Hepatitis A; Hepatitis B |
| 6 | Celtura | Novartis | \$441 million | Swine flu |
| 7 | Varivax | Merck & Co. | \$392 million | Varicella virus |
| 8 | Cervarix | GlaxoSmithKline | \$285 million | HPV |
| 9 | RotaTeq | Merck & Co. | \$284 million | Rotaviral gastroenteritis |
| 10 | Synflorix | GlaxoSmithKline | \$274 million | Pneumococcal infection; Otitis media |
| 11 | Rotarix | GlaxoSmithKline | \$266 million | Rotaviral gastroenteritis |

Total sales First half 2012 (2)



| | Vaccine | Company | H1 Sales | Use |
|----|------------------|-----------------------|---------------|---|
| 12 | Zostavax | Merck & Co. | \$224 million | Shingles; Herpes |
| 13 | Prevnar 7 | Pfizer | \$222 million | Pneumococcal infection; Otitis media |
| 14 | Fluzone/Vaxigrip | Sanofi | \$219 million | Influenza |
| 15 | Menactra | Sanofi | \$217 million | Meningitis |
| 16 | Pneumovax | Merck & Co. | \$213 million | Pneumococcal infection |
| 17 | Adacel | Sanofi | \$207 million | Diphtheria; Pertussis/whooping cough; Tetanus |
| 18 | MMR-II | Merck & Co. | \$180 million | Measles, Mumps, Rubella |
| 19 | Boostrix | GlaxoSmithKline | \$165 million | Diphtheria; Tetanus; Pertussis/whooping cough |
| 20 | Biothrax | Emergent BioSolutions | \$88 million | Anthrax |

Sources: EvaluatePharma; Fiercevaccines, Sep 2012

VACCINE MARKET : GROWTH FACTORS ?

Combination of :

- Importance of communicable diseases and new threats
- Cost effectiveness of immunizations
- New funding opportunities (Gov, PPP, donors, Foundations,...)
- New research techniques and manufacturing technologies
- Increasing demand, new target population, larger emerging markets
- Higher prices, improved profitability for the industry (blockbuster vaccines..)



Developing countries: vaccine market share and trends

Developing country market

80 % of population / less than 20% of global market

Regular and rapid growth in volume and dollar value

Emerging
economies and
markets

UN market

Private sector in
Low and Middle
income countries

MNC : Key strategies for developing countries

3 main targets:

- Emerging economies
- UN markets (UNICEF/GAVI and PAHO)
- Private sector, middle income group markets

3 main strategies

- Partnerships with emerging economies and manufacturers
- Accelerated uptake and Differential pricing
- Field presence and active marketing, different presentations

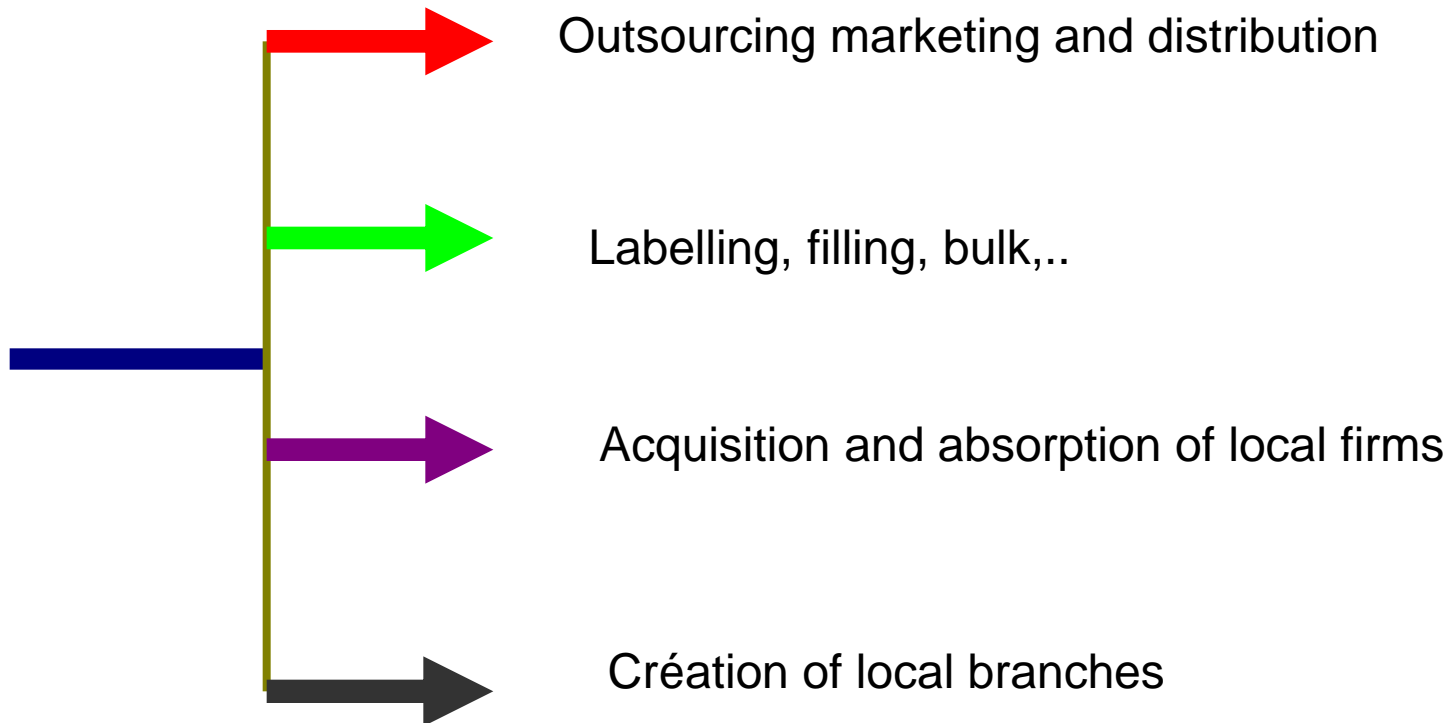
Arrangements with emerging economies and manufacturers

- Various types of arrangements, contracts and partnerships
- Taking into account country potentials and particularities:
 - size of population and potential market,
 - legislation favouring or not domestic production and TT,
 - production costs, scientific and technical capacity, price regulation,
 - NIP, immunization in the private sector,
 - regional influence,..
- Directly with countries and local manufacturers or through PPP or PDP

Various types of arrangements

Objectives:

lower costs, increase production capacity, competitive position
access to large public and private market, ...



A new trend: more active vaccine marketing in DC

- ❑ Emerging markets such as Mexico, Brazil, Turkey, Indonesia, Russia, China and India are among key priorities for MNC
- ❑ Singapour, Malaysia, Vietnam, Philippines, Egypt, GCC and others: second line
- ❑ Wide licensing and registration of new and innovative vaccines
- ❑ Increased presence of sale forces and MNC representatives : "pharma like model"

New business MNC model is emerging?

- More mapping, market segmentation and price differentiation
- Outsourcing selected part of R&D, production and commercialization/Access to promising markets and local capacities, low costs
- Risk sharing with countries and funders
- Collaborative networks and active presence at GHIs

UN Market: UNICEF and PAHO



Spectacular increase in the last 10 years



Both UNICEF SD and PAHO



Polio, measles, new vaccines



National, regional and global priority



MDGs, GIVS, GAVI, AMC, IFFim, GPEI,
Measles partnership, BMGF, DOV/GVAP

UN MARKET (in value)

| | 2002 | 2011 | % |
|------------------|----------------|-----------------|--------|
| UNICEF SD | \$ 220 million | \$ 1,03 Billion | + 468% |
| PAHO RF | \$ 120 million | \$ 400 million | + 333% |
| Total | \$ 340 million | \$1,430 billion | + 420% |



Around 7, 5 % of total vaccine sales

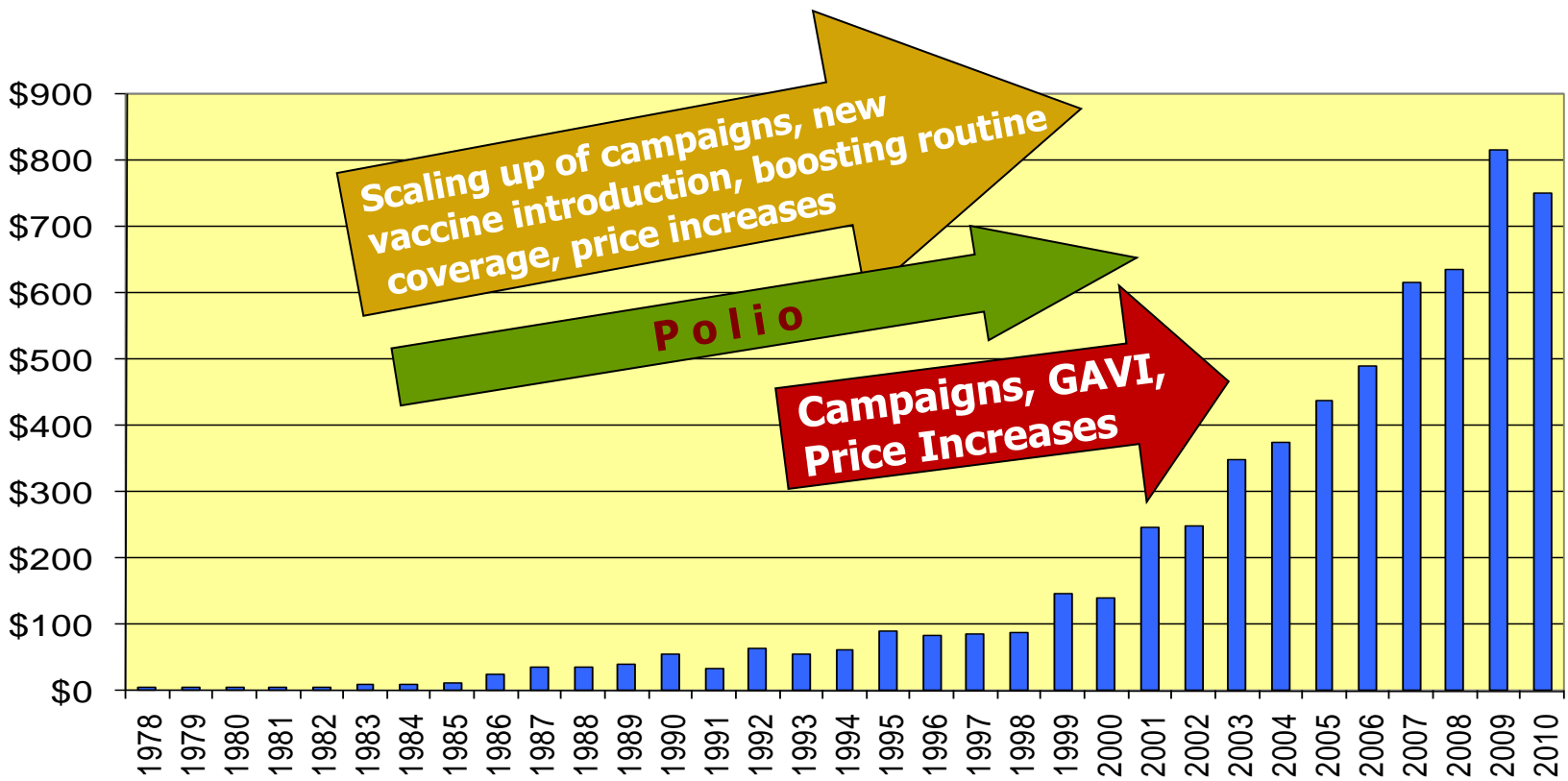
Sources: our WHO estimates based on UNICEF SD and PAHO RF data



**World Health
Organization**

UNICEF annual **vaccine procurement** has increased five fold since 2000 - supporting UNICEF Programmes and on behalf of Partners, Global Programmes Governments and NGO's

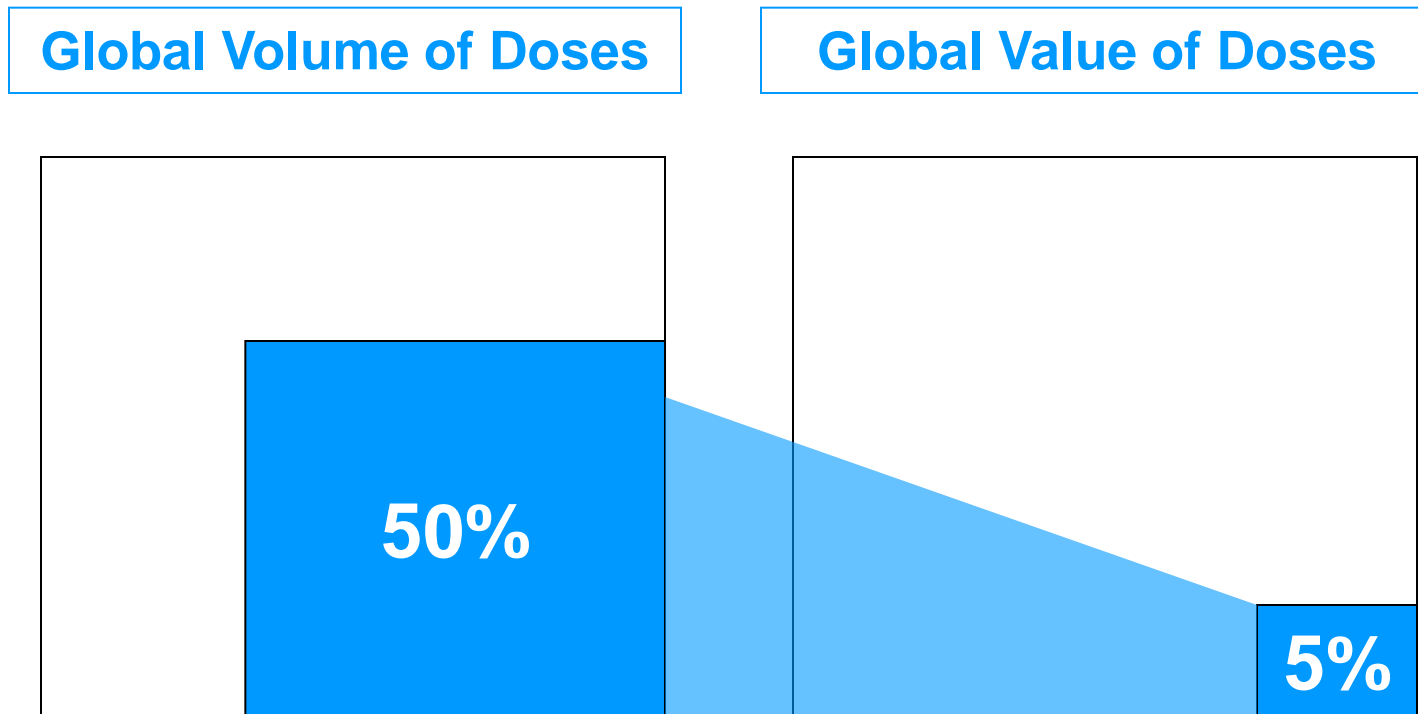
UNICEF SD Annual procurement value of vaccines, in million USD



The arrows indicate the main programme drivers for the increased procurement value.

Source UNICEF Supply Division

The UNICEF 2012: buying 50% of the global volume of vaccine doses, mainly EPI vaccines, but representing only 5% of total market value

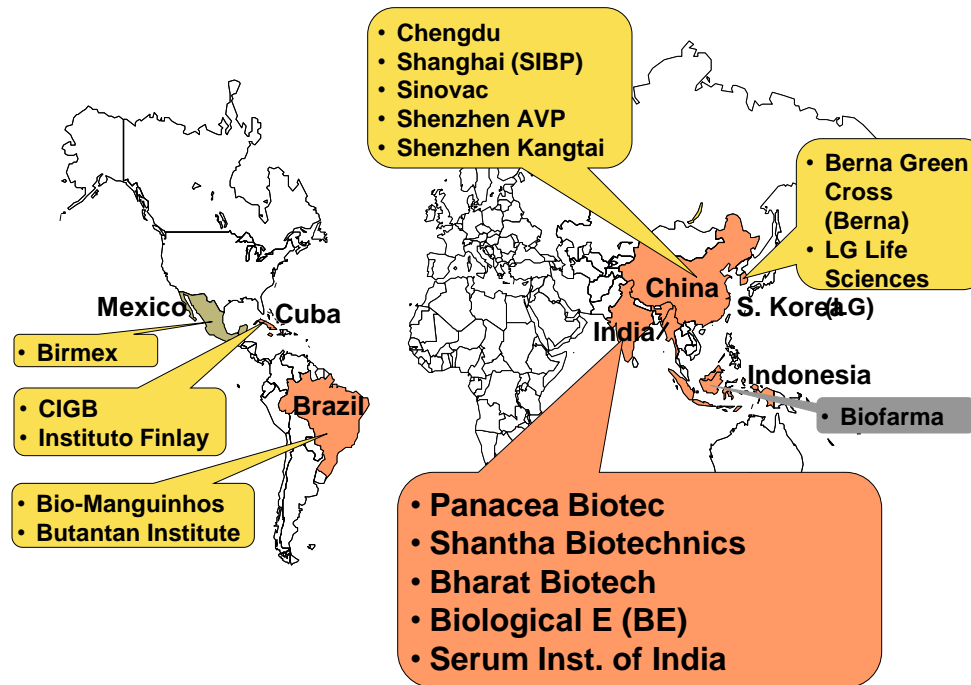


Sources. UNICEF SD



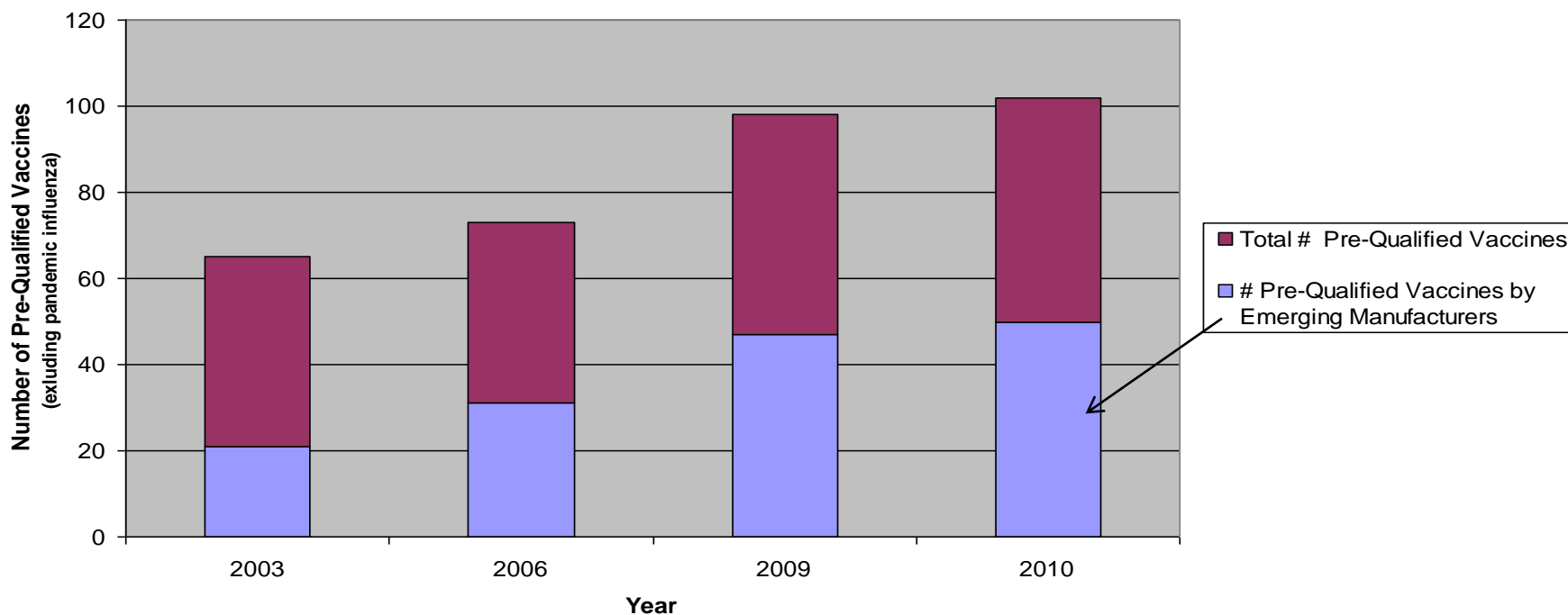
World Health
Organization

EMERGING MANUFACTURERS ARE PLAYING AN ACTIVE ROLE



| Year | Total # Pre-Qualified Vaccines (excluding pandemic influenza) | # Pre-Qualified Vaccines by Emerging Manufacturers (excluding pandemic influenza) | % of Pre-Qualified Vaccines by Emerging Manufacturers | # Emerging Manufacturer Countries with Functional NRA's |
|-------------|--|--|---|---|
| 2003 | 66 | 21 | 32.3% | 6 |
| 2006 | 73 | 31 | 42.5% | 6 |
| 2009 | 98 | 47 | 48.0% | 6 |
| 2010 | 102 | 50 | 49.0% | 7 |

Number of Pre-Qualified Vaccines by Year with Shares from Emerging Manufacturers

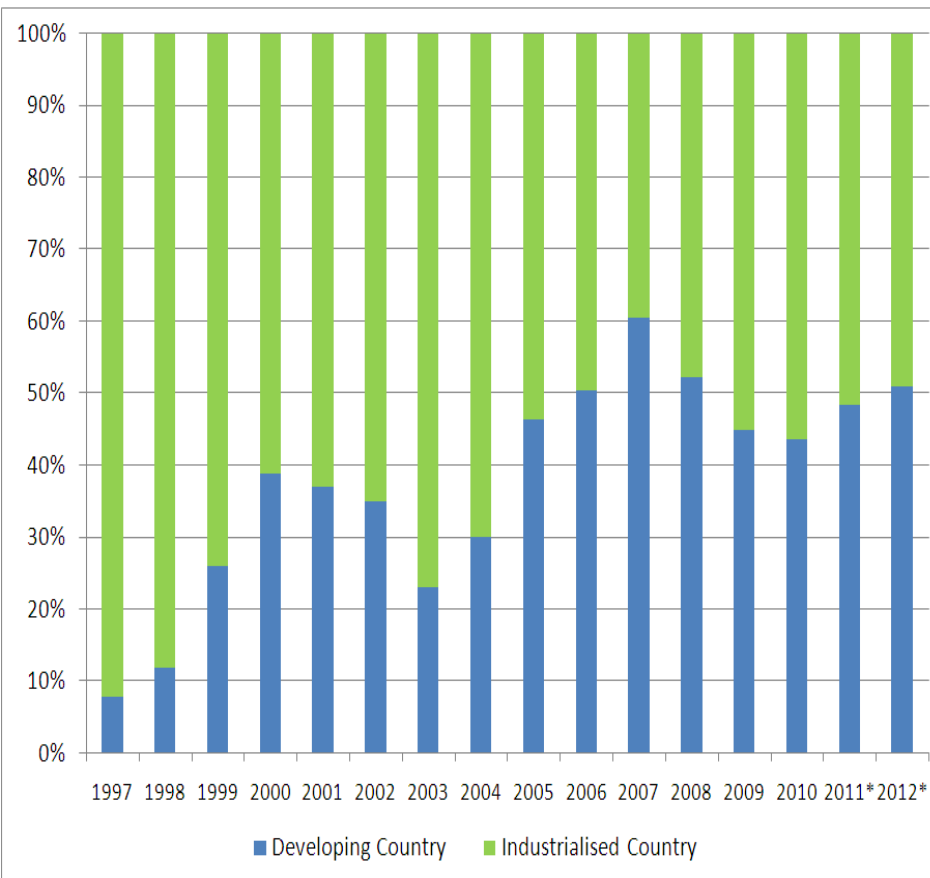


UNICEF SD

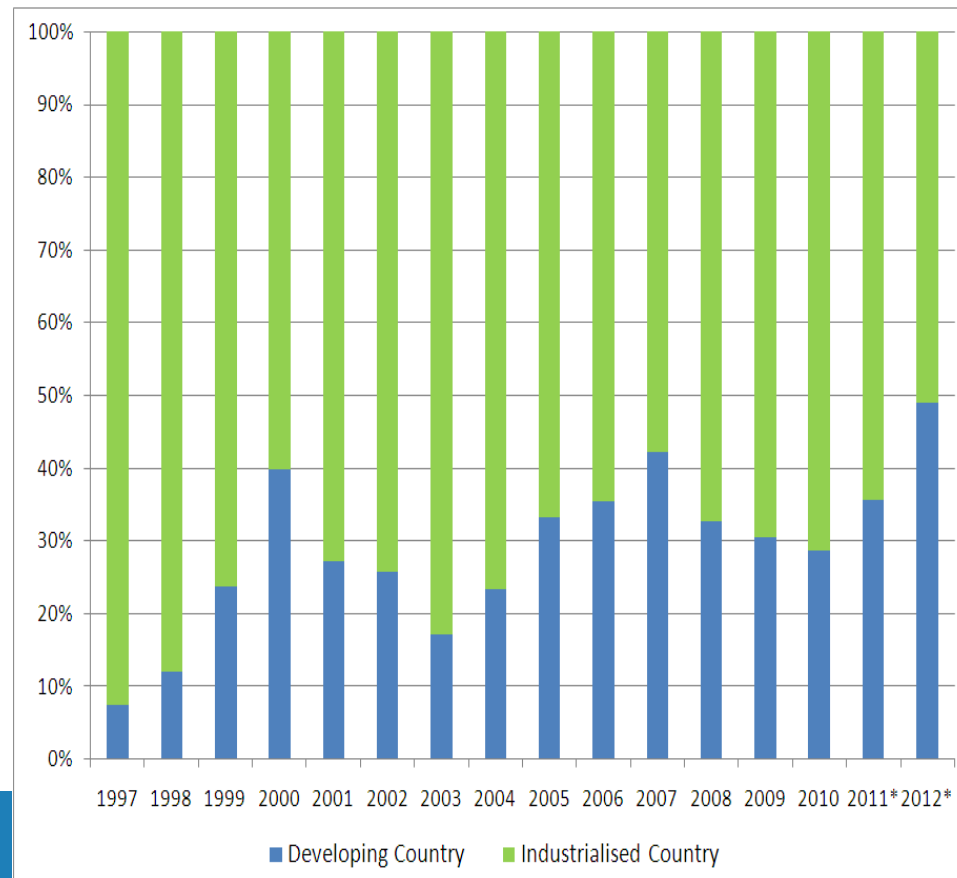
Emerging vs. Industrialized manufacturers

Emerging Market Country Manufacturers make up approximately 50% of procurement volumes in 2010 and 30% by value, predominantly due to lower but increasing participation in new vaccine markets and differing cost bases

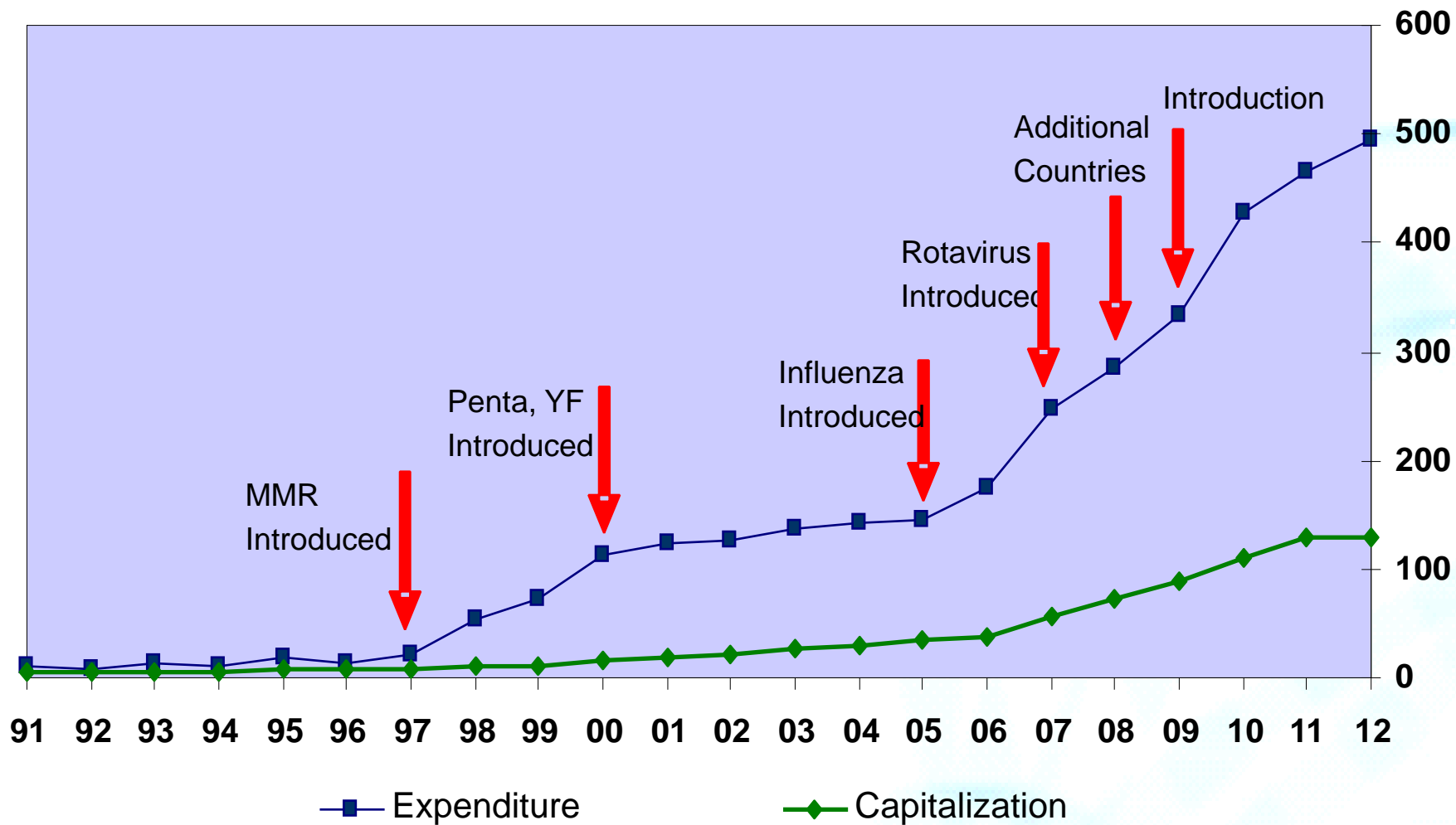
By Volume



By Value



Growth of the PAHO Revolving Fund



The PAHO Revolving Fund

Update: 2012



60 products
28 antigens

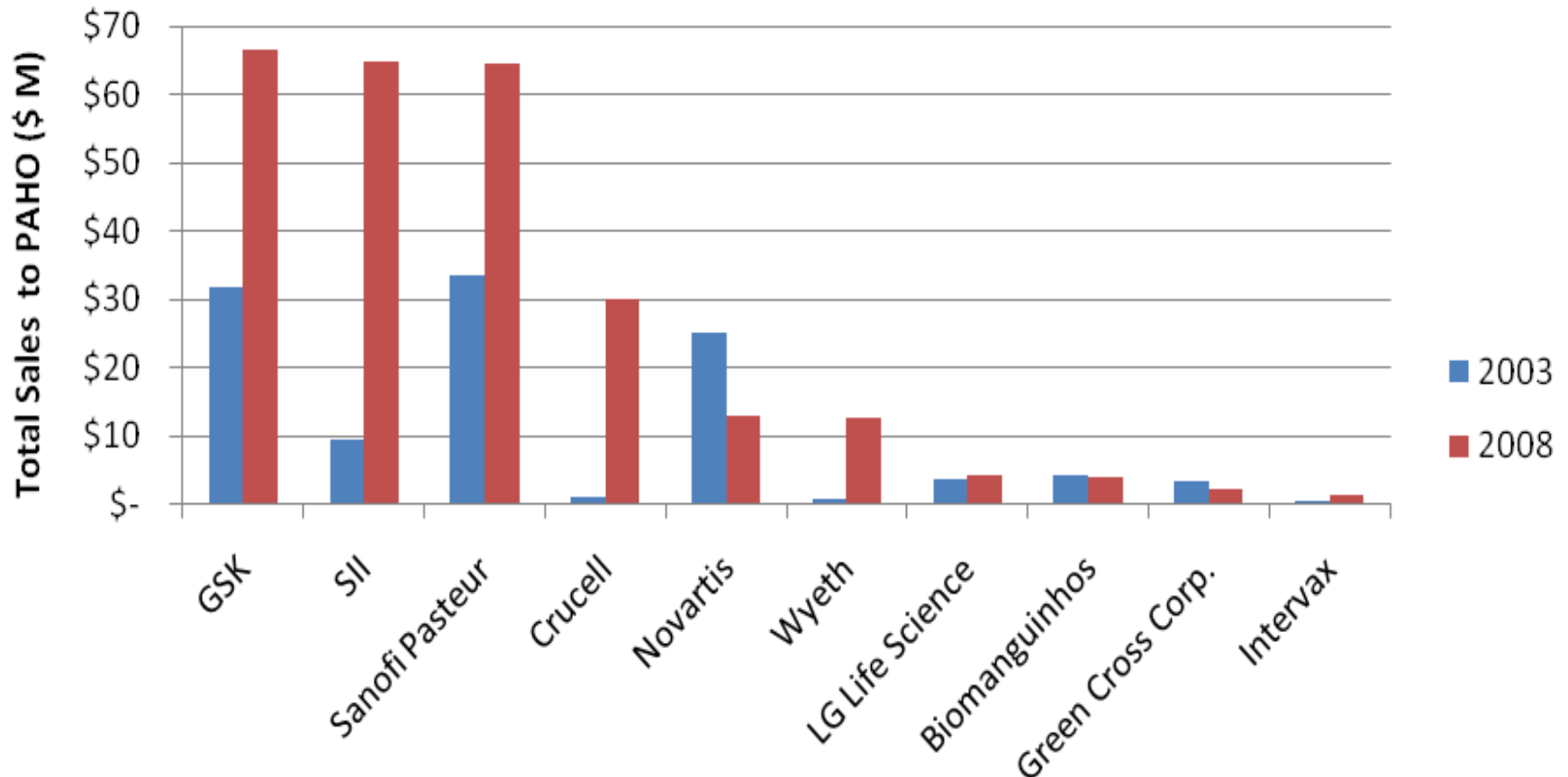


39 countries & territories



Expected Purchases: US\$ 405 million
Capital Fund: US\$ 100 million

Top ten suppliers of PAHO RF 2003-2008



In 2008, no one manufacturer accounted for more than 23% of PAHO purchases

NEW TRENDS ?

New trends ?

Demand side

- Vaccines and vaccinations : on the top of GoV and UN agenda, unmet needs
- Accelerate uptake and increasing demand in LIC
- Middle Income countries including emerging Countries

Supply

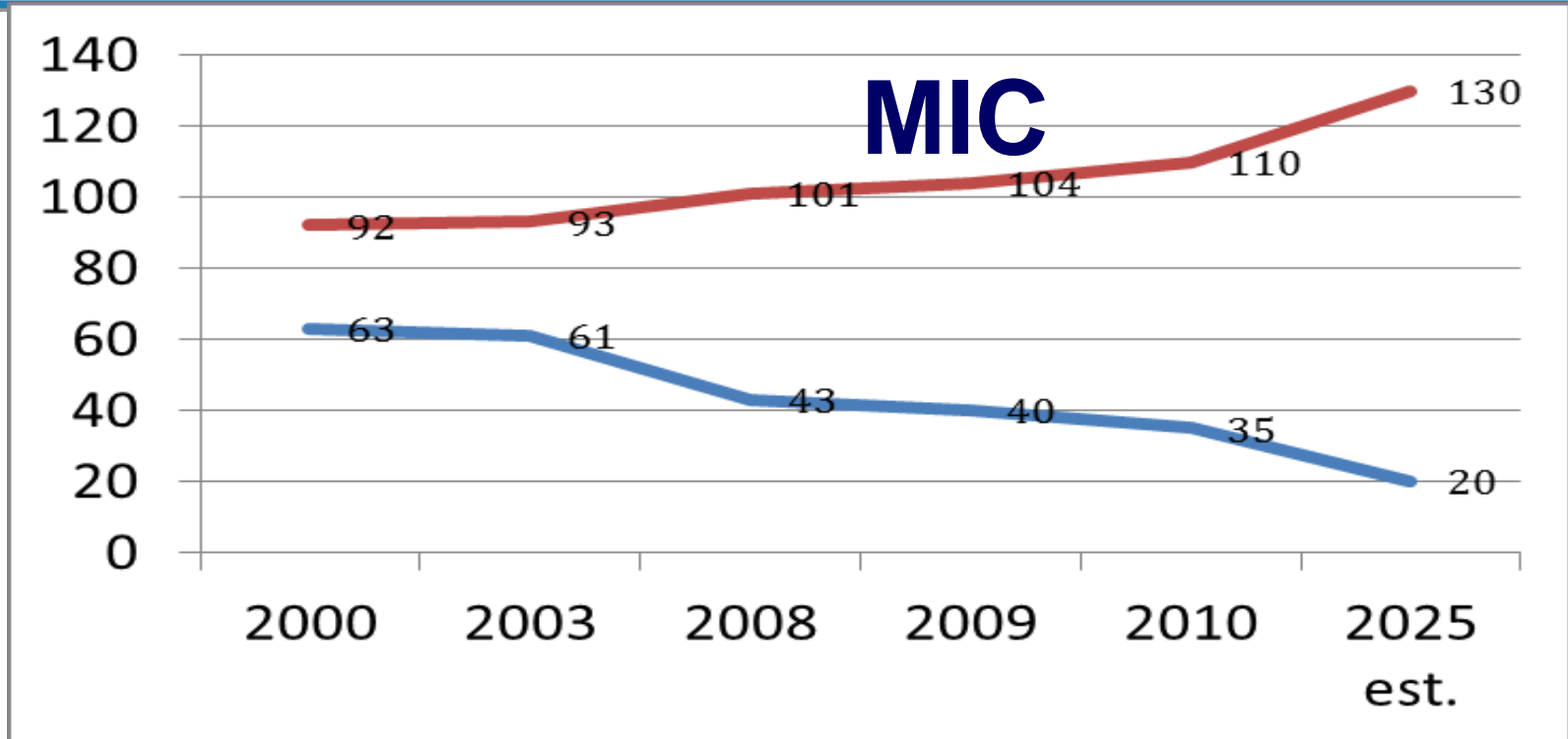
- Increasing capacity
- Remaining tensions on products
- New production and supply strategies

Funding

- GoV resources
- Donors
- Private foundations

More players on demand, supply and financing

By 2025, there will only be 20 LICs

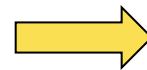


Number of countries by income classification and year

RED = MIC;

BLUE = LIC

Source: Leo and Moss, 2011
CGD A. Glassman



Development of "MIC vaccine market products"

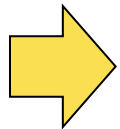
New trends in the last 5 years and their implications

1) Supply side

- Newcomers: Pfizer, Novartis, Johnson and Johnson,...
- New contractual arrangements between MNF/EM/EE
- Outsourcing of production in developing countries
- New commercial and marketing strategies (high volume/lower price, donation, active marketing,...)
- Product/market segmentation and differential pricing
- MNC: new products and presentations with high return,
- EM: basic and underutilized products high volume/low price
- Persistent supply tensions (basic and new vaccines)

Variety of tools to accelerate new vaccine access and to manage risks

- Innovative procurement approaches as pull mechanisms (AMC)
- Push mechanisms to accelerate vaccine supply (such as Men A)
- Long term commitments may be needed to fund vaccines to stimulate capacity expansion (such as YF)



New supply and procurement strategies

- Reduce risks for both producers and purchasers
- Increase predictability and co-responsibilities

Innovative Finance Achieving Results

| Tools Used | Transaction Examples | Goal |
|--|---|---|
| Volume Guarantee & Prepayment | <p>Rotavirus Vaccine:</p> <ul style="list-style-type: none"> Volume guarantee provided for a portion of the quantities with some volumes paid for in advance Contract duration of 5-years covering 132M doses New vaccine launched and sustained at lower price Financing provided by GAVI, with strategic and technical support from the Gates Foundation ("BMGF") | <ul style="list-style-type: none"> \$15 per course → €3.76 per course >\$400M in savings over 5 years Prepayment understood to facilitate expected expansion of manufacturing capacity Accelerated introduction of Rotavirus vaccine made possible through certainty provided by commitment in new markets |
| Volume Guarantee | <p>Oral Polio Vaccine (OPV):</p> <ul style="list-style-type: none"> Firm contract signed for 2011-2012 with large bulk and fill-finish manufacturer who at the time was considering exit of market Duration of 2-years originally covering 270M doses per year (540M doses total) Financing provided by BMGF | <ul style="list-style-type: none"> Decrease in price offered to <\$0.118 per dose generated significant savings versus current WAP of >\$0.13 Delayed exit of manufacturer by >2 years Increased visibility for manufacturer and certainty of UNICEF procurement during fragile OPV market |
| Volume Guarantee & Prepayment | <p>Pentavalent Vaccine (lyophilised):</p> <ul style="list-style-type: none"> Contract signed with new entrant to Pentavalent market with volume paid for in advance Duration for <1 year covering 10M doses Financing provided by GAVI | <ul style="list-style-type: none"> New entrant to market secured volume and able to offer extremely attractive price of \$1.80 per dose, Expanded vaccine security with expanded manufacturing capacity in a fragile market |
| Volume Guarantee | <p>PCV</p> <ul style="list-style-type: none"> Volume guarantees for 20/10/5% of quantities or years 1/2/3 of 10 year contract Financing provided by GAVI and WB | <ul style="list-style-type: none"> Part of overall AMC structure to achieve tail price of max. \$3.50 and sufficient production quantities to meet demand |

Source: UNICEF SD, DCVMN meeting, Nov 2012

Vaccine Market:

Positive trends and Main Issues

- Positive trends
 - Immunizations: on the top of the agenda: DOV and GVAP
 - Promising vaccine pipeline, R&D
 - Growing support: GAVI partners + Gov funding
 - Multiple initiatives, PDPs and PPPs
 - New players on supply and funding
 - More WHO PQ vaccines leading to competition, price decrease
 - Strategic role of UNICEF SD and PAHO and increasing role of funders
- Concerns :
 - Oligopoly, limited supply for DC and Shortage risks
 - Upstream factors : Technology transfer and IPRs, R&D for most needed vaccines, DCVM R&D capacity , ..
 - New vaccine costs and prices
 - Financial sustainability ? Govt responsibilities role
 - Future of International initiatives
 - Future of Emerging Manufacturers
 - Impact of the financial crisis?