

# How Companies Choose Projects

Stanley A. Plotkin

# Reasons Why Vaccine Manufacturers Launch a Development Program

---

**1) Market**

**2) Market**

**3) Market**

# How Market is Determined

---

1. Demand from consumers in developed countries  
e.g. Lyme Disease, Acellular Pertussis
2. Demand from authorities in developed countries  
e.g. Mening C
3. Epidemiologic data  
e.g. Pneumococcal conjugate
4. Expert opinion  
e.g. Mumps
5. Guesses, buttressed by precise but inaccurate data. e.g. Hepatitis B

# Reasons Why Vaccine Manufacturers Launch a Development Program

---

**4) Public Health interest**

**5) Technical Feasibility**

**6) Intellectual Property**

**7) Fit with Other Vaccines**

# Public Health Interest

---

**Development programs for HIV vaccines based more on this than on expectation of profit**

# Technical Feasibility

---

**Breakthroughs come from academia and government, and now biotech**

**However, as in Hollywood, a concept must be developed as an idea.**

**An idea is useless unless it can be scaled up.  
e.g. vectors**

**Mice lie, or at least exaggerate. e.g. DNA**

# Intellectual Property

**A quagmire**

**May block development or sale**

**e.g. Hepatitis B  
Lyme**

# **Fit with Other Vaccines**

---

**Combinations**

**Travel Vaccines**

**Syndrome Coverage**

**e.g. Meningitis**

# **The Road to Vaccine Development**

---

## **Academic**

- 1. Identify the mechanism of natural protection**
- 2. Isolate the antigen(s) responsible for the protection**
- 3. Show in animals that the vaccine protects**
- 4. Find the best formulation of the antigen**

## **Industry**

- 5. Increase yield and purity of vaccine**
- 6. Show the safety of the vaccine in animals**
- 7. Produce a lot under GMP**
- 8. Perform Phase 1, 2, 3, 4 clinical trials**

## Estimates of Transitional and Cumulative Success Probabilities for Vaccines

<b>Transition Probability</b>	
<b>Preclinical to Phase 1</b>	<b>0.57</b>
<b>Phase 1 to Phase II</b>	<b>0.72</b>
<b>Phase II to Phase III</b>	<b>0.79</b>
<b>Phase III to Registration</b>	<b>0.71</b>
<b>Registration to Launch</b>	<b>0.96</b>
<b>Cumulative Launch Probability</b>	
<b>Preclinical to Launch</b>	<b>0.22</b>
<b>Phase I to Launch</b>	<b>0.39</b>
<b>Phase II to Launch</b>	<b>0.64</b>
<b>Phase III to Launch</b>	<b>0.68</b>
<b>Registration to Launch</b>	<b>0.96</b>

## Estimates of Clinical Development and Approval Times Mean Time Duration in Months

---

<b>Study</b>	
<b>Phase</b>	<b>BioTech</b>
Preclinical	NA
Phase I	19.5
Phase II	29.3
Phase III	32.9
Registration, Review and Launch	16.0
Total Excluding Preclinical	97.7 (8+ Yrs.)

# Lyme Disease Vaccine

**20,000 cases/yr**

**Geographically localized**

**Joint, heart, CNS complications**

**Outer surface Protein A vaccine**

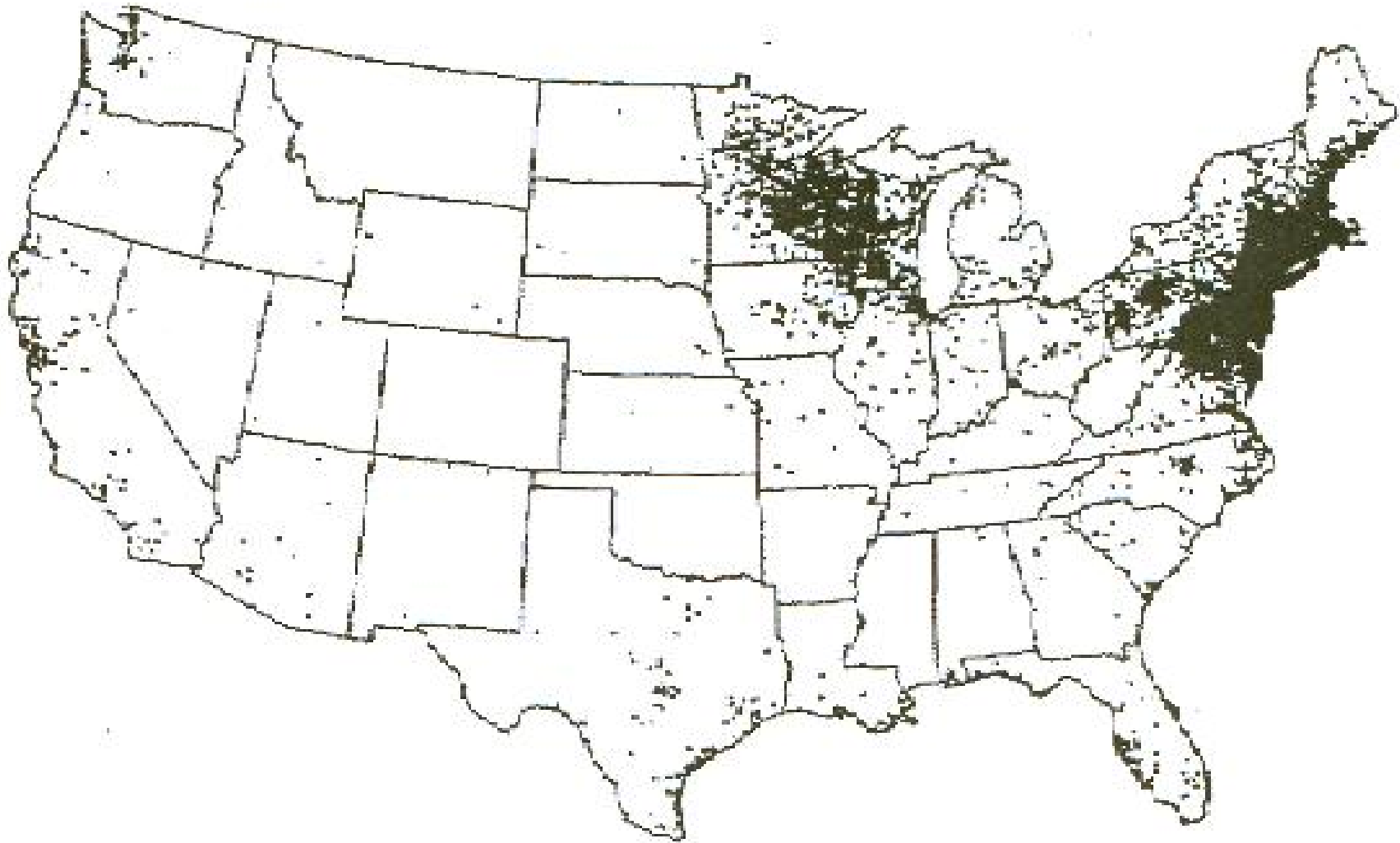
**licensed in 1999 (GSK + Sanofi Past)**

**?Autoimmune epitope**

**Cost-effective, but poor sales**

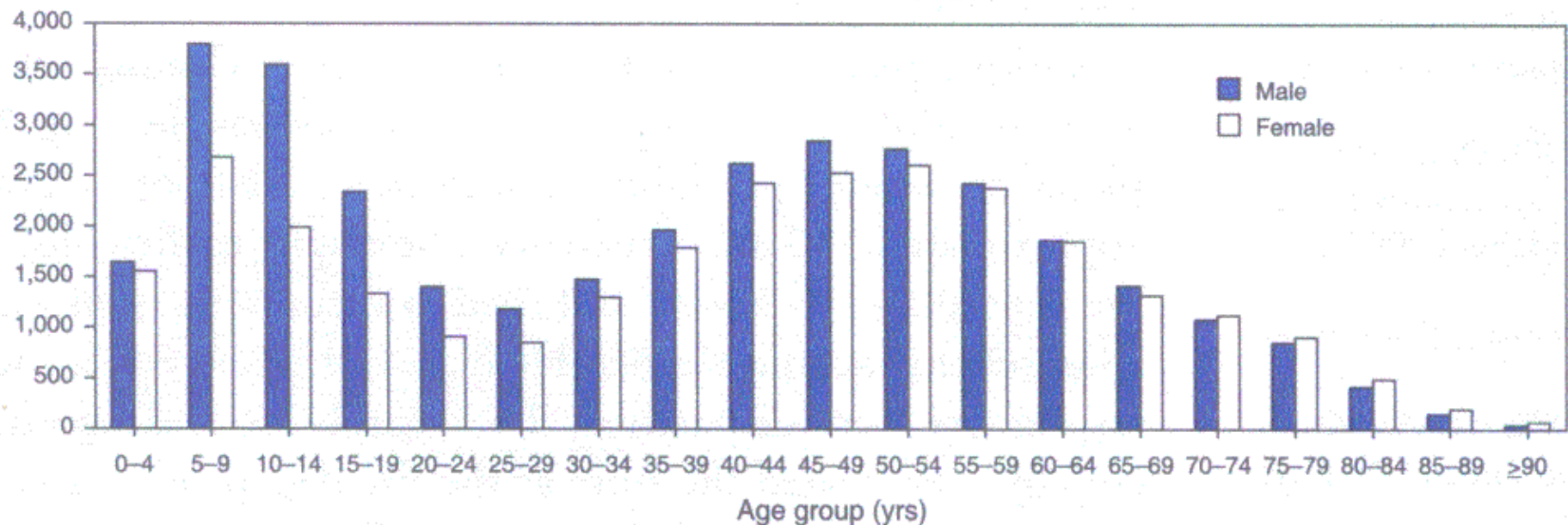
**Withdrawn 2002**

## Number of newly reported Lyme disease cases, United States, 2006



Medicine & Health, Rhode Island 91(7):229-230.

# Number of newly reported Lyme disease cases, by sex and age group – United States, 2003 - 2005



## **“From Lyme Disease Vaccine Recommendations”**

**Lyme disease vaccination may be considered for persons 15-70 years who are exposed to tick-infested habitat but whose exposure is neither frequent nor prolonged. The benefit of vaccination beyond that provided by basic personal protection and early diagnosis and treatment of infection is uncertain.**

## **Estimated Yearly Congenital CMV Infections and Disease in US**

<b>Live Births/yr</b>	<b>4,000,000</b>
<b>Congenital Infections</b>	<b>28,000</b>
<b>Symptomatic at Birth</b>	<b>3,640</b>
<b>    Sequelae</b>	<b>1,820</b>
<b>Asymptomatic at Birth</b>	<b>24,360</b>
<b>    Sequelae</b>	<b>3,410</b>
<b>Estimated Sequelae in Seropos.</b>	<b>2,350</b>
<hr/> <b>Total Sequelae</b>	<hr/> <b>9,400</b>

# **CMV Vaccines - History**

---

**1975      Attenuated Vaccines (Elek, Plotkin)**

**1975 – 1979      GSK sponsorship**

**1980-1985      Merck sponsorship**

**1985-1990      Orphan drug, Sanofi Pasteur**

**1991      NAID**

**1991      Subunit gB (Chiron)**

**1995      Canarypox – CMV (Sanofi Pasteur)**

**1996      Recombinants (Aviron)**

**2001      gB (Sanofi Pasteur)**

**2000      IOM Report**

# Experimental CMV Vaccines

---

- **Live attenuated Towne strain**
- **Subunit gB glycoprotein (SP, GSK)**
- **Recombinant of Towne with genes from Toledo virulent virus (MedImmune)**
- **Canarypox-pp65 (SP)**
- **Multiple genes in MVA (City of Hope)**
- **Alphavirus replicons (Alphavax)**
- **DNA plasmids (Vical)**
- **gB in adenovirus vector (Australia)**
- **Purified dense bodies (Germany)**

# **Immunization Alliance Members**

**(Selective list)**

**AAFP**

**AAP**

**ACOG**

**AMA**

**APHA**

**Every Child by Two**

**IDSA**

**March of Dimes**

**NFID**

**PIDS**

# **Voices for Vaccines**

---

**Supposed to be voice of pro-vaccination people**

**Website plus personal testimony**

**Fact-based**

**No financial support from industry or government**

**Who will support?**