THE PHARMACEUTICAL INDUSTRY: AN OVERVIEW

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Focus Areas

- Brief historical review of the U.S. pharmaceutical industry.
- Societal benefits and challenges associated with the pharmaceutical industry.
- Overview of drug product marketing and sales issues.
- Interactions between health professionals and the pharmaceutical industry.

Historical Development

1700’s
- Patent medicines and remedies
- Apothecaries dispense pills and potions

1800’s
- Pharmaceutical manufacturers are established in seaports (e.g., Philadelphia, New York)
- Civil War increases demand for drugs

1900 – 1940
- 1910’s – Fat and water soluble vitamins
- 1921 – Insulin extracted from the pancreas
- 1930’s – Sulfonamides
- 1940’s – Penicillin (Initially isolated in 1928)
- World War II begins era of research and development; large scale production begins

1950 – Present
- Technological innovations lead to new expensive products
- The U.S. accounted for nearly 65% of the world wide drug innovations
- Antineoplastics, Cardiovascular agents, Diagnostic agents, Antiulcer drugs, Hormones, Ophthalmic agents, Antihistamines, Bronchodilators, Oral Contraceptives, Analgesics, Antidepressants, Antibiotics

Pharmaceutical Industry

- PhRMA Companies
  - Pfizer, GlaxoSmithKline, Merck
- Branded Products, Research Intensive
- Biotechnology Companies
  - Amgen, Biogen, Immunex
- Generic Drug Companies
  - Mylan, Teva, Watson
Top 10 Pharmaceutical Manufacturers
(Source: www.imshealth.com)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>2003 U.S. Sales in Billion $</th>
<th>Ticker Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>29.2</td>
<td>PFE</td>
</tr>
<tr>
<td>2</td>
<td>GlaxoSmithKline</td>
<td>18.6</td>
<td>GSK</td>
</tr>
<tr>
<td>3</td>
<td>Johnson &amp; Johnson</td>
<td>15.2</td>
<td>JNJ</td>
</tr>
<tr>
<td>4</td>
<td>Merck and Company</td>
<td>14.3</td>
<td>MRK</td>
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<tr>
<td>5</td>
<td>AstraZeneca</td>
<td>10.6</td>
<td>AZN</td>
</tr>
<tr>
<td>6</td>
<td>Bristol-Myers Squibb</td>
<td>9.6</td>
<td>BMY</td>
</tr>
<tr>
<td>7</td>
<td>Novartis</td>
<td>9.5</td>
<td>NVS</td>
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<tr>
<td>8</td>
<td>Amgen</td>
<td>7.7</td>
<td>AMGN</td>
</tr>
<tr>
<td>9</td>
<td>Wyeth</td>
<td>7.6</td>
<td>WYE</td>
</tr>
<tr>
<td>10</td>
<td>Lilly</td>
<td>7.5</td>
<td>LLY</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>129.4</td>
<td></td>
</tr>
</tbody>
</table>

Industry Trends

Mergers and Acquisitions are Strategies to Enhance Research Pipeline and Shareholder Value

"In a surprise move today, everything merged"

Value of Pharmaceuticals
- Medical, Social and Economic
- Decrease morbidity and mortality
- Improve quality of life
- Increase productivity of Americans
- Assist in reducing overall health care costs

Health Care Expenditures
$1.00 Spent in 2001

Hospital Care 31%
Dental 5%
Nursing Homes 7%
Rx Drugs 10%
MD Services 22%

Drug Development: Overwhelming Odds

<table>
<thead>
<tr>
<th>Phase</th>
<th>Test Subject</th>
<th>Purpose</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Laboratory and animal studies</td>
<td>Pharmacology, Toxicology</td>
<td>5,000 - 10,000 new compounds synthesized</td>
</tr>
<tr>
<td>II</td>
<td>Safety PK PD</td>
<td>Safety, PK, PD</td>
<td>60 - 90 enter trials</td>
</tr>
<tr>
<td>III</td>
<td>200 - 500 Patient Volunteers</td>
<td>Efficacy, Dose response</td>
<td>1,000 - 3,000 Patient Volunteers</td>
</tr>
<tr>
<td>IV</td>
<td>1,000 - 3,000 Patient Volunteers</td>
<td>Benefits vs. risk under typical clinical conditions</td>
<td>Review process approved</td>
</tr>
</tbody>
</table>

Drug Development Costs

Expenditures per Drug in Millions $

Source: www.cms.hhs.gov
Drug Patents

- U.S. Patents protect property rights to inventors of new products for 20 years from the date of application filing.
- Pharmaceutical manufacturers typically apply for a patent when a promising compound is discovered.
- May take up to 3 years for a patent to be issued.
- Considering another 10 or more years for testing and review, patent protection lasts about 7 years after FDA approval.

Average Annual Profit Margins

Source: www.cms.hhs.gov

Promotional Spending
$21.2 Billion in 2002

Source: www.imshealth.com
Indirect Marketing Influence – Direct-to-Consumer Advertising

Pro
- Education of public about disease states and medications
- Some physicians report benefit since patients ask better questions
- Promote consumer involvement and empowerment
- Economic benefit to pharmaceutical industry and advertising industry

Con
- Print, radio, television and internet advertising
- Focus on population that has less sophistication than traditional targets (i.e., those prescribing, dispensing and administering drugs)
- Use of athletes and celebrities
- Lack of reliable studies to demonstrate benefit

Average Out-of-Pocket Drug Expense

Source: www.cms.hhs.gov

Prescription Drugs via Internet

Lipitor 40mg Cost ($)
- Costco.com: 95.37
- Drugstore.com: 94.99
- CVS.com: 109.99

Celebrex 200mg ($)
- Costco.com: 80.07
- Drugstore.com: 76.99
- CVS.com: 92.99

Nexium 40mg ($)
- Costco.com: 122.77
- Drugstore.com: 120.99
- CVS.com: 147.99

Source: Richmond Times-Dispatch April 18, 2004

Drug Importation Controversy

Product Quality Concerns
- Counterfeit Drugs – labeling or adulteration issues
- Wholesalers (Amerisource Bergen, Cardinal Health McKesson) comprise 90% of the market
- Use of barcodes and radio-frequency identification
Consumer Concerns

- Increased number of new and expensive drugs
- Increased aging population on chronic drug therapy without adequate insurance coverage
- Decreasing coverage by private insurers with increasing co-payments for branded drugs

Generic Drugs

- A copy of the innovator drug with the same active ingredients and comparable strength, quality and therapeutic effectiveness
- Average Prescription price for trade vs. generic product was $76.29 vs. 22.79
- Hatch-Waxman Act of 1984 and drug substitution laws at the state level supported generic drug use

Generic Drug Industry

- Companies
  - Barr, Bertek, ENDO, Eon Labs, Fougera, Geneva, Global, IVAX, Teva, Watson
- Patent Issues
  - a new generic alternative discounts the innovator product by approximately 40% and captures approximately 40% market share initially
  - a generic drug captures approximately 70% market share after 3 years

Consumer Response - Implications for Physicians

Source: www.ag.state.mn.us

Office of Inspector General Compliance Guidance for Pharmaceutical Manufacturers (June 2001)

- PhRMA Code (July 1, 2002)
  - General Interaction with Healthcare Professionals (Focus on information)
  - Entertainment (Avoid)
  - Continuing Education (Support conference, but not individual participants)
  - Consultants (Avoid token arrangements)
  - Educational and Healthcare Practice-related Items (For healthcare benefit of patients and value of $100 or less)

Pharmaceutical Sales Representatives

- 90,000 - 95,000 Employed in U.S.
- Estimate Cost of $ 150,000 per Representative per Year (salary, bonus, incentives, training, automobile, other expenses)
- Approximately One Representative for every Two General Practice Physicians
- Promotional Messages Restricted to FDA Labeling
Drug Samples

- Widespread industry practice
- Distribution controlled by Prescription Drug Marketing Act of 1987
- Sale is forbidden
- Drug use control issues

Housestaff Attitudes Toward Promotions

Percent Who Consider Appropriate

<table>
<thead>
<tr>
<th>Percent</th>
<th>Very appropriate</th>
<th>Somewhat appropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>abs</td>
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<td>20</td>
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<td>CME</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>luggage</td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Residents and Brand Promotion

Frequency of items found in residents' white coats

- % Carrying item
- % Carrying item with pharmaceutical brand

New Age Representatives

- Specialist/Liaison Positions
  - Medical Science Liaison, Clinical Education Specialist, Regional Scientific Manager
  - Pharmacists (Pharm.D.) or Physicians
  - Collaboration with Sales Force
  - Lack of Financial Incentives for Sales
  - Ability to discuss "off-label" indications
  - Primary Focus is on Thought Leaders

Thought Leaders

- Other Nomenclature
  - Key Opinion Leader
  - Subject Matter Expert
  - Thought Leader
  - Influence Leader
- Focus
  - Local
  - Regional
  - National
Medical Science Liaison Reporting Structure

Authors of Clinical Practice Guidelines and Relationships with the Pharmaceutical Industry

Corporate Philanthropy

Other Common Oxymorons
- Managed Care
- Authentic Replica
- Clearly Ambiguous
- Plastic Silverware
- Unbiased Opinion

Industry Challenges
- Product Pipeline Issues
- Expensive and Unpredictable Research
- Negative Industry Publicity
- Legislative Issues
- Globalization of Marketplace
- Current Marketing Practices
- Mergers and Acquisitions
- FDA Relationship
- Projections for Increased Spending on Drugs

Pharma’s Political Influence

$ 29 Million in Contributions to National Parties and Candidates in Last Election (10th Largest Amount of 80 Industries)

$94.1 Million Spent in 2003 for 675 Lobbyists in Washington

Challenge to All Health Professionals

- Remember Covenantal Relationship with Patients
- Weight the Ethical Issues
- Be Alert to Conflicts of Interest
- Develop a Personal Code of Conduct