

An Overview of the United States Regulatory Environment (FDA and Healthcare) for Global Pharmaceutical Compliance Professionals

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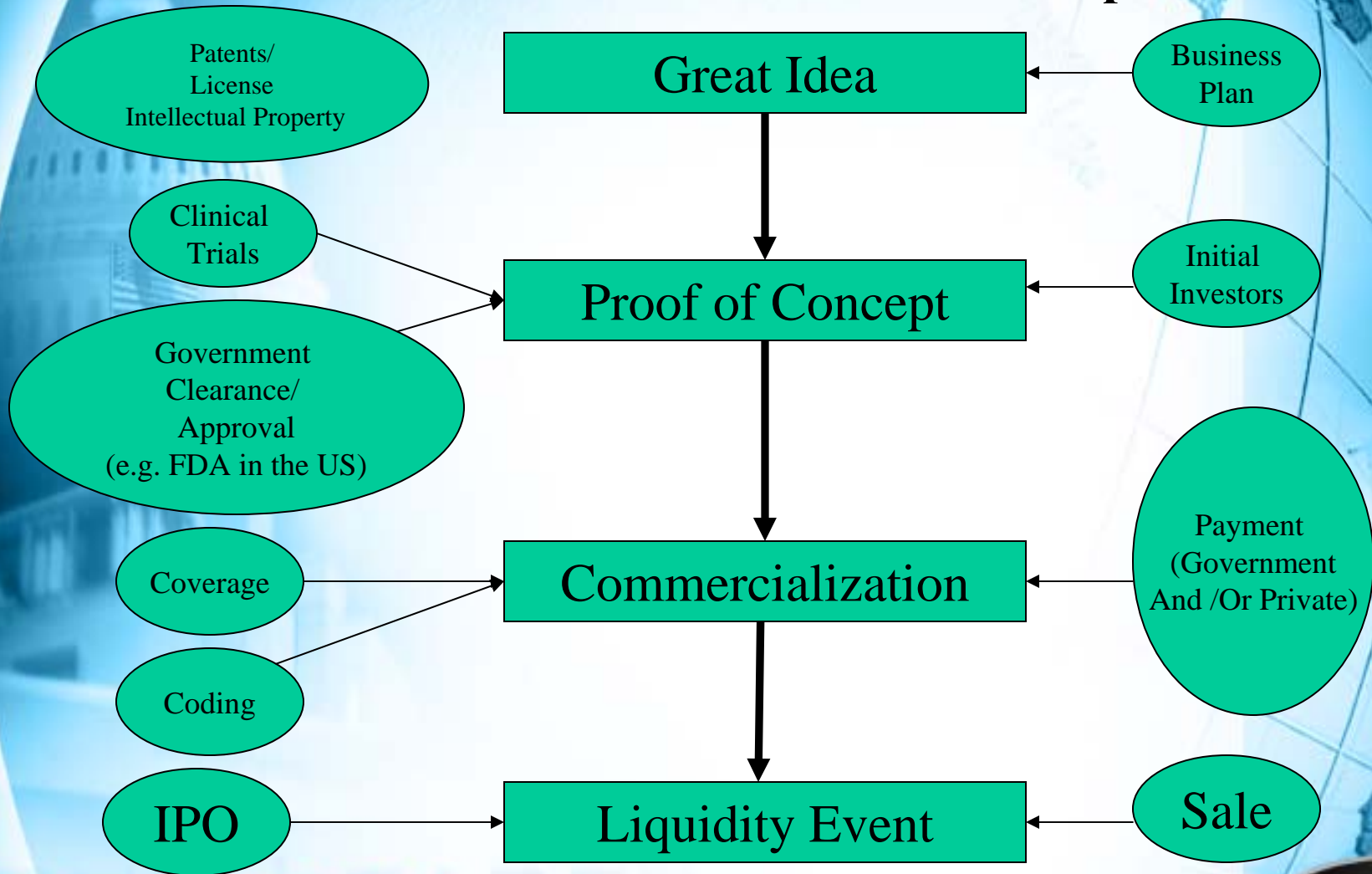
US Regulatory Environment

Focusing on FDA and Other Health Regulatory Commercialization Issues

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Critical Milestones In Drug or Device Product Commercialization – Universal Concepts



United States Food and Drug Administration (FDA)

- Basics – Regulatory Scheme
 - Clinical Trials
 - Product Approval
 - Post Market Enforcement
- FDAAA – The Food and Drug Administration Amendments Act of 2007

FDAAA - User Fees

- Reauthorize drug and device review user fees (PDUFA and MDUFMA)
 - Expanded use for post-market safety
 - Use for enforcement
 - Voluntary review of DTC advertisements

FDAAA: Pediatric Drug Incentives

- Pediatric Research Equity Act
 - Revised standards for requiring pediatric clinical trials
- Best Pharmaceuticals for Children Act
 - Exclusivity incentives for conducting pediatric clinical trials

FDAAA: Key Issues

- Drug Safety: Post Market Studies, Labeling Changes
- Clinical Trial Registry
- Risk Evaluation and Mitigation Strategies (REMS)
- Post Approval Trials

FDAAA: Key Issues

- FDA Drug Safety Surveillance
- DTC Advertising
- Citizen Petitions
- Anti Counterfeiting
- Reagan Udall Foundation

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FDA Clearance / Drug and Device Approval

- **Initial Drug Testing:** Before clinical testing of new products begins, companies must submit an investigational new drug application (IND)
- **Investigational Device Exemption (IDE)**
 - manufacturer must apply for exemption before clinical trials begin

FDA Clearance / Drug and Device Approval

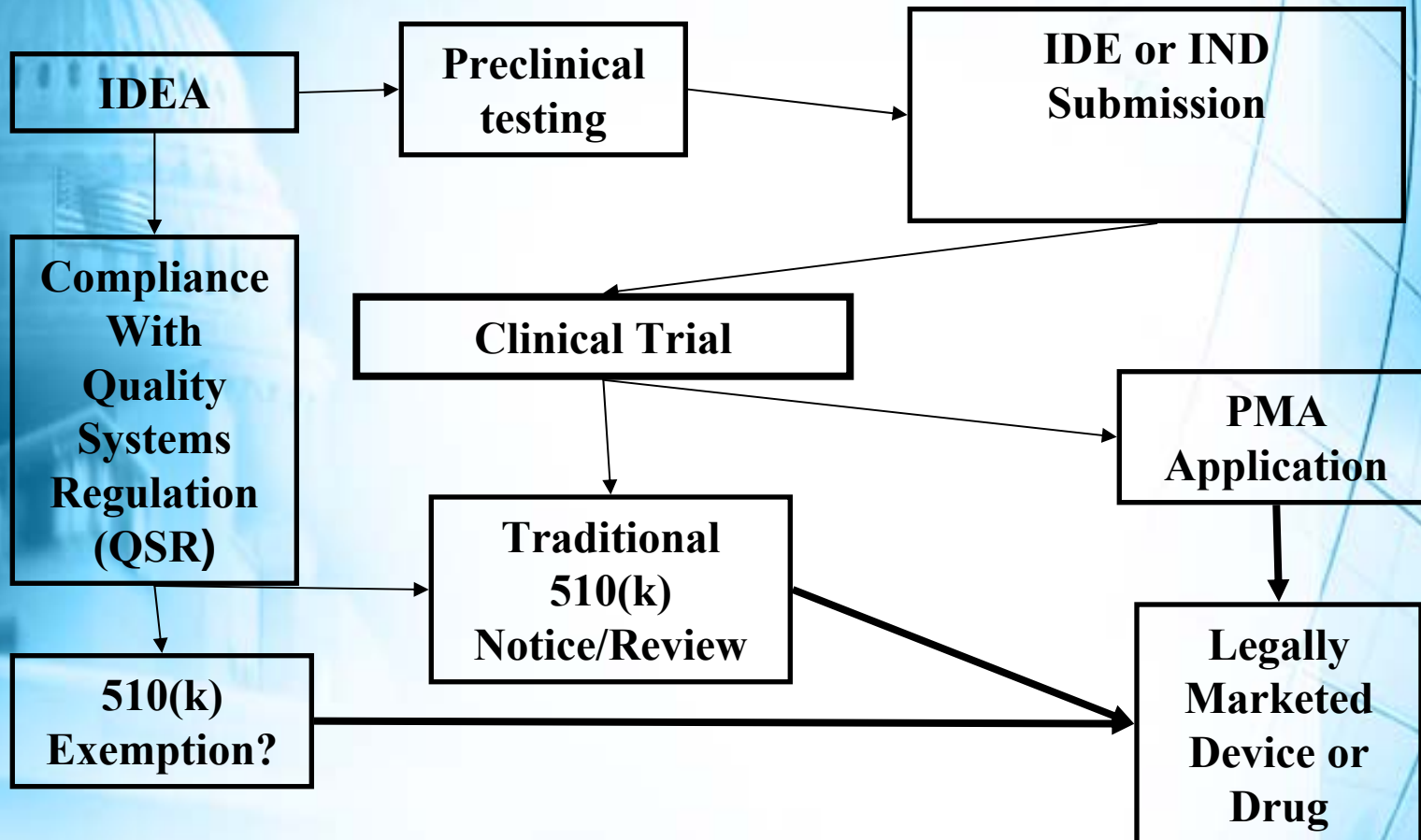
Clinical Trials: There are 3 phases of clinical trials.

- **Phase I Trials** – help determine how the drug is metabolized, help establish the optimal dose, and involve fewer than 100 people.
- **Phase II Trials** – may involve 100-200 patients and explore the safety and effectiveness of the product as well as side effects. Early phase II studies may try to assess the efficacy of the drug, while later studies may evaluate how much better (if at all) the drug is than a placebo given to patients with similar conditions and characteristics.
- **Phase III Trials** – examine the long-term safety and efficacy of the product and often involve thousands of patients throughout the country.

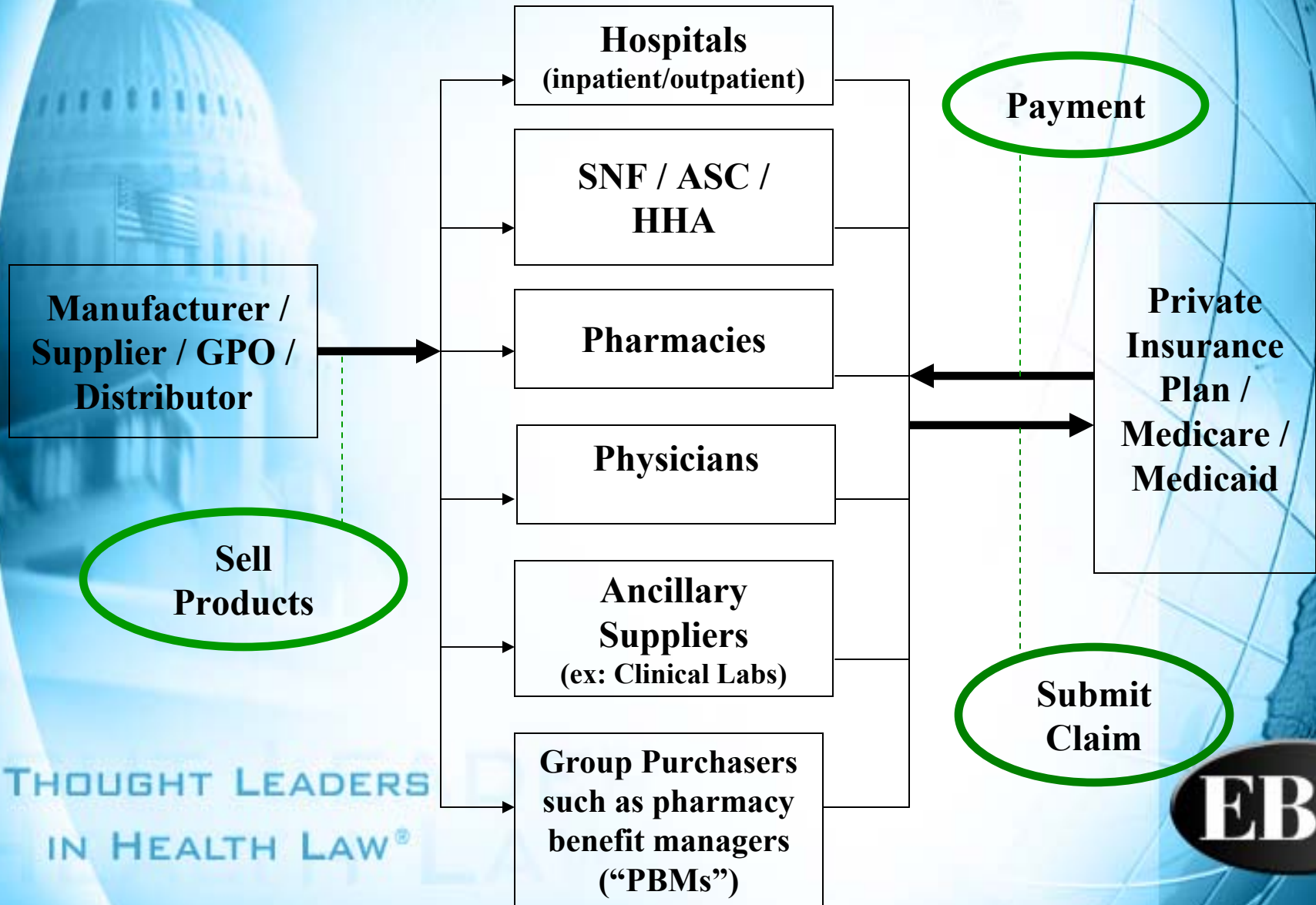
FDA Clearance / Drug and Device Approval Cont.

- **Institutional Review Boards (IRB)** – Institutions conducting clinical trials must establish IRBs, which ensure that studies are conducted ethically and with due regard for patient safety
- **Pre-market notification (Devices) – 510(k)** – contains labeling information, manufacturing information, and information about how the device will be used and devices to which it is substantially equivalent
 - For substantial equivalents, Class I and Class II devices
- **Pre-market approval (PMA)** – more detailed review
- **FDA and Fast Track Review**

FDA Clearance / Drug and Device Approval: the Pre-Market Process



How Does A New Drug or Device Fit Into The U.S. Health Care System?



Who Are The Payers?

Private Payers

Employers

- self-funded or not

Unions

Health Plans

- Blue Cross/Blue Shield Plans
- United Healthcare
- Aetna US Healthcare
- Anthem Wellpoint
- Others

Public Payers

Medicare

- federal
- seniors, disabled, ESRD

Medicaid

- federal/state
- indigent, women, children, indigent seniors, chronically ill

TriCare

- Federal
- military dependants and Retirees

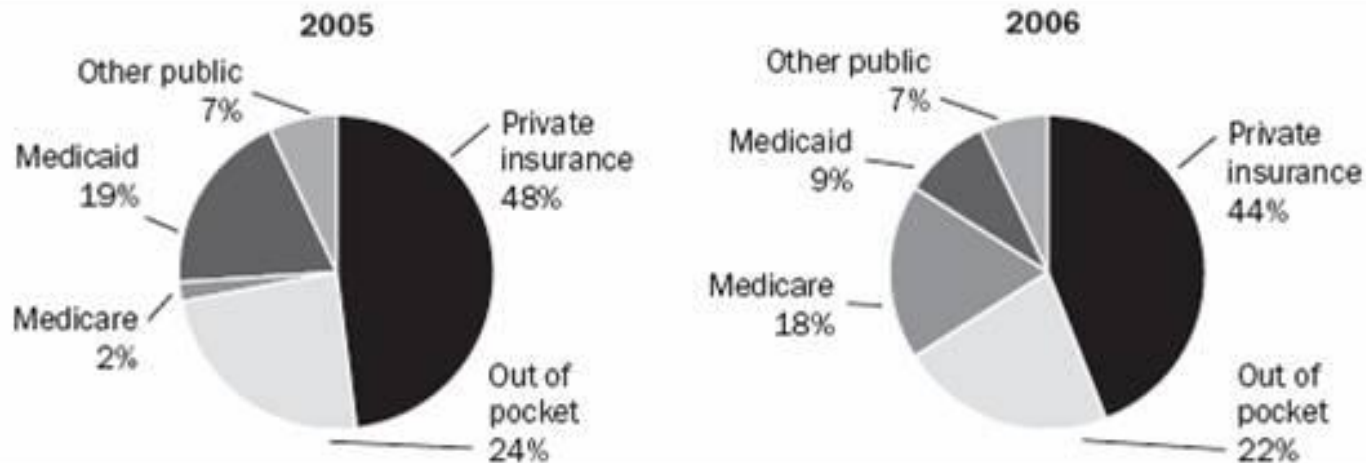
State Children's Health Insurance Program (SCHIP)

- federal/state
- children

Others

Retail Prescription Drug Spending: Commercial and Public Sectors

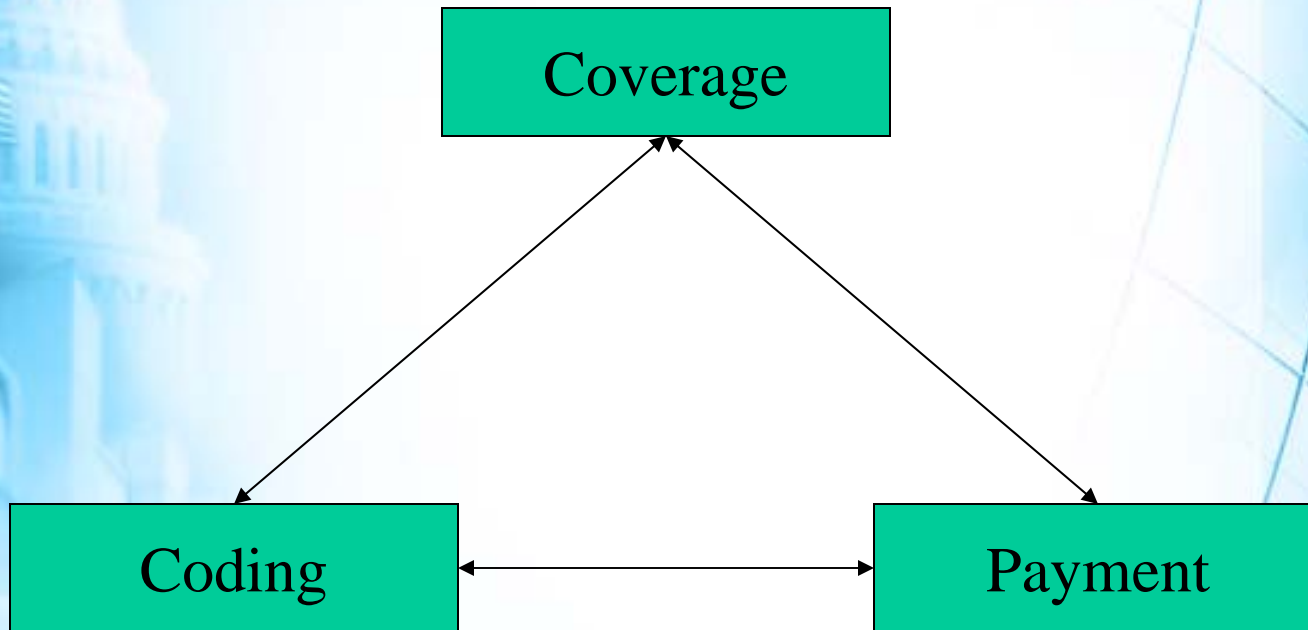
Sources Of Funds For Retail Prescription Drugs, 2005 And 2006



SOURCE: Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Group.

NOTES: Numbers might not add to 100 percent because of rounding. "Other public" includes programs such as workers' compensation, public health activity, Department of Defense, Department of Veterans Affairs, Indian Health Service, state and local hospital subsidies, and school health.

Commercialization Concepts



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FDA Approval ≠ Coverage

- “We do not see why the Secretary [of Health and Human Services] would be bound . . . by any earlier acceptance of MRI by the Food and Drug Administration”

Goodman v. Sullivan, 891 F.2d 449, 451 (2d Cir. 1989)

- FDA approval, alone, does not equate to successful commercialization in the United States

Coding, Coverage and Payment : How Are These Concepts Different?

Coding – Unique identifiers for diagnoses, procedures, devices & diagnostics, inpatient services, and outpatient services

- Links coverage and payment and provides for rapid claims processing and health policy research
- Does not guarantee coverage
- Does not guarantee favorable reimbursement
- Types of Codes
 - ICD-9-CM: Diagnosis & Inpatient Hospital Procedures
 - CPT: Procedures
 - HCPCS: Drugs and Devices

Coding, Coverage and Payment: How Are These Concepts Different?

Coverage - Terms and conditions for payment

- Is not guaranteed when you receive FDA approval/clearance
- Does not guarantee a new or favorable billing code
- Does not guarantee favorable reimbursement

Payment - Remuneration by health insurance plans,
government-funded programs

- Function of coverage and coding
- May be subject to limits
- May be stand-alone or bundled
- May be driven by breakthrough or existing technologies

Commercialization Strategy

- Commercialization process related to coding, coverage and payment should start well in advance of product launch
 - Thinking about coding, coverage and payment at all times beginning with the earliest product R & D discussions as well as when designing clinical trials
- Understanding realistic timeframes is critical

Coverage and Payment Basics

General Rule:

Coverage and Payment of Drugs and Devices Depend upon:

1. Site of Service
2. Enumerated Benefits
3. Enumerated Exclusion
4. Coverage determinations (nationally/locally)

A Closer Look at Select US Federal Government Health Benefits Programs

Medicare

Medicaid

**Veterans
Administration
(VA)**

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Federal Government Programs: Key Points

- No two programs are the same
- Most recent changes focus on competitive market system

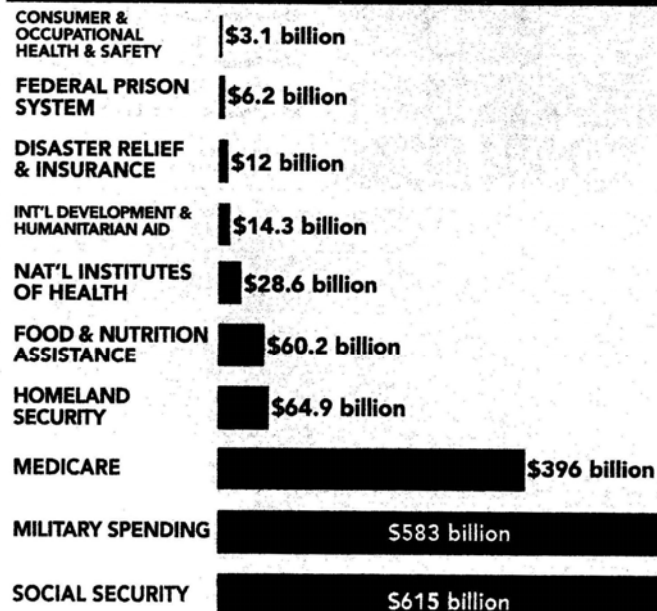
Medicare Spending

IntelligenceReport® Parade.com/intel

GOVERNMENT WATCH **Where Your Money Goes**

Total estimated federal spending for 2008 will be about \$2.93 trillion, a 7% increase over last year. This is a staggering figure, but where exactly does the money go? Here's a partial list of categories that are financed by your tax dollars, according to the Office of Management and Budget. To see the entire 2008 federal budget, go to Parade.com.

2008 Federal Spending



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Medicare Program Basics

Part A – inpatient service benefits

Part B – outpatient service benefits, including physician administered drugs

Part C – Managed Care Contracting for Parts A, B, and maybe D

Part D – outpatient prescription drug benefits (only through private managed care plans)

Aged – Disabled – ESRD Patients

Medicare Program Basics

- A la carte fee-for-service
- Managed Care: bundled benefits; bundled payment
- Administered through a federal agency – the Centers for Medicare & Medicaid Services (“**CMS**”) and through contractors hired by CMS

Medicare Program: Coverage and Payment Basics

- Medicare will pay only for an item or service that is reasonable and necessary for the treatment of an illness, injury, or malformed body member
- Medicare pays providers for most items and services using prospective payment methodologies or fee schedules which vary by provider, provider site, and type of service

Medicare Outpatient Benefit

Example: Diabetes Related Coverage

Part B – physician visits, drugs “incident to” a physician’s visit (*e.g.*, not self-injectible drugs), laboratory tests, test strips, glucose monitors, new screenings

Part D – outpatient prescription drugs (*e.g.*, oral drugs), insulin, insulin syringes, insulin delivery devices not otherwise covered under Part B Durable Medical Equipment (DME) benefit

A Closer Look at Medicare Coverage and Payment for Drugs and Devices

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Medicare Program Drug Coverage Basics: Enumerated Part B Drugs

1. Drugs billed by physicians and provided *incident to physician service* for that patient (e.g., chemotherapy drugs)
2. Drugs billed by pharmacy suppliers and administered through durable medical equipment (DME) benefit (e.g., respiratory drugs given via nebulizer, injectables)
3. Some drugs billed by pharmacy suppliers and self-administered by the patient (e.g., immunosuppressive drugs, some oral anti-cancer drugs).
4. Separately billable drugs provided in hospital outpatient clinics.
5. Separately billable End Stage Renal Disease (ESRD) drugs (e.g., erythropoietin).

Medicare Part B Program Payment Basics for Drugs and Devices

Payment Methodologies for Drugs

- Fee schedules (old “AWP” concept) (new “ASP” concept)
- Manufacturer Average Sales Price (ASP) Price Reporting to CMS
 - ASP is the Average Sales Price to all purchasers (excluding certain nominal charge sales and sales exempted from Best Price) net of all discounts
- Reimbursement Formula: 106% of ASP

Payment Methodologies for Devices

- Not a separate reimbursable event
- Pass-through
- Fee schedules
- Competitive bidding

Medicare Part D

- Medicare Prescription Drug Improvement and Modernization Act of 2003 (MMA) created new Part D, the new Medicare outpatient prescription drug benefit.
 - Greatly expands Medicare beneficiaries access to outpatient drugs. Embraces private sector delivery and private competition.

Medicare Part D

- **Covered “D” Drug** – a drug available only by prescription, approved by FDA, used and sold in the United States, and used for a medically accepted indication (as defined in section 1927(k)(6) of the Act).
- A covered Part D drug includes prescription drugs, biological products, insulin as described in specified paragraphs of section 1927(k) of the Act, and vaccines licensed under section 351 of the Public Health Service Act. The definition also includes “medical supplies associated with the injection of insulin (as defined in regulations of the Secretary).” FDA defines those medical supplies to include syringes, needles, alcohol swabs, and gauze.

Medicare Part D

- Fundamental differences between Medicare Part B and Part D
 - Part D completely delivered through private plans
 - No government reimbursement formula
 - Government pays plans based on competitive bid
 - Plans pay pharmacies and manufacturers based on plan negotiation.
- Plans bear financial risk for providing the benefit. Patients pay a subsidized premium and federal government makes certain risk sharing payments.

Part B drugs vs. Part D drugs: The Implications on Commercialization

- CMS Guidance: Medicare Part B versus Part D Coverage Issues (July 27, 2005 Draft)
- Medicare Parts B/D Coverage Issues Chart available at:
http://www.cms.hhs.gov/Pharmacy/08_Parts%20B%20&%20D%20Information.asp

Medicare Part D Balances Affordability And Access

- Plans provide standard benefit which includes deductible, cost-sharing, coverage gap and catastrophic coverage, or actuarially equivalent benefit.
- Plans allowed to use formularies, tiering, utilization management tools, e.g., prior authorization and step therapy.
- Beneficiary rights include exceptions and appeals to change tiering (or obtain non-formulary drug), pharmacy access.

Medicare Part D - Formularies

- Part D Plan Pharmacy and Therapeutic (P&T) Committees decide which drugs will be included
 - P&T Committee includes majority of members who are practicing physicians or pharmacist; at least one independent member (without conflict of interest with Plan or manufacturer).
 - Formulary must include at least two drugs within each class or category. Class is not defined.
 - P&T Committee must base clinical decision on the strength of scientific evidence and standards of practice... pharmacoeconomic studies, outcome research data....

Medicare Part D - Formularies

- Formulary Guidance in PDP Manual -
http://www.cms.hhs.gov/PrescriptionDrugCovContra/Downloads/PDBMChap6FormularyReqrmts_03.09.07.pdf
- Special Rules
 - 6 special categories and class requirements
 - Specialty drug tier
 - Transition guidance
 - Patient protections when removing a drug from the formulary

Centers For Medicare & Medicaid Services Approval

- CMS (the government agency) reviews bids which include benefit design, formulary, premium, cost-sharing.
- Formularies and benefit design reviewed for non-discrimination – cannot substantially discourage enrollment of certain individuals.
- CMS then contracts with plans with accepted bids.
- Once plan year begins, CMS receives claims data and other data to determine whether reinsurance or risk corridor payments are payable and for general oversight purposes.

Medicare Part D – Pricing Issues

- No government reimbursement formula
- PDPs privately negotiate discounts with pharmacies and rebate and other price concessions with manufacturers
- Non-Interference Provision: By law, Secretary may not “interfere with the negotiations between drug manufacturers and pharmacies and PDP sponsors” or “require a particular formulary or institute a price structure for the reimbursement of covered Part D drugs.”

Medicare Part D Successes

- Cost are much lower than projected. Competition has reduced CBO's estimated total Part D costs by \$438 Billion over 10 years.¹
- Premiums paid by patients are much lower than originally projected.
- Average premium for 2008 is \$25 and was originally projected at \$41.
- Very high patient satisfaction rate (over 80% in repeated polls).
 - Numerous studies show that despite concerns about confusion, patients have chosen plans with high value.²

1. "Fact Sheet for CBO's March 2007 Baseline: Medicare" and "Fact Sheet for CBO's March 2006 Baseline: Medicare" available at www.cbo.gov.
2. University of Michigan News Service, "Most seniors now have drug coverage, U-M study shows," August 9, 2007, available at www.ns.umich.edu.

Medicare Part D Successes

- Part D plans have broad coverage. In a study of 132 brand drugs in top 300 drugs used by seniors, 97% were covered in Part D Plans with highest enrollment in contrast to 42% of those brand name drugs covered on VA formulary³
- Beneficiaries are saving more than \$1200 and low income subsidiary recipients are saving more than \$3000⁴

3. The Lewin Group; Comparison of VA National Formulary and Formularies of the Highest Enrollment Plan in Medicare Part D and the Federal Employee Health Benefit Program, Jan. 12, 2007

4. CMS Fact Sheet, August 13, 2007.

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**A Closer Look at
Medicaid Coverage and
Payment for Drugs and
Devices**

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Medicaid Program Basics

- Federal/State joint program:
 - Federal minimum requirements
 - Manufacturers pay statutory rebate – which is split between federal and state government
 - Federal matches payments
 - Administered at the state level
 - Payment through retail pharmacy distribution channel –states pay pharmacy on the basis of state formula subject to a federal cap
- Medicaid population includes:
 - “Categorically needy” persons
 - “Medically needy” persons
 - Those who, but for slightly higher incomes, could qualify as “categorically needy”
 - States have option of covering “medically needy”
 - Medicaid expenditures for prescription drugs, net of rebates, represented about 9% of US Market for prescription drugs in 2006.⁵

5. A. Caitlin, et.al, “National Health Spending in 2006: A Year of Change for Prescription Drugs; Health Affairs, (January/February 2008) :19

Medicaid Program Basics

- Medicaid “minimum” benefits
- Medicaid “optional” benefits
 - Home health services
 - Private duty nursing services
 - Clinic services
 - Dental services
 - Physical therapy and related services
 - Prescribed drugs, dentures, prosthetic devices, eyeglasses
 - Respiratory Care services

Medicaid Program Basics

- A la carte fee-for-service
- Managed Care Plans: Bundled benefits;
Capitation payment

Medicaid Program Basics

Pharmacy Payment Methodologies for Drugs

- fee schedules subject to federal upper limits (“FUL”)
- Managed care arrangements (private party negotiations)

Medicare / Medicaid

– “Dual eligible” individuals

- Persons who are entitled to Medicare (Part A and/or Part B) and who are also eligible for Medicaid
- Chronically ill frail elderly
- Total number as of 2007 over 7 million
- Total number as of 2003 over 6 million
 - As a percentage of total Medicare beneficiaries in 2003
 - 17%
 - 29% of all Medicare expenditures in 2003
 - As a percentage of total Medicaid beneficiaries in 2003
 - 14%
 - 40% of all Medicaid expenditures in 2003

Dual Eligibles

- Outpatient drug benefit now provided through Part D
- Only Medicaid drugs for dual eligible beneficiaries ARE those drugs not included in the covered drug benefit under Medicare Part D but otherwise covered under the state's Medicaid program for its Medicaid only beneficiaries.

Medicaid Program Drug Pricing Basics

Medicaid Drug Rebate Statute (Drugs only)

- Contract between CMS and Pharmaceutical Manufacturer
- Condition of coverage of drugs is the payment of quarterly rebate
- Required participation in certain other federal programs
- Concepts
 - “Average Manufacturer’s Price” (AMP) and “Best Price”
 - Statutory rebate formula based on greater of 15.1% of AMP or the difference between AMP and Best Price plus additional rebate paid if AMP increases more than CPI compared to baseline AMP

MEDICAID: Average Manufacturer Price (AMP) and “Best Price”

- Manufacturer must report to CMS: (1) monthly: AMP; (2) quarterly: AMP, “Best Price,” value of customary prompt pay discounts, and value of nominally priced sales
 - AMP: “the average price paid to the manufacturer for the drug in the United States by wholesalers for drugs distributed to the retail pharmacy class of trade . . . without regard to customary prompt pay discounts extended to wholesalers”
 - Best Price: generally, “the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, HMO, nonprofit entity or governmental entity within the United States”
 - Recent Developments

A Closer Look at the 340B Drug Discount Program

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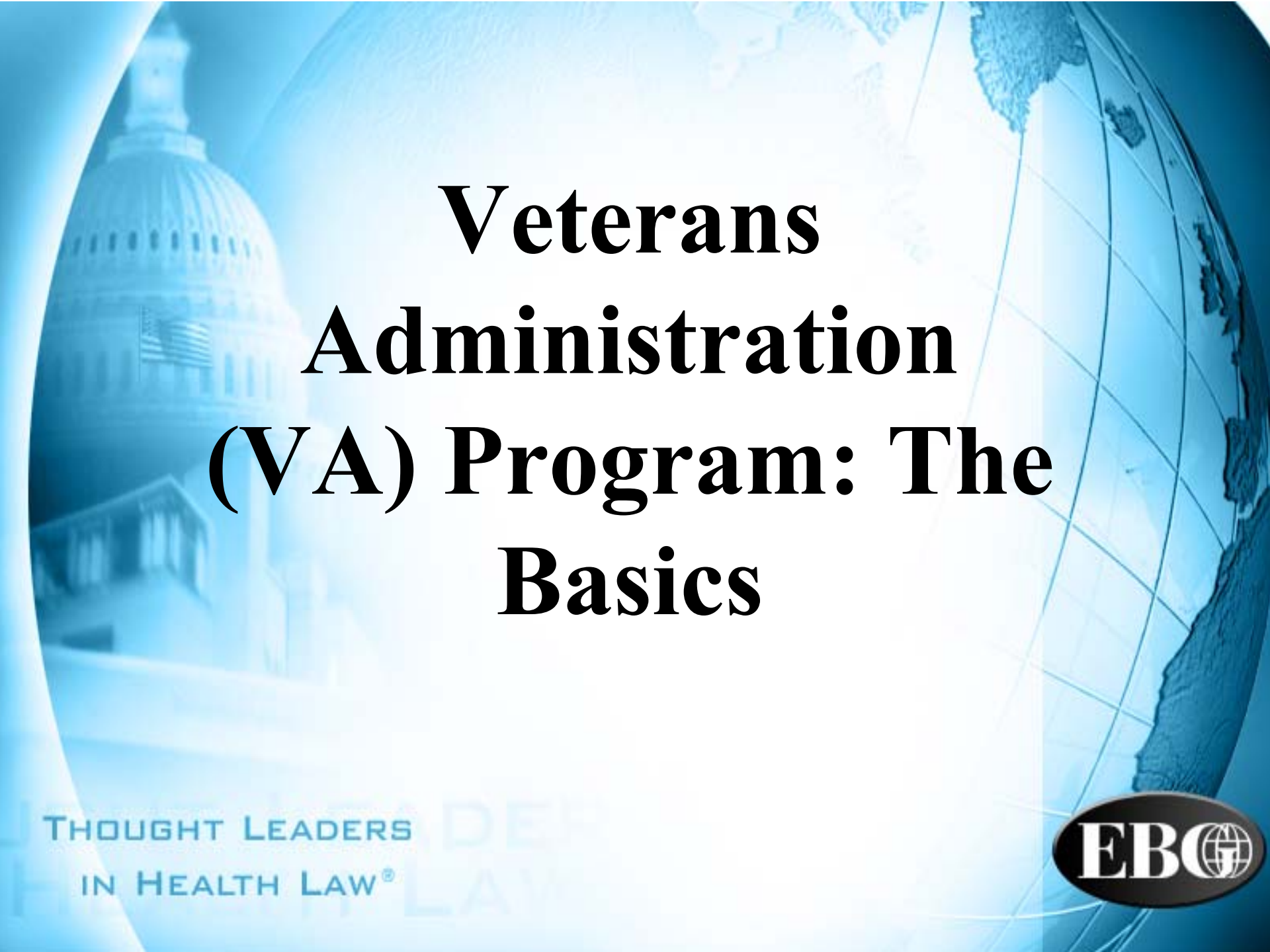


340B Drug Discount Program

- Program was created by Section 602 of the Veterans Health Care Act of 1992
- Requirements are codified at Section 340B of the Public Health Service Act (42 U.S.C. § 256b)
- Mandates that certain “covered entities” receive discounted prices
- Response to market changes resulting from OBRA 90 which created the Medicaid Rebate Statute
- Program is administered by the Health Resources and Services Administration, Office of Pharmacy Affairs (“HRSA” or “OPA”)
 - Technical assistance provided through Pharmacy Services Support Center contract
- 340B statutory discount formula tied to AMP and Unit Rebate Amount

340B Drug Discount Program: Covered Entities

- “Covered Entities”
 - Generally thought of as medical “safety net” providers
 - 12,300+ entities registered in HRSA’s database (<http://opanel.hrsa.gov/opa>)
 - Include:
 - Federally Qualified Health Centers and “look-alikes,” including Consolidated Health Centers, Migrant Health Centers, Health Care for the Homeless Clinics, Healthy Schools/Healthy Communities, Health Centers for Residents of Public Housing
 - PHS Grantees; specifically:
 - Family Planning Clinics
 - Ryan White CARE Act Programs (Titles I, II and III)
 - State-Operated AIDS Drug Assistance Programs
 - Black Lung Clinics
 - Hemophilia Treatment Centers
 - Native Hawaiian Health Centers
 - Urban Indian Clinics
 - Tuberculosis Clinics
 - Sexually Transmitted Disease Clinics



Veterans Administration (VA) Program: The Basics

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Veterans Administration (VA) Program: The Basics

- Covers veterans who generally must enroll with VA.
- Prescription usually first obtained at VA facility and then through mail order.
- No retail benefit.
- Prescriptions usually written by VA employed physicians.
- VA represents about 2% of US Market for prescription drugs.⁶

6. Prices for Brand New Drugs Under Selected Programs, Congressional Budget Office, June 2005 (CBO Paper).

VA Drug Pricing Under Veterans Health Care Act

- Manufacturer must make each covered drug available under Federal Supply Schedule contract (FSS) as a condition of participation in certain other government programs.
- Manufacturers must agree to charge VA, DoD, Public Health Service, and Coast Guard (Big 4) for drugs purchased under FSS or depot contracts, no more than federal ceiling price (FCP). FCP is based on 76% of non-FAMP which is generally average manufacturer price to wholesalers for non federal purchasers.
- CPI adjustments
- National Formulary creates opportunity for VA to obtain further discounts.

Veterans Administration Program: What Makes It Different?

- One national formulary; certain classes are closed.
- New drugs approved by FDA cannot be added to the VA's national formulary until reviewed by Medical Advisory Panel (MAP) and regional Formulary leaders committee. MAP performs "evidence-based drug class review".
- Where drug class review finds drugs in therapeutic class to have equal safety, efficacy and side effect profiles, one agent is selected "based on cost".
- VA uses national contracts and negotiates for drugs in closed classes with the statutory ceiling as a starting point.
- 40% of Medicare eligible veterans enrolled in the VA health care system also enrolled in Part D either directly or through their employer plan.⁷

7. Source: HHS Press Release; June 14, 2006; "Over 38 Million People with Medicare Now Receiving Prescription Drug Coverage" (found at <http://www.hhs.gov/news/press/2006pres/20060614.html>)



**Basic Federal
Health Care
Program
Compliance
Concepts for Drugs
and Medical Device
Manufacturers**

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Key Drug or Device Product Compliance Statutes (other than FDA)

- Federal Anti-Kickback Statute
 - federal health care programs – applies to most financial relationships with prescribers and customers
- State law Anti-Kickback Counterparts

Key Drug or Device Product Compliance Statutes (other than FDA)

- Federal False Claims Statute
 - federal funds
- State false claims statutes

Key Drug or Device Product Compliance Statutes (other than FDA)

- Medicaid Drug Rebate Statute (drugs)
 - Medicaid coverage of drugs involves reporting of AMP and Best Price, payment of rebates and participation in other related government programs
 - Penalties
 - \$100,000 civil monetary penalty for each item of false information provided
- State supplemental rebate statutes (drugs)

Federal Health Care Program Compliance Concepts

Medicare Enforcement / Compliance – Federal Programs Only

1. CMS Contractors
2. DHHS – Office of Inspector General
 - <http://oig.hhs.gov/>
 - Office of Investigations
 - <http://oig.hhs.gov/organization/OI/index.html>
 - Office of Audit Services
 - <http://oig.hhs.gov/organization/OAS/index.html>
 - Office of Evaluation and Inspections
 - <http://oig.hhs.gov/organization/OEI/index.html>
3. Department of Justice
 - Main Justice, Washington, D.C.
 - Branch Offices Nationwide

Federal Health Care Program Compliance Concepts

- Medicaid
 - Enforcement/Compliance
 - Federal/State Sharing
- CMS/State
 - Contractors
 - DHHS – Office of Inspector General
 - Department of Justice
 - Medicaid Fraud Control Units (state level)
 - State Attorney General Consumer Fraud Unit

Medicare / Medicaid Enforcement / Compliance

Pharmaceutical Product Manufacturers

- direct CMS relationships through Medicaid Drug Rebate Statute and related programs

The Concept of Manufacturers of Drugs and Devices as “Indirect” Providers

- OIG pronouncements
 - “causing” false claims
 - Anti-Kickback issues
 - financial relationships with prescribers and formulary decision-makers

Medicare / Medicaid Enforcement / Compliance

- **OIG Industry Guidance: The Pharmaceutical Industry**
 - Compliance Program
 - Kickbacks and Other Illegal Remuneration
 - Relationships with Purchasers and Agents
 - Formulary and Formulary Support Activities
 - AWP
 - Relationships with Referral Sources
 - Relationships with Sales Agents
 - Auditing and Enforcement of Policies/Procedures
 - Education and Training

Medicare / Medicaid Enforcement / Compliance

Off-Label Coverage: What are the Part B Coverage Rules?

- The Social Security Act mandates coverage of off-label use of an FDA approved drug used in an anti-cancer chemotherapeutic regimen if:
 - The use of the drug is supported as a “medically accepted indication” by a citation in one OF THE compendium identified by CMS.
 - The use of the drug is determined to be medically accepted based on clinical evidence in peer reviewed literature identified by CMS.
 - Section 50.4.5 of the Medicare Benefit Policy Manual lists 26 peer-reviewed journals that a Medicare contractor must use to determine "whether there is supportive clinical evidence for a particular use of a drug."
 - Medicare contractors have discretion to cover off-label uses of cancer drugs not listed in a compendium and for which no support exists among peer-reviewed literature.

Medicare / Medicaid Enforcement / Compliance

Off-Label Coverage: What are the Part D Coverage Rules?

- Part D drug means:
 - used for “medically accepted indication”
 - defined in Medicaid Drug Rebate statutes
 - FDA approved label indication
 - Compendia citations (AHFSDI, USP-DI, DrugDEX)
- Dispensed only upon prescription
- Includes certain biologics, insulin and associated medical supplies, vaccines

Medicare / Medicaid Enforcement / Compliance

Off-Label Promotion: FDA Compliance Issues

- Promotional activities
 - “Off-label promotion” is any communication of favorable information by a pharmaceutical company about a use of a drug product that is not covered by the approved FDA labeling
 - A pharmaceutical company may provide for a controlled dissemination of balanced peer-reviewed studies of off-label use of one of its products (*See Draft FDA Reprint Guidance*).
 - A physician may prescribe a drug for any indication
 - Promotion of an investigational new drug, not yet approved for marketing, is prohibited

Medicare / Medicaid Enforcement / Compliance

Compliance Focus: Special Issues Regarding Off Label Promotion

- Schering-Plough (2006)
 - Government alleged that the company sought to induce “off label” use of its drugs by physicians for treating bladder cancer and brain tumors through a combination of improper preceptorships, sham advisory boards, lavish entertainment, and improper placement of clinical trials
 - Government alleged that the company caused reimbursement claims to be submitted to federal health care programs in violation of the False Claims Act
 - Government also alleged that “off label” promotion violated the FDCA
 - \$435 Million settlement

Medicare / Medicaid Enforcement / Compliance

Relationship Between Drug Manufacturers and the Federal Government

- On February 20, 2008, the FDA made available for comment draft guidance titled "Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices"
- Draft FDA Reprint Guidance establishes rules for:
 - Publishing Organizations
 - Channels of Distribution
 - Influence of the Manufacturer
 - Content of Disseminated Information
 - Manner of Dissemination

Medicare / Medicaid Enforcement / Compliance

False Claims Act (FCA) Compliance Issues

- Overview and Elements
 - “Don’t give false or faulty data to the government”
 - The FCA prohibits a pharmaceutical manufacturer, as well as its employees, agents and contractors, from “knowingly”:
 - submitting (or causing to be submitted) false claims (which have been interpreted broadly by the courts) for government payment, or
 - making a false record or statement in order to be paid from the federal government
 - “Knowingly” is interpreted very broadly, to mean:
 - Actual knowledge;
 - Deliberate Ignorance; or
 - Reckless Disregard
 - Provides for cause of action by individual whistleblowers (“relators”) – typically disgruntled employees

Medicare / Medicaid Enforcement / Compliance

Pharmaceutical Research and Manufacturers of America
(PhRMA) Code on Interactions with Healthcare Professionals

- Code adopted in 2002
- Covers company interactions with healthcare professionals, including
 - Informational Presentations
 - CME and other Third Party Educational Meetings
 - Consultants
 - Speaker Programs
 - Educational and Practice Related Items
- Interactions should:
 - Meet all legal requirements
 - Follow highest ethical standards
 - Enhance knowledge for the patient's benefit

Medicare / Medicaid Enforcement / Compliance

– “Although compliance with the PhRMA Code will not protect a manufacturer as a matter of law under the Anti-Kickback statute, it will *substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable health care program requirements.*”

- OIG Compliance Program Guidance for Pharmaceutical Manufacturers, May 5, 2003

Examples of Drug and Device Enforcement Actions

- **Drug Manufacturers**

- Pfizer Lipitor (2004)

- allegations: Medicaid fraud involving Lipitor marketing through a \$250,000 “unrestricted educational grant” made to a health plan in exchange for favorable formulary placement that was not reported to Medicaid as a cash discount
 - total settlement: \$49 million and entered into Corporate Integrity Agreement

- Pfizer Neurontin (2004)

- allegations: off-label promotion of Neurontin
 - total settlement: \$430 million settlement and entered into Corporate Integrity Agreement

Examples of Drug and Device Enforcement Actions (cont.)

- **Drug Manufacturers**

- Purdue Pharma (2007)

- allegations: felony misbranding of Oxycontin
- total settlement: \$634 million (including \$35 million plus \$15,000 in criminal fines paid by top executives) and entered into Corporate Integrity Agreement

- Merck (2008)

- allegations: improper Medicaid billing and improper inducements to healthcare professionals
- total settlement: \$399 million for Zocor and Vioxx + \$250 million for Pepcid and enter into a Corporate Integrity Agreement

Examples of Drug and Device Enforcement Actions (cont.)

- **Device Manufacturers**

- Medtronic Sofamor Danek USA, Inc. (2006)


- allegations: improper payments made to health care providers to induce the use of Medtronic spine-implant products
 - total settlement: \$40 million and entered into Corporate Integrity Agreement

- Artificial Hip and Knee Manufacturers (2007)

- allegations: companies violated anti kickback statutes by paying physicians for the purpose of using their artificial hip and knee products for their patients
 - total settlement: \$311 million (Zimmer - \$169.5 million; Depuy - \$84.7 million; Smith & Nephew - \$28.9 million; and Biomet - \$26.9 million) and entered into Deferred Prosecution Agreements and Corporate Integrity Agreements

Individuals vs. Companies

- Individuals
 - InterMune, Inc. (2008)
 - former CEO indicted
 - Purdue Pharma, LP (2007)
 - 3 top executives plead guilty to strict liability misdemeanor for misbranding
 - Serono SA of Geneva (2007)
 - 4 former employees were acquitted in kickback case
 - TAP Pharmaceuticals, Inc. (2004)
 - 7 sales representatives were acquitted of kickback related charges
- Companies
 - CVS Caremark Corporation (2008)
 - agreed to pay \$36.7 million to resolve claims it improperly switched patients from a tablet version of a generic drug to a more expensive capsule version to increase Medicaid reimbursement



**Examples of Key
Integrity Provisions
Found in the DPAs of
the Artificial Hip and
Knee Manufacturers**

THOUGHT LEADERS
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Hip and Knee DPAs – Integrity Obligations

- Implement and maintain a Compliance Program
- Adhere to the AdvaMed Code of Ethics on Interactions with Health Care Professionals
- Retain a Monitor
- Conduct annual needs assessment to determine the reasonable needs for educational consulting services, and new product-development consultants.
- Rules applying to Consultant and royalty payments
- Internet publication of consulting payments to physicians on company websites

OIG Corporate Integrity Agreement (CIA) Obligations Generally

- Compliance Program
 - Written procedures
 - Training and education
 - Review procedures
 - Disclosure program
 - Reporting requirements
- Independent Review Organization (IRO)
 - Review government reimbursement
 - Review of government payments
 - Review of financial relationships
 - Review of price reporting to the government
 - Review of compliance with on label promotion obligations
 - System reviews and transactional reviews
- Notify OIG of New Business Units/Locations
- Implementation and Annual Reports to OIG
- OIG Inspection, Audit and Review
- Document Retention
- Change of Ownership
- Term of CIA

An Overview of the United States Regulatory Environment (FDA and Healthcare) for Global Pharmaceutical Compliance Professionals

- Monitor Key Government Websites
 - Department of Justice
 - <http://www.usdoj.gov/>
 - Office of the Inspector General
 - <http://oig.hhs.gov/>
 - Department of Health & Human Services
 - <http://www.os.dhhs.gov/>
- Monitor Key Sub-Regulatory Websites
 - Food and Drug Administration
 - <http://www.fda.gov/>
 - Centers for Medicare and Medicaid Services
 - <http://www.cms.hhs.gov/>