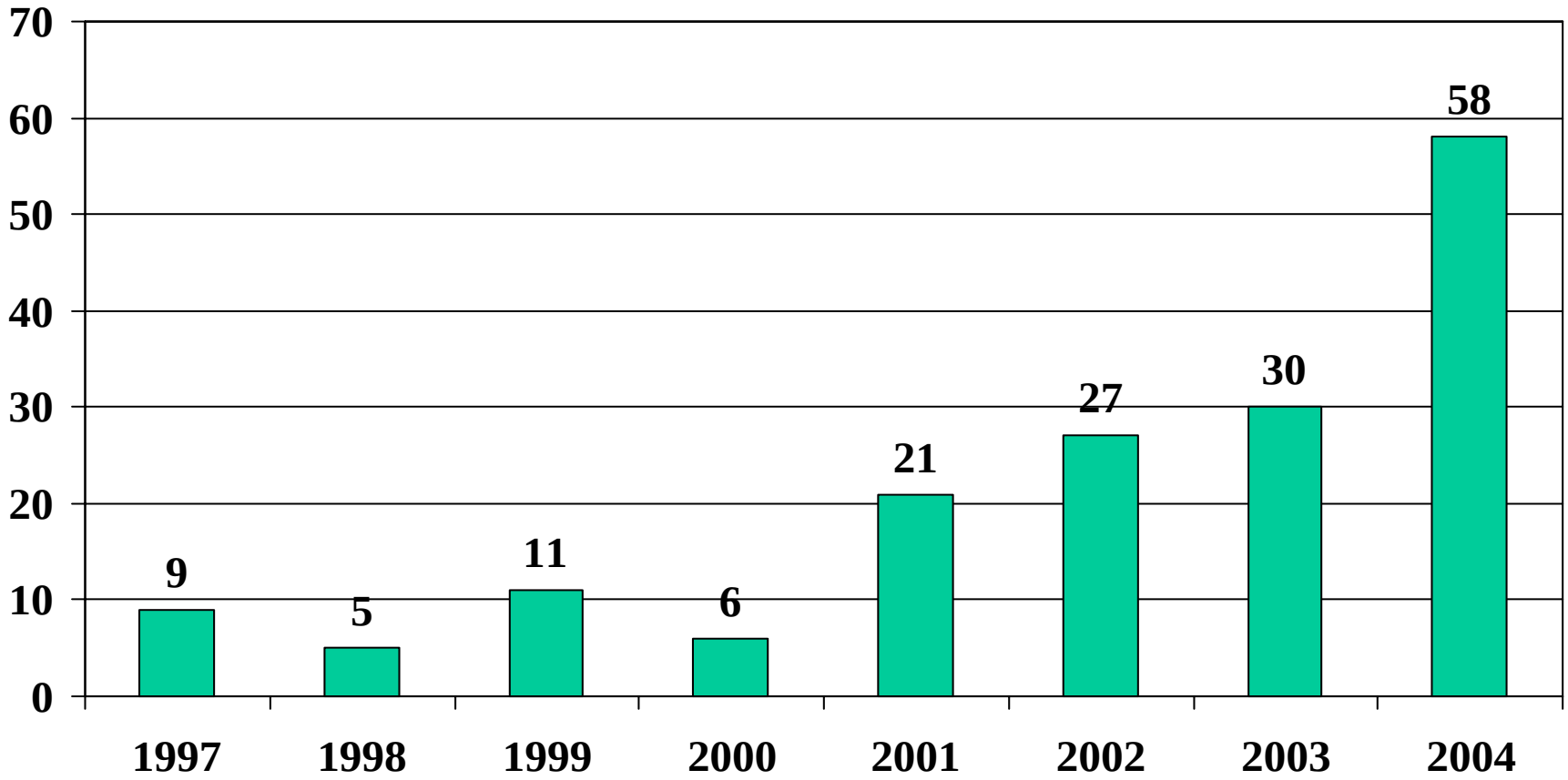
FDA UPDATE

C. Michelle Limoli, Pharm. D.
Office of International Programs
U.S. Food and Drug Administration

Counterfeit Drug Cases Opened by FDA per Year



Track and Trace Technology (1)

REPORT:

"The adoption and common use of *reliable* track and trace technology is feasible in 2007."

- *Electronic* track and trace
- RFID is most promising technology

ANNUAL UPDATE:

"Stakeholders have made tremendous progress in the development and implementation of EPC/RFID."

"…we continue to support [the efforts] today."

Track and Trace Technology (2)

- Standards development progress
- FDA RFID Compliance Policy Guide issued
- Major pharma companies announce tagging
- FDA cross-agency RFID Workgroup formed
- Studies
  - PQRI
  - FDA's Center for Devices and Radiological Health
    - Analysis of heating and radio-frequency field strengths in certain liquid pharmaceuticals
    - Auto-ID Labs – Health Research Initiative

Track and Trace Technology (3)

NEXT STEPS:

- "FDA will continue to play an active role in private an public sector efforts…including the adoption and widespread use of reliable track and trace technology by 2007."
- Continue to facilitate and monitor standard-setting activities..including efforts by epcGlobal (numbering systems, chip frequency, e-pedigree, data-sharing, security)
- Continue to encourage and foster research on use and potential impact of RFID on drug and biological products
- Regularly review the extent and pace at which RFID is being adopted

Authentication Technology

REPORT:

"Authentication techologies (such as color-shifting inks, holograms, taggants, or chemical markers imbedded in a drug or its label) have been sufficiently perfected that they can now serve as a critical component of any strategy to protect products against counterfeiting."

ANNUAL REPORT:

Companies are increasing their use of authentication technologies in products and packaging

NEXT STEPS:

Continue to work with companies and organizations to facilitate use of authentication technologies

Electronic Pedigree (1)

REPORT:

Adoption of electronic track and trace technology will help stakeholders meet and surpass goals of Prescription Drug Marketing Act (PDMA)

ANNUAL REPORT:

"We are pleased with the progress stakeholders, standard-setting bodies, and software and hardware companies have made thus far toward implementing an electronic pedigree for drug products."

- Recognize that there have been challenges along the way
- Optimistic that progress will continue in an expeditious manner toward meeting the 2007 goal

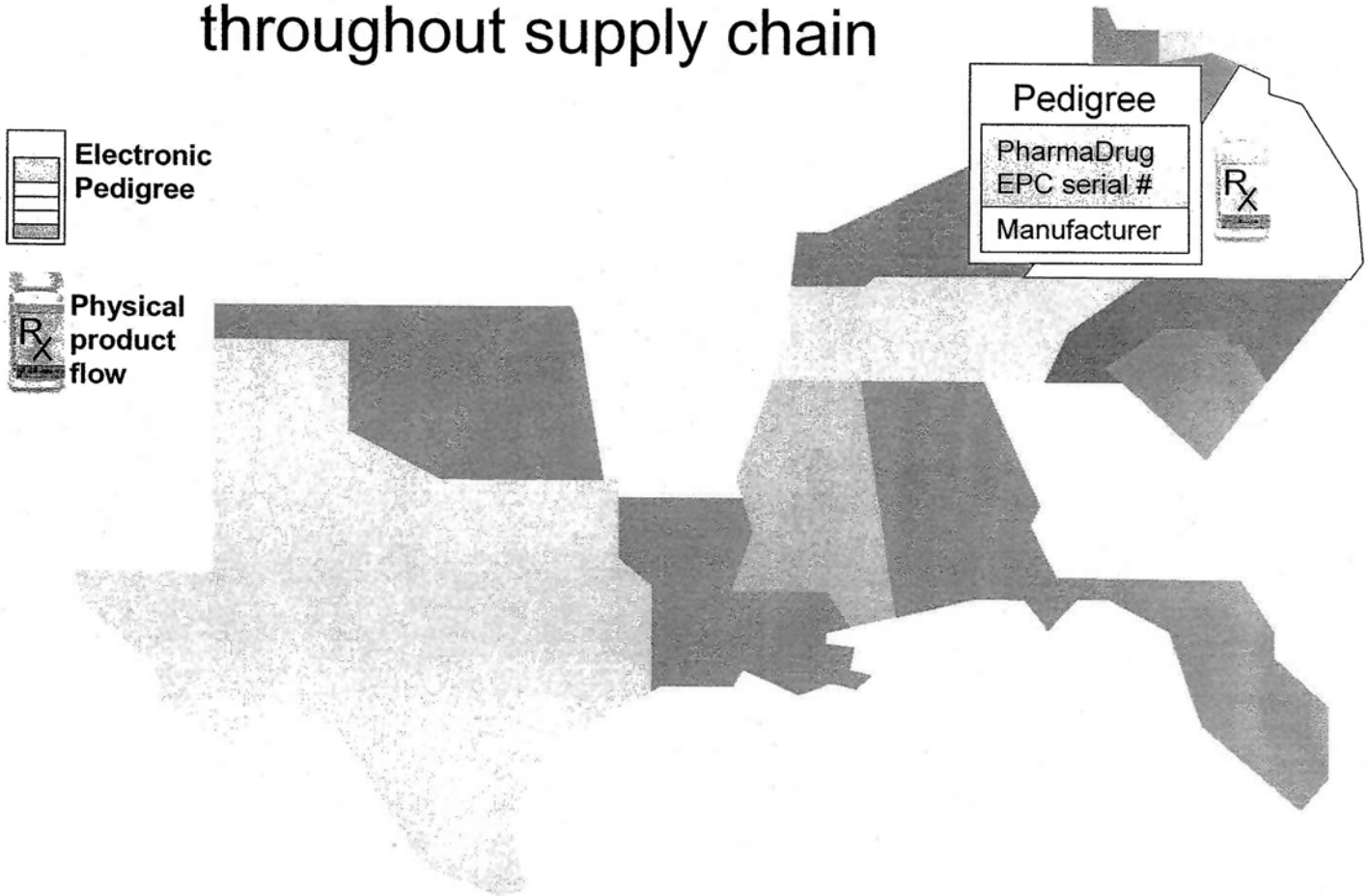
Electronic Pedigree (2)

NEXT STEPS:

- "We are closely monitoring the progress of widespread use of electronic pedigree as we assess whether to lift, maintain, or pursue other options regarding the stay…."

- Will continue to work with stakeholders to facilitate implementation.

Electronic Pedigree tracks drug throughout supply chain

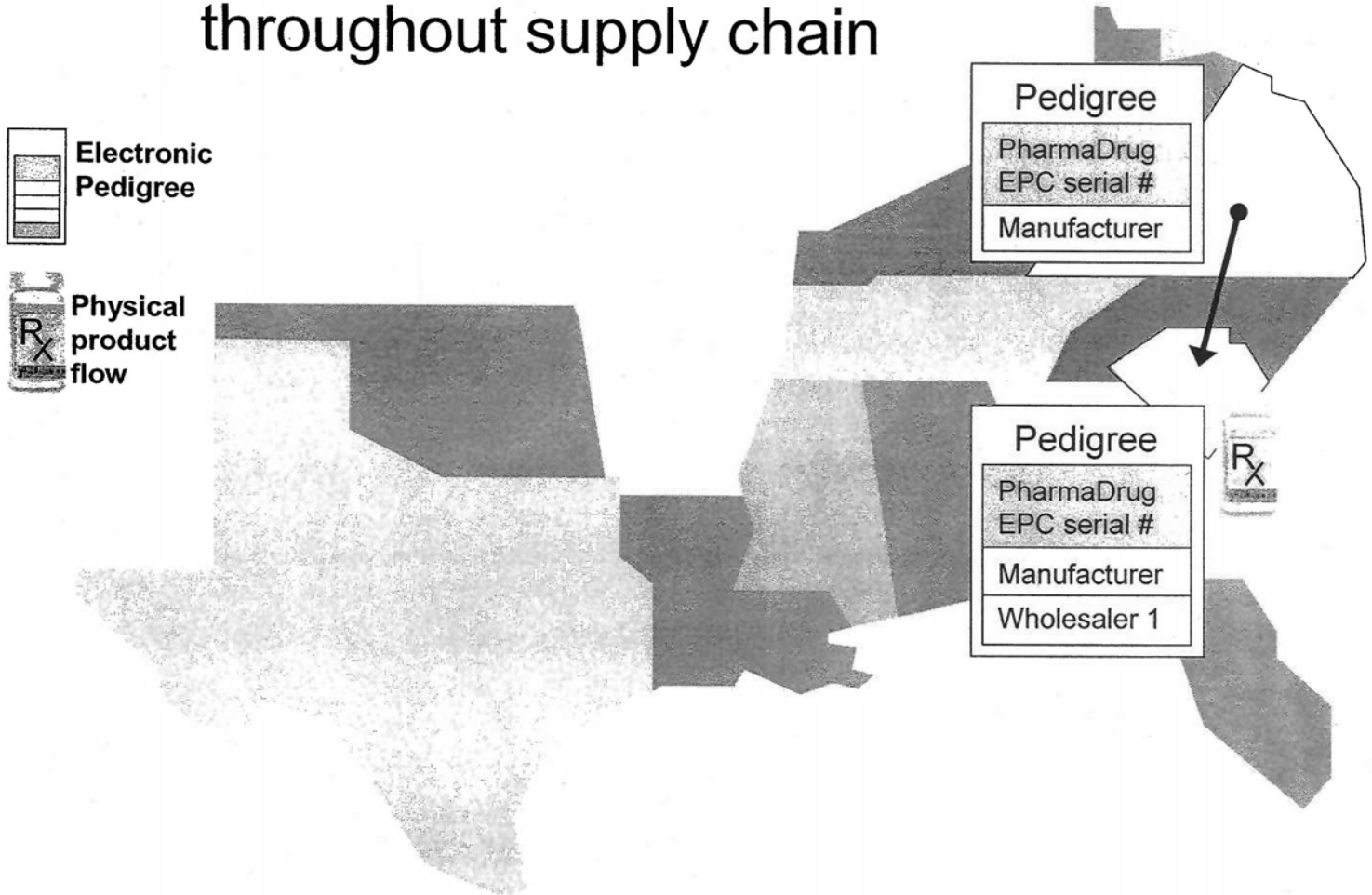


Prescription Drug Pedigree: History of Drug Sales and Distributions

Pharma Manufacturer → Wholesaler 1 → Wholesaler 2 → Retail Pharmacy

Authenticity	Product Information	Lot Information	EPC Serial Number
Genuine	 **PharmaDrug** 10 mg; 200 tablets NDC 0978-0451-02 Anti-counterfeit measures	Lot A231556 Manufactured: 12-Nov-2003 Expires: 15-Dec-2006	01.0.0.00978.000451.1234567890

Electronic Pedigree tracks drug throughout supply chain



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Drug Sales and Distributions

Sale 1: Wholesaler 1 purchase from Pharma Manufacturer

Business Name:	**Wholesaler 1**	**Acquired From:**	**Pharma Manufacturer**
Purchased By:	John Brown, Account Manager	**Released By:**	Michael Garcia, Quality Manager
Address:	200 Distribution Drive, York, SC 29745 USA	**Address:**	500 Manufacturer Road, Danville, VA 24540 USA
Phone:	803-555-6000	**Phone:**	434-555-2500
Date Acquired:	13-Dec-2003	**Date Released:**	12-Dec-2003

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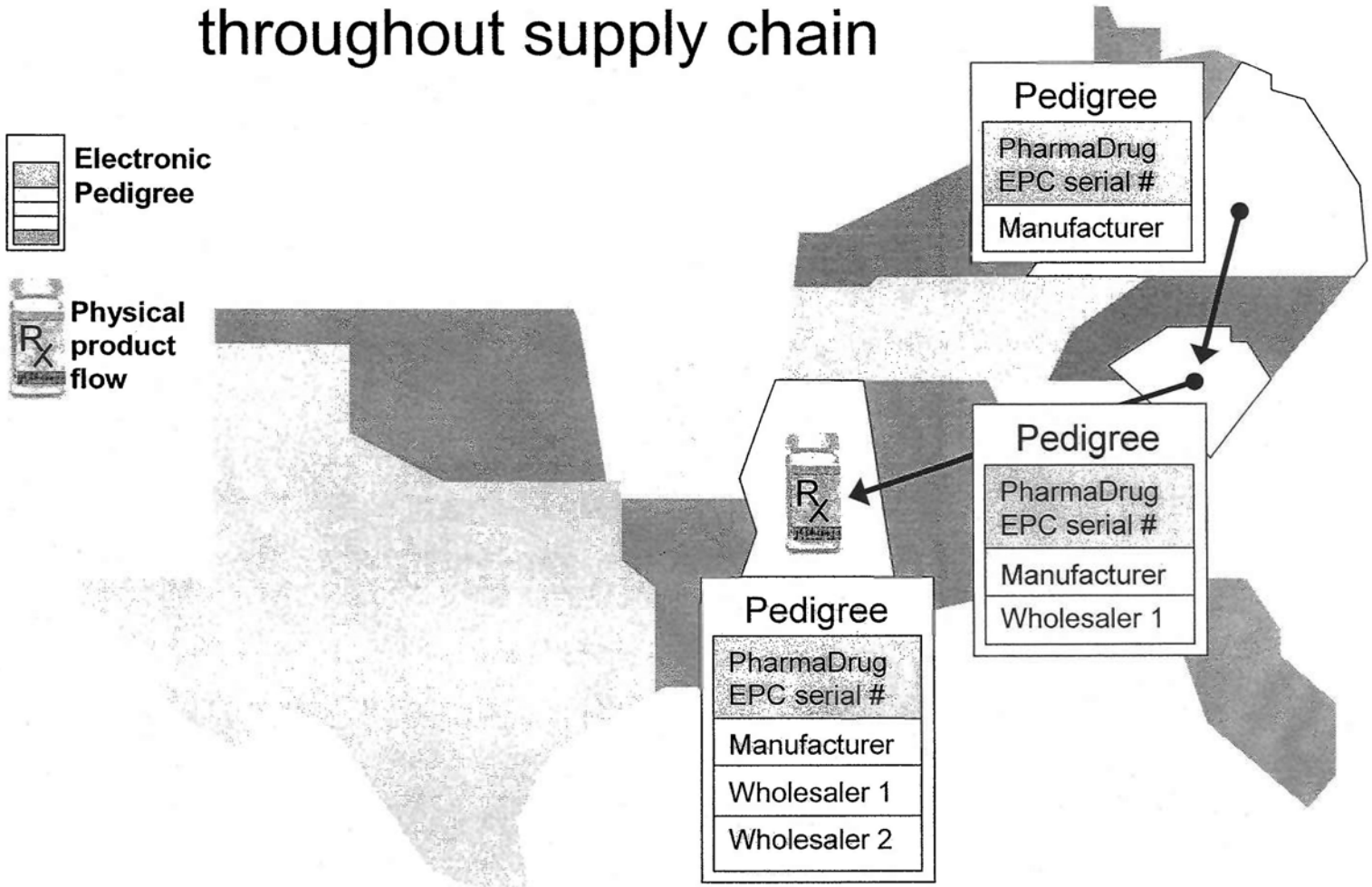

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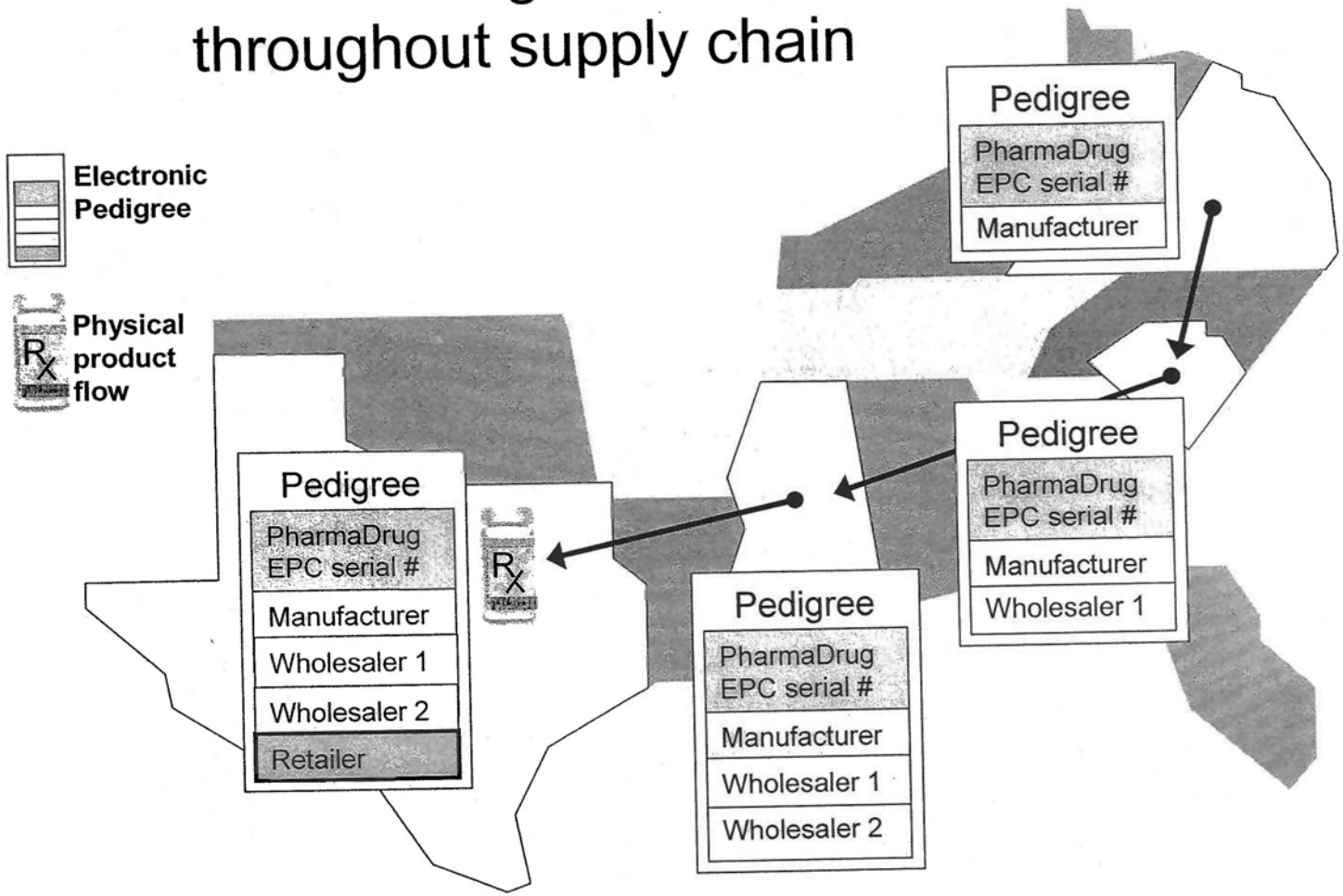
Sale 2: Wholesaler 2 purchase from Wholesaler 1

Business Name:	**Wholesaler 2**	**Acquired From:**	**Wholesaler 1**
Purchased By:	Amy Jones, Account Manager	**Released By:**	William Davis, Quality Manager
Address:	305 Wholesaler Place, Greenville, MS 38701 USA	**Address:**	200 Distribution Drive, York, SC 29745 USA
Phone:	662-555-3300	**Phone:**	803-555-6000
Date Acquired:	3-Jan-2004	**Date Released:**	2-Jan-2004

Electronic Pedigree tracks drug throughout supply chain



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Phone:	662-555-3300	**Phone:**	803-555-6000
Date Acquired:	3-Jan-2004	**Date Released:**	2-Jan-2004

Sale 3: Retail Pharmacy purchase from Wholesaler 2

Business Name:	**Retail Pharmacy**	**Acquired From:**	**Wholesaler 2**
Purchased By:	Patti White, Pharmacist	**Released By:**	Wendy Smith, Quality Manager
Address:	600 Pharmacy Road, San Antonio, TX 78201 USA	**Address:**	305 Wholesaler Place, Greenville, MS 38701 USA
Phone:	210-555-4200	**Phone:**	662-555-3300
Date Acquired:	18-Jan-2004	**Date Released:**	17-Jan-2004

Prescription Drug Pedigree: History of Drug Sales and Distributions

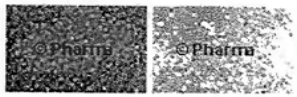
Pharma Manufacturer → Wholesaler 1. → Wholesaler 2 → Retail Pharmacy

Authenticity Pro… … ber

Genuine

Overt Anti-counterfeit Measures

Color-shifting carton seals



A carton seal with color-shifting ink is affixed to both flap closures of the carton. The seals shift color from blue to silver when viewed at different angles.

Residue visible on carton flaps when seal is broken

The closure seals are designed to break away when the carton flap is opened and leave behind a blue and silver residue.

Product markings

Pills are round tablets, with a smooth, white surface. The name of the product is imprinted in raised lettering on one side of the pill.

Close

Drug Sales and Distrib

Sale 1: Wholesaler 1 pi

Business Name:	Whole
Purchased By:	John E
Address:	200 Di
Phone:	803-55
Date Acquired:	13-De

Sale 2: Wholesaler 2 pi

Business Name:	Whole
Purchased By:	Amy J
Address:	305 W
Phone:	662-55
Date Acquired:	3-Jan-

Sale 3: Retail Pharmac

Business Name:	Retail
Purchased By:	Patti W
Address:	600 Pharmacy Road, San Antonio, TX 78201 USA
Phone:	210-555-4200
Date Acquired:	18-Jan-2004

0451.1234567890

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State Efforts

REPORT:

- Recognize the important role the states have in regulating the drug supply chain
- Support efforts of NABP in revising Model Rules for licensure of wholesale distributors

ANNUAL REPORT:

- 4 states have stricter laws in place
- Several states considering new legislation

NEXT STEPS:

- Continue to support efforts by states to adopt and enforce stricter laws

Other Activities

- **Heightened Vigilance and Awareness**
- **Educating Consumers and Health Professionals**
- **International Collaboration**

- **Continued advice/guidance as needed**
- **www.fda.gov/counterfeit**
- **THANK YOU**

Bar Code Final Rule

Principal Themes and Issues

U.S. Food and Drug Administration

The Rule's Origins

- May, 2001 – Secretary Thompson, in an appearance before a Senate committee, notes that technology, such as bar codes, could help save lives and money
- July, 2001 – the American Society for Health System Pharmacists asks Secretary Thompson to have FDA "develop regulations that mandate that drug manufacturers provide a standardized machine-readable code (bar coding) on all drug containers…."

The Rule's Origins (cont.)

- In late 2001, DHHS asks FDA to begin working on a bar code proposal
- FDA begins researching the issues and visits the Veterans Administration hospital in Washington, DC. The VA has a bar code system in place
- July 26, 2002 – as public interest grows, FDA holds a public meeting to discuss bar code issues. Nearly 400 people attend.

The Rule's Origins (cont.)

- Attendees at the public meeting include:
  - American Society for Health System Pharmacists
  - American Medical Association
  - American Hospital Association
  - American Academy of Nursing
  - Pharmaceutical Research and Manufacturers of America, the Generic Pharmaceutical Association, and the Consumer HealthCare Products Association
- Private meetings are held, too, from August 19, 2002 to October 9, 2002.

The Proposal

- Published on March 14, 2003
- Would apply to manufacturers, repackers, relabelers, private label distributors, and blood establishments
- Would apply to prescription drugs (except samples), OTC drugs commonly used in hospitals and dispensed pursuant to an order, blood, and blood components

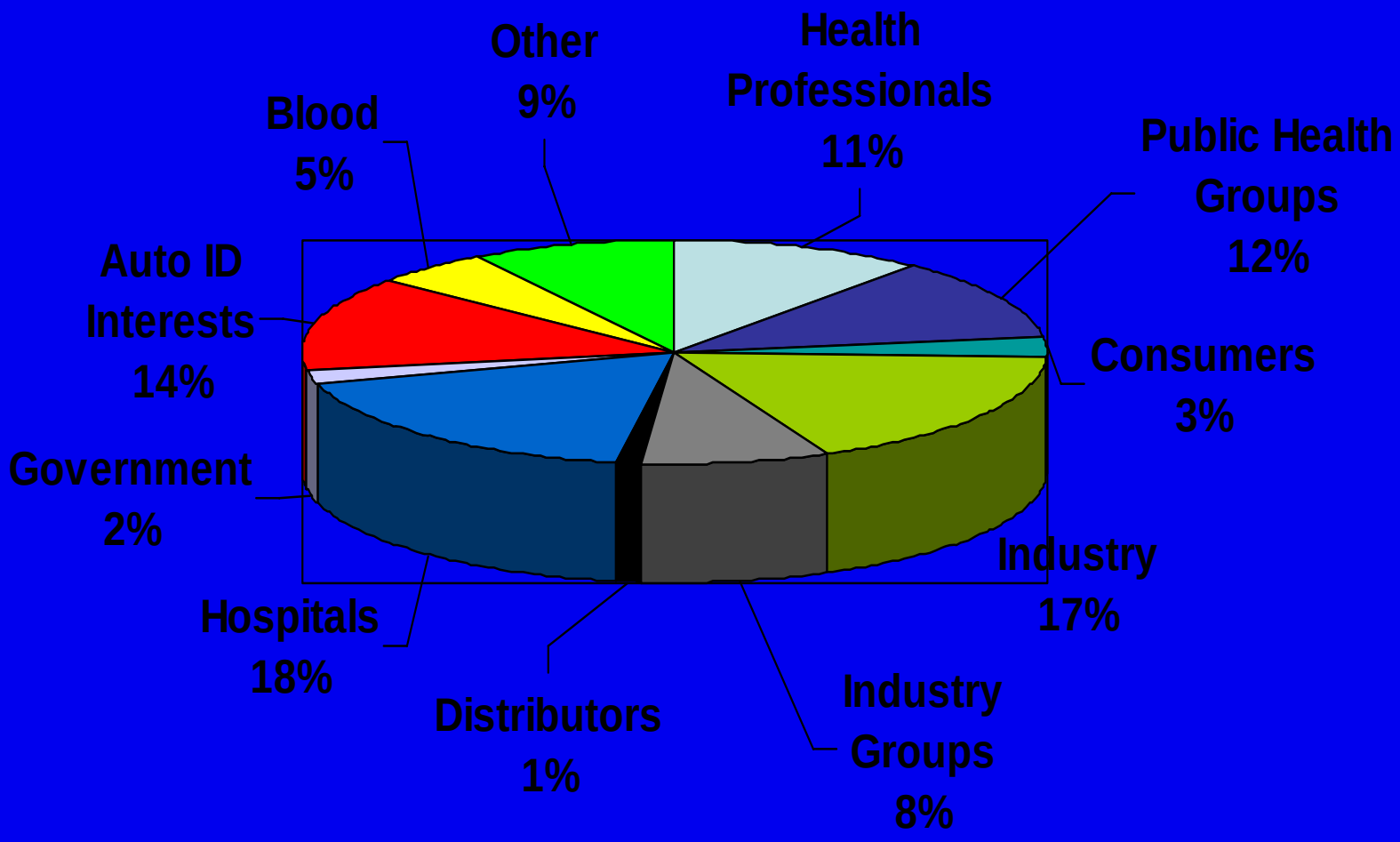
The Proposal (continued)

- For drugs:
  - Would require a linear bar code that meets UCC standards
  - Would require the bar code to contain, at a minimum, the drug's NDC number

The Proposal (continued)

- For blood and blood components:
  - Would require “machine-readable information” approved for use by CBER. The last approved version is ISBT 128.
  - Would encode, at a minimum, the facility identifier, lot number relating to the donor, product code, and donor’s ABO and Rh

Who Submitted Comments?



Technology (Bar Code vs. Other)
(58 comments)

- Many comments, particularly from industry and automatic identification interests, oppose requiring the use of linear bar codes
- However, comments advocating the use of other technologies do not agree on any particular alternative. Some endorse two-dimensional symbologies, whereas others would let firms decide on a technology, regardless of whether hospitals would be able to read that technology
- The tension, therefore, is between predictability and innovation

Technology – Pros and Cons

- **Linear Bar Codes**

  Pros: simple; easy to use proven technology; low costs to users

  Cons: limited opportunity for innovation, limited data encoding capabilities

- **Non-Linear Codes**

  Pros: can encode more data; some may even identify individual products; greater potential for innovation

  Cons: uncertain impact on device functions; some technologies have not matured; costs

FDA Response

- Final rule continues to require use of a linear bar code
- FDA commits to re-examining technology issues 2 years after the final rule's publication
- FDA notes issues regarding other technologies, such as possible electromagnetic interference with other medical devices inside a hospital, and read/error rates compared to linear bar codes

Information to be Encoded
(67 comments)

- Nearly all comments agree on encoding the NDC number
- Many comments continue to advocate encoding lot number and expiration date information, but do not provide data to show the benefits of encoding such information

FDA Response

- NDC number must be encoded
- Lot number and expiration date information is not required, but FDA will not object if a firm voluntarily encodes such information
- FDA suggests that hospitals consider equipment purchases carefully if they choose to buy drugs with lot number and expiration date information encoded
- For blood and blood components, the machine-readable information contains, at a minimum:
  - A unique facility identifier
  - Lot number relating to the donor
  - Product code, and
  - ABO and Rh of the donor

Implementation
(35 comments)

- Many comments from public health interests sought a shorter implementation period (from the proposed rule's 3 year period). In contrast, most industry comments felt 3 years was appropriate.
- Other comments would offer a different implementation period if industry would agree to encoding lot number and expiration date information.

FDA Response

- Effective date is 60 days after rule's publication date
- For drugs that receive approval on or after the effective date, compliance must occur within 60 days of the drug's approval date
- For drugs that received approval before the effective date, compliance must occur within 2 years from the rule's effective date. A third year can be obtained if technological reasons prevent compliance within 2 years
- For blood and blood components, compliance must occur within 2 years from the rule's effective date

Exemptions
(60 comments)

- Most comments seeking an exemption involve specific drugs or types of drugs
- Public health groups and health professionals oppose exemptions, but industry groups favor specific and general exemptions
- No comments address FDA's concerns regarding a general exemption provision (how to ensure that such a provision is not abused)

FDA Response

- Individual exemptions granted for allergenic extracts, intrauterine contraceptive devices, medical gases, radiopharmaceuticals, low-density polyethylene form fill and seal containers, and prescription drugs sold directly to patients
- General exemption provision created, but it would only apply if:
  - Compliance would adversely affect the drug's safety, effectiveness, purity, or potency or would not be technologically feasible or
  - An alternative regulatory program or method of product use makes the bar code unnecessary

Over-the-Counter Drugs
(17 comments)

- Most comments would refer to “non-prescription drugs used therapeutically pursuant to a prescriber’s order”
- Other comments sought case-by-case review of OTC drugs, either on an individual drug or class basis
- Some comments sought exclusion of all or most OTC drugs, even if those drugs were sold to hospitals

FDA Response

- Retains the construct of “OTC drugs commonly used in hospitals and dispensed pursuant to an order.” The comments’ alternatives were either overly inclusive or offered no advantage over the rule
- Rejects case-by-case review of OTC drugs
- Allows firms to make bar-coded and non-bar-coded OTC package lines

Summary of Principal Changes

- Exemptions granted for allergenic extracts, intrauterine contraceptive devices regulated as drugs, medical gases, radiopharmaceuticals, low-density polyethylene form fill and seal containers, and prescription drugs sold directly to patients
- General exemption provision created
- Compliance period shortened to 60 days after drug approval (if the drug is approved on or after the rule's effective date) or, for approved drugs, 2 years after the rule's effective date
- FDA commits to reconsidering technology issues