# INCENTIVIZING NEW VETERINARY PHARMACEUTICAL PRODUCTS TO COMBAT ANTIBIOTIC RESISTANCE

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Challenges to Changing Antibiotic Use in Food Animal Production: Economics, Data, and Policy
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# POLICY CONTEXT

- Recent calls to incentivize new veterinary pharmaceutical products to reduce the use of medically important antibiotics in food animal production.
- *"...the time is right to stimulate the development of novel approaches that will reduce the need for antibiotic use in food animals as well as make therapeutic uses more strategic and effective"* (p. 25)

RECOMMENDATIONS FOR INCENTIVIZING THE DEVELOPMENT OF VACCINES, DIAGNOSTICS, AND THERAPEUTICS TO COMBAT ANTIBIOTIC-RESISTANCE

SEPTEMBER 2017

PACCARB

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria

# Research Questions

1. What are the aspects of the human and animal pharma industries that are similar and different? How are they linked?

2. How do these similarities, differences, and linkages impact the efficacy of incentive mechanisms designed human pharma in animal pharma?

3. How much does a new animal drug cost to bring to market?

# Methods and Data

- Very little academic literature describing the animal pharma industry
- Sources of information:
  - Interviews with industry stakeholders
  - Statistics available through industry groups
  - Firm-level annual reports
  - Literature available through consulting firms, industry publications
- Data:
  - Collection of veterinary pharma approvals from websites and historical government documents
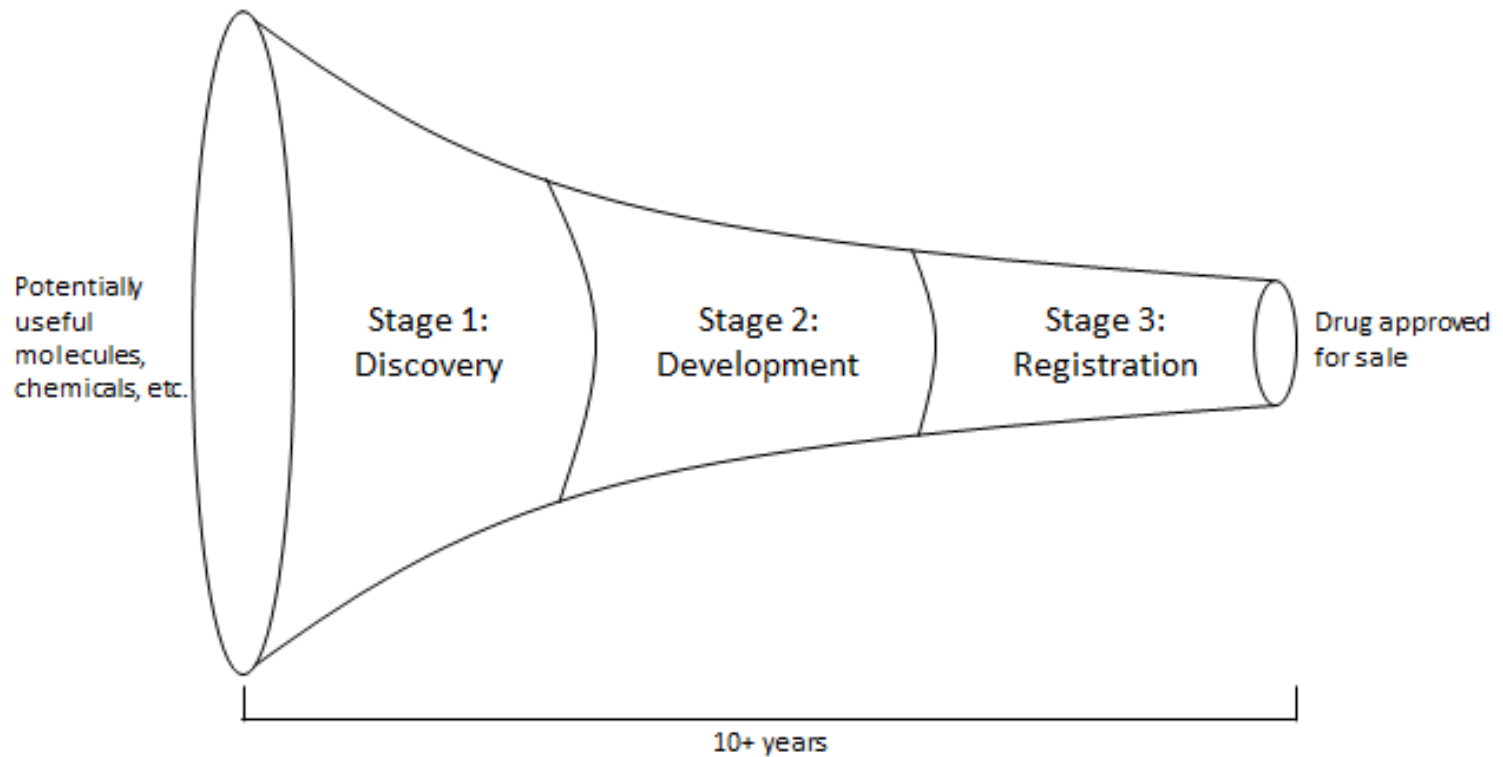  - Estimates of R&D spending from animal pharma firm annual reports

# SIMILARITIES BETWEEN HUMAN AND ANIMAL PHARMA

- Drugs available over the counter or through professional (doctor or veterinarian)

- Extensive use of patents

- Research intensive:
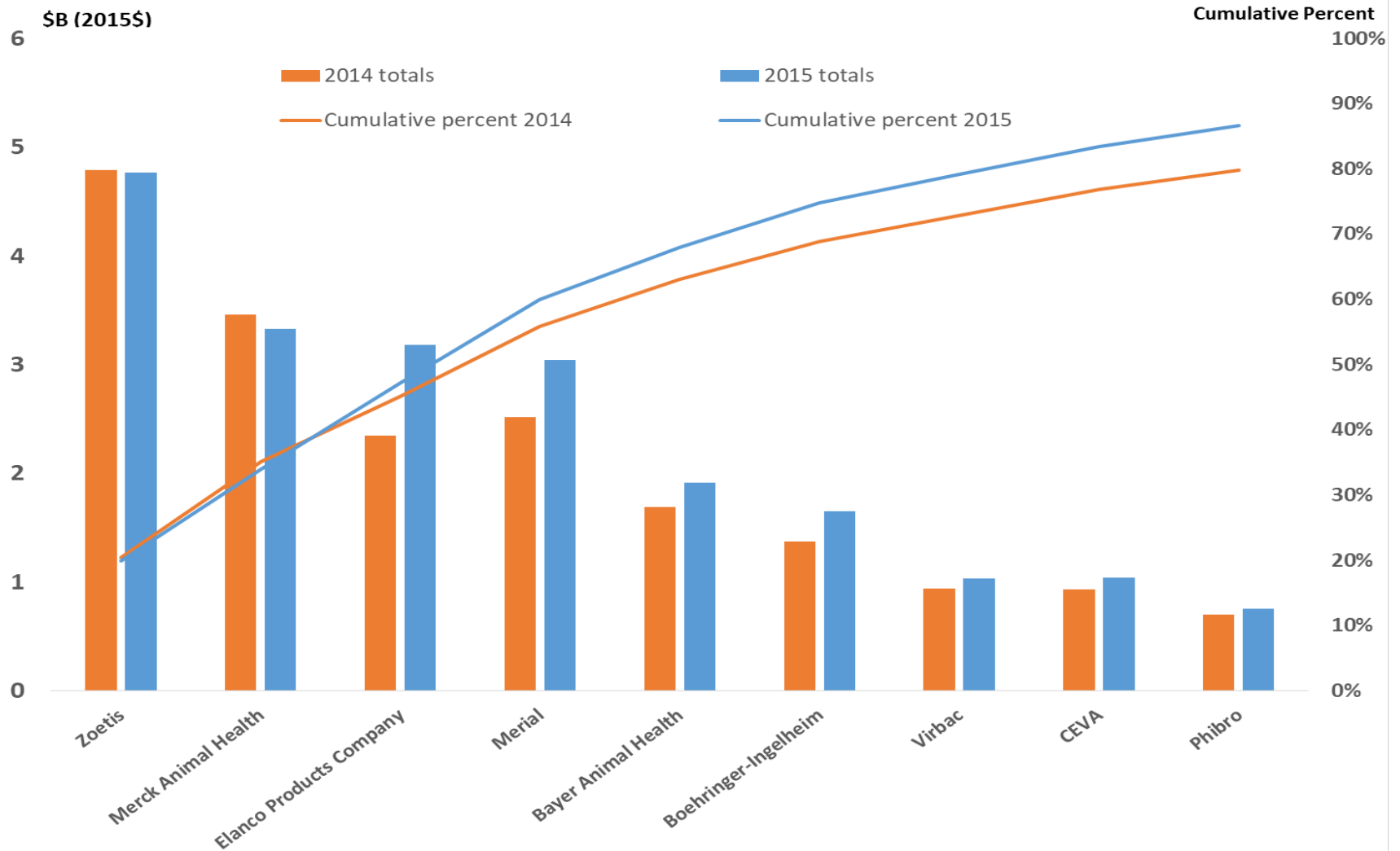  - R&D/Sales in human pharma: 12.7%
  - R&D/Sales in animal pharma:  7.8%

# New products take many years to go from discovery to market, and there is significant attrition of products from start to finish

Potentially useful molecules, chemicals, etc.

Stage 1: Discovery

Stage 2: Development

Stage 3: Registration

Drug approved for sale

10+ years

Source: ERS, USDA.

# Pharma Industries are Highly Concentrated:
## Major Animal Pharmaceutical Companies' Sales, and Cumulative Percentage of Global Industry Sales, 2014 and 2015

**$B (2015$)**

**Cumulative Percent**

Legend:
- 2014 totals
- 2015 totals
- Cumulative percent 2014
- Cumulative percent 2015

Categories: Zoetis, Merck Animal Health, Elanco Products Company, Merial, Bayer Animal Health, Boehringer-Ingelheim, Virbac, CEVA, Phibro

Sources: ERS calculations from company annual reports for 2014 and 2015; Bayer (2014, 2015); Boehringer-Ingelheim (2014, 2015); CEVA (2014, 2015); Eli Lilly and Co. (2014, 2015); Merck & Co., Inc. (2015, 2016); Novartis (2014; 2015); Phibro (2015, 2016); Sanofi (2015, 2016); Virbac (2015, 2016); Zoetis (2014; 2015). Total sales are from Health for Animals, 2015 and 2013. Total sales for 2014 are not reported, thus the total is a linear extrapolation of totals for years 2013 and 2015.  Note: Sanofi sold its animal health business (Merial) in 2017 to Boehringer-Ingelheim. Chart predates this merger.

# CONNECTIONS BETWEEN HUMAN AND ANIMAL PHARMA

- 6 of 7 top-selling animal pharma companies are divisions of human pharma companies

- The 7$^{th}$ was spun off from a human pharma company in 2013

- Many animal drugs "cast-offs" of human drugs

- Similarities in basic research

# DIFFERENCES BETWEEN HUMAN AND ANIMAL PHARMA

- Human pharma is 42 times larger:
  - Human pharma sales: $1,057B
  - Animal pharma sales: $25B
- Human pharma has government intervention in pricing
- Humans have insurance
- Patents protection *may* be less meaningful in animal pharma

# HUMAN PHARMA DEVELOPS PRODUCTS FOR ONE SPECIES, WHILE ANIMAL PHARMA DEVELOPS PRODUCTS FOR MANY SPECIES

**Percentage of Animal Pharmaceutical Sales by End User Species, 2009**
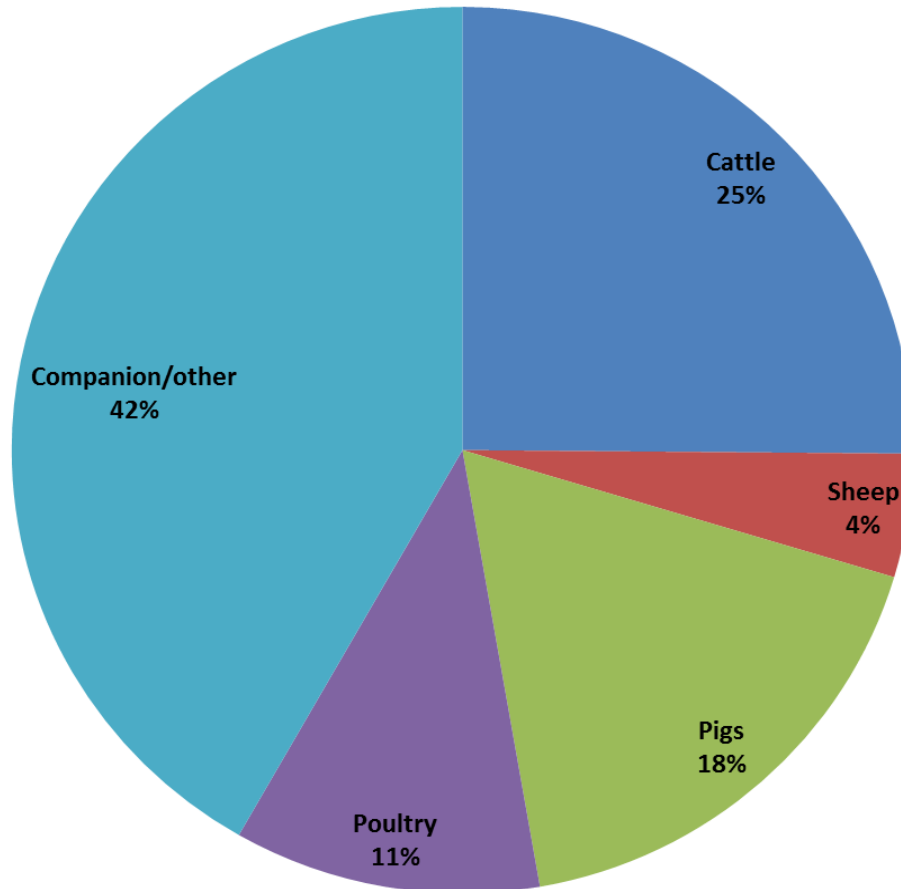


- Food animals constitute 58% of global animal pharmaceutical sales ($11B).
- Cattle constitute the largest share of sales to food animals ($4.7B).

Source: Vetnosis data published by IFAH.

# QUESTION:

## WHAT ARE THE TYPES OF INCENTIVE PROGRAMS PROPOSED FOR NEW HUMAN ANTIBIOTICS, AND WOULD THESE KINDS OF INCENTIVE PROGRAMS WORK FOR ANIMAL PHARMA?

# DECISION TO
# CARRY A DRUG TO MARKET

- A research project is worth doing whenever:
$$P \times V - K \geq 0$$

- $P$: *probability* research does what you hope.

- $V$: *value* researcher obtains if research works.

- $K$: *costs* of research.

# INCENTIVE MECHANISMS FOR NEW HUMAN ANTIBIOTICS

- Reduce cost of research (lower $K$)
- Speed time to approval (lower $K$)
- Increase revenues (increase $V$)
- Reward end product (increase $V$)
- Increase probability of approval (increase $P$)

Review on Antimicrobial Resistance

SECURING NEW DRUGS FOR FUTURE GENERATIONS: THE PIPELINE OF ANTIBIOTICS

THE REVIEW ON ANTIMICROBIAL RESISTANCE
CHAIRED BY JIM O'NEILL

MAY 2015

NEW DRUGS TO TACKLE ANTIMICROBIAL RESISTANCE

ANALYSIS OF EU POLICY OPTIONS

PRIYA SHARMA AND ADRIAN TOWSE

OHE
Office of Health Economics

Biomedical Advanced Research and Development Authority

BARDA Broad Spectrum Antimicrobials (BSA) program

imi innovative medicines initiative

COMBACTE
Combatting Bacterial Resistance in Europe

# CAN AN INCENTIVE PROGRAM SIMILAR TO HUMAN PHARMA BE DESIGNED FOR ANIMAL PHARMA?

DIFFERENCES BETWEEN HUMAN AND ANIMAL PHARMA (1/3)

| Para-meter | Policy interventions | Comparison between HP and AP | Result |
|---|---|---|---|
| *V* | Prizes, patent extensions, buying agreements, price setting | HP is much larger than AP | The amount to incentivize a new product might be lower in AP |
| | | Government intervention in pricing in HP. | Without this intervention in AP, the mechanism is less possible. |
| | | Patents less important in AP | Probably less signal from extending patents in AP |

HP = Human Pharma        AP = Animal Pharma

Economic Research Service
www.ers.usda.gov

# CAN AN INCENTIVE PROGRAM SIMILAR TO HUMAN PHARMA BE DESIGNED FOR ANIMAL PHARMA?

DIFFERENCES BETWEEN HUMAN AND ANIMAL PHARMA (2/3)

| Para-meter | Policy interventions | Comparison between HP and AP | Result |
|---|---|---|---|
| $K$ | Funding of research | HP is more expensive than AP | Less $ to fund research in AP |
| | | Multiple species in AP | Adds complexity and length in AP |

HP = Human Pharma            AP = Animal Pharma

# CAN AN INCENTIVE PROGRAM SIMILAR TO HUMAN PHARMA BE DESIGNED FOR ANIMAL PHARMA?

DIFFERENCES BETWEEN HUMAN AND ANIMAL PHARMA (3/3)

| Para-meter | Policy interventions | Comparison between HP and AP | Result |
|---|---|---|---|
| P | Funding of primary research, changes in approval process | AP needs to be more likely to pass registration | More fundamental research would be needed in AP to increase likelihood of a new drug, or regulatory hurdles would need to be lowered more |
| | | Can test the efficacy of a drug in AP on a lot of animals; can't do this in HP | Lowering regulatory hurdles for efficacy more possibility |

HP = Human Pharma          AP = Animal Pharma

# WHAT DO THE CONNECTIONS BETWEEN ANIMAL AND HUMAN PHARMA MEAN FOR INCENTIVE PROGRAMS?

- Large human pharma industry means more basic discovery than would otherwise exist for animal pharma
  - BUT
    - Reliance on human pharma means that animal pharma is limited in its ability to research animal-specific disease
    - Research is not necessarily transferred
    - A poor performer for human pharma is not necessarily going to go to animal pharma

# Further Disparities Between Human and Animal Pharma with Ramifications for Developing an Incentive Program

| | Human pharma | Animal pharma |
|---|---|---|
| Desired end products of incentive program | • New antibiotics | • Animal-only non-shared class antibiotics<br>• Animal-only shared class antibiotics?<br>• Large array of products termed "antibiotic alternatives" |
| Regulatory pathways | • One | • Several |
| Targeted bacteria | • Antibiotic resistant bacteria that impacts humans | • Anything that gets treated with shared-class antibiotics |
| Stewardship | • Any new products used sparingly to prevent more AMR | • Certain new (non-antibiotic) products encouraged to be used widely to prevent more AMR |

# PRELIMINARY CONCLUSIONS ON INCENTIVES PROGRAM FOR ANIMAL PHARMA

- Human pharma is very large, relative to animal pharma
  - Drives research into new drugs
  - Drives research about drug development incentives
  - Dominates policy development
- Animal pharma may be able to leverage human pharma
  - Overlap in biology and economics
  - Human drug development may be a pipeline for some animal drugs
- Significant differences remain
  - Animal pharma less studied
  - Animal specific needs may not be met by human pharma programs

# HOW MUCH DOES IT COST TO BRING A VETERINARY DRUG TO MARKET?

- Prior research:
  - Nothing for animal pharma (that we can find)
  - For human pharma:
    - Studies relying on major human pharma companies providing non-random samples of drug approvals to researchers
    - Estimates of lagged total R&D divided by total approvals
    - Estimates range from $69M - $884M per new drug

# DATA

- Human pharma
  - Already constructed by others
    - Industry-wide R&D estimates provided by National Science Foundation
    - FDA provides historical series of human drug approvals

- Animal pharma
  - We construct ourselves
    - Construct R&D estimates from firm-level annual reports
    - Text-scraping of historical documents (Greenbooks) for drug approvals

# BASIC METHOD

- Calculate R&D spending per drug approval as a centered nine-year moving average of real R&D divided by nine-year moving average of approvals, lagged five years.

- Reflects the lag between the R&D investment in the pharmaceutical industry and when products are approved.
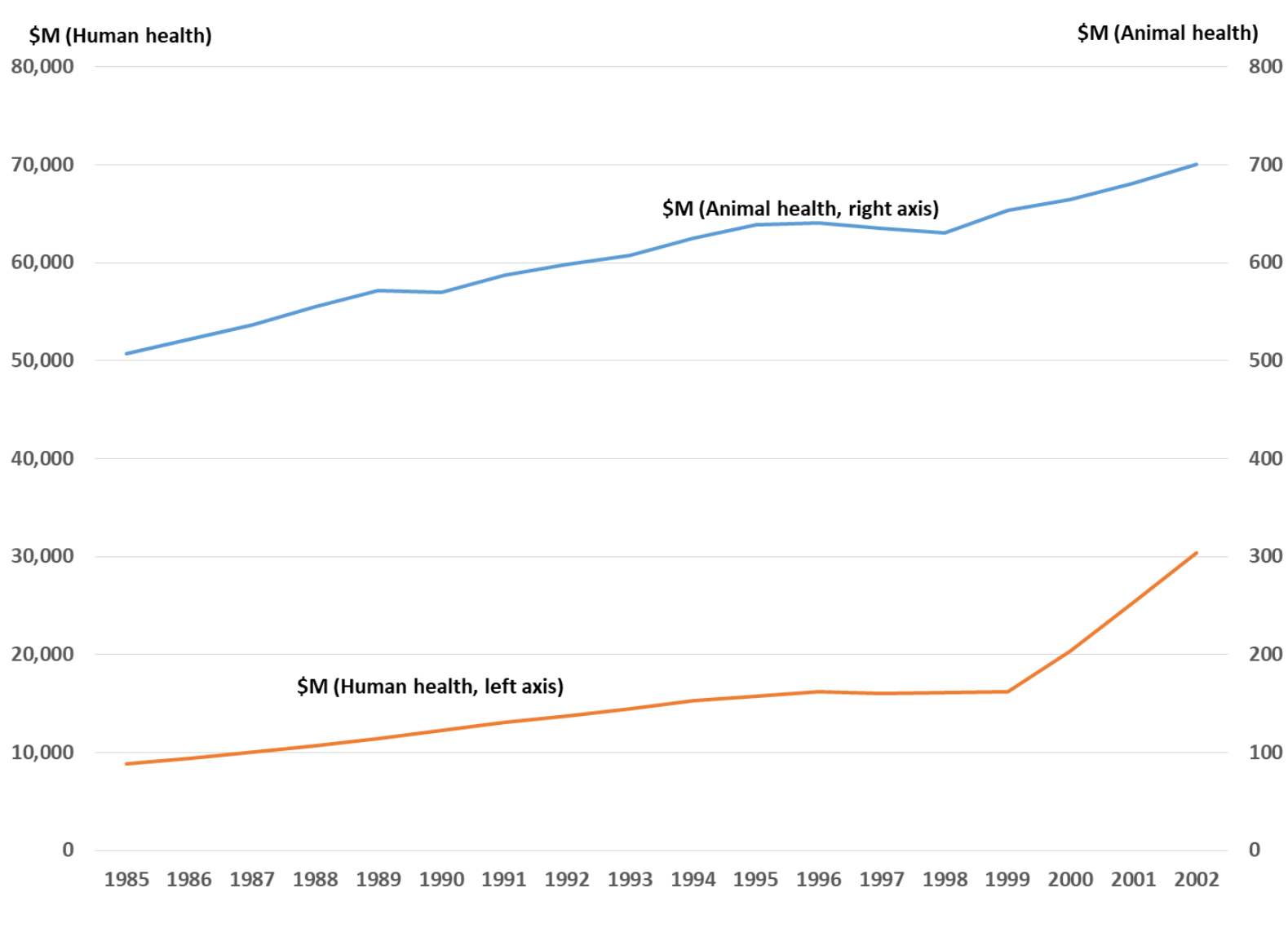
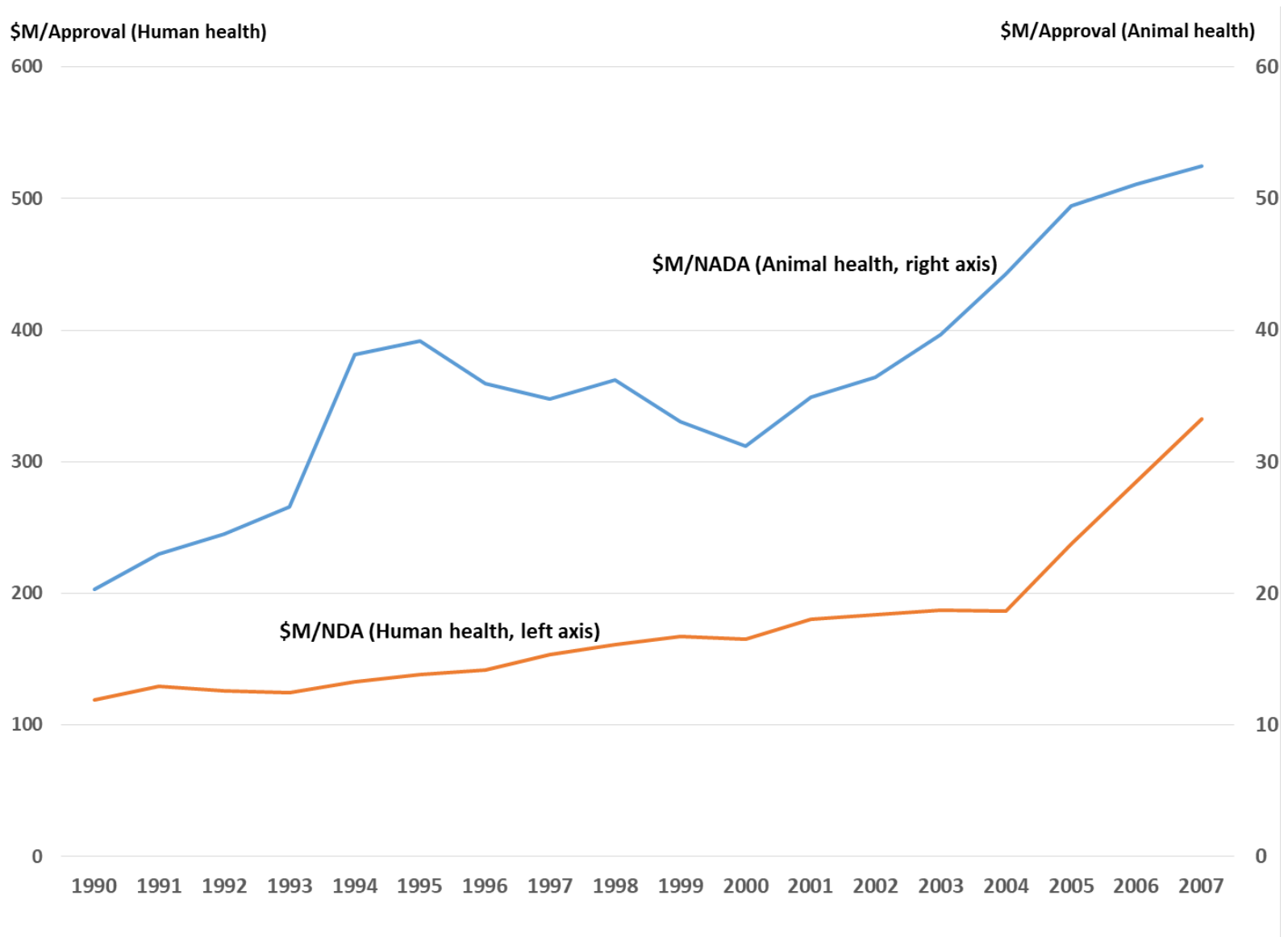# New Human and Animal Drug Approvals, 1990-2007, 9-Year Moving Averages

**Human Drug Approvals**

**Animal Drug Approvals**

**Human New Drug Approvals (left axis)**

**Animal New Drug Approvals (right axis)**
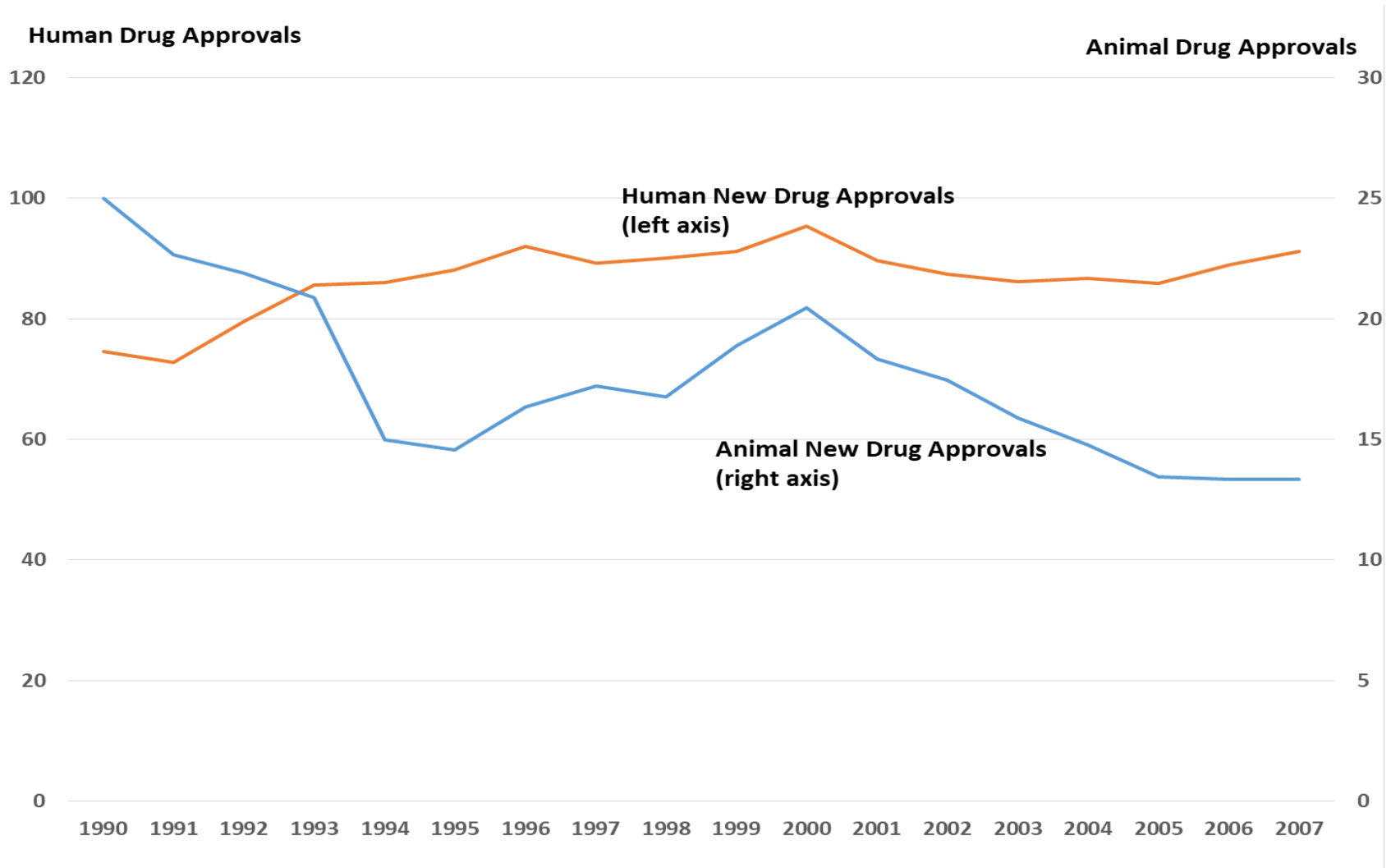


Source:  ERS calculations from FDA (2014) and FDA Greenbook data.

# R&D Spending in Human and Animal Pharma, 1985-2002, 9-Year Moving Averages



$M (Human health)

$M (Animal health)

$M (Animal health, right axis)

$M (Human health, left axis)

Source: ERS calculations from FDA (2014) and FDA Greenbook data.

# R&D per New Drug Approval, Human Versus Animal Drugs, 1990-2007

$M/Approval (Human health)

$M/Approval (Animal health)

$M/NADA (Animal health, right axis)

$M/NDA (Human health, left axis)



Sources:  ERS calculations from FDA Greenbooks, FDA (2014), NSF, and firm-level annual reports.  Dollars are in 2014$.

# COMPARISONS OF COSTS FOR HUMAN VERSUS ANIMAL DRUG APPROVALS

|  | Human drug approvals | Animal drug approvals | Ratio (Human/Animal) |
|---|---|---|---|
| Average drug approvals per year (1990-2007) | 87 | 18 | ~5 |
| Average R&D spending per year (1985-2002) | $15,302M | $607M | ~25 |
| Average Lagged R&D/Approval (1990-2007) | $175M | $36M | ~5 |

# CONCLUSIONS FROM ESTIMATION

- Levels
  - Human drugs cost approximately 5x more to develop than animal drugs

- Trends
  - Costs for both are rising
    - Average about 6.4% per year between 1990 and 2011
    - Human drugs: 180% in entire period
    - Animal drugs:  159% in entire period