

# THE PRESERVATION OF ANTIBIOTICS FOR MEDICAL TREATMENT ACT OF 2011

Columbia University  
School of International and Public Affairs & The Earth Institute  
Master of Public Administration in Environmental Science and Policy  
Workshop in Applied Earth Systems Management  
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## **Final Report**

Columbia University  
School of International and Public Affairs  
Master of Public Administration in Environmental Science and Policy  
Fall Workshop in Applied Earth Systems Management

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# ACRONYMS AND ABBREVIATIONS

APHIS - Animal and Plant Health Inspection Service

CDC - Center for Disease Control and Prevention

CVM - Center for Veterinary Medicine

EPA - Environmental Protection Agency

FDA - Food and Drug Administration

FoodNet - Foodborne Diseases Active Surveillance Network

GAO - Government Accountability Office

GDP - Gross domestic product

HHS - Department of Health and Human Services

IES - Investigative and Enforcement Services

NAHMS - The National Animal Health Monitoring System

NARMS - National Antimicrobial Resistance Monitoring System

NIFA - National Institute of Food and Agriculture

NRC - National Research Council

ONADE - The Office of New Animal Drug Evaluation

OS&C - Office of Surveillance and Compliance

PAMP - Post-Approval Monitoring Programs

USDA - United States Department of Agriculture



## EXECUTIVE SUMMARY

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Increasing bacterial resistance to antibiotics is widely recognized as a critical and growing public health issue. For over half a century, we have depended on antibiotics to fight infection and cure illness, but as resistance increases, these antibiotics are becoming less and less effective. The growing threat of antibiotic resistance is not only a matter of public health but also an economic and social concern, as resistant infections are more difficult to treat, making hospital stays longer and more expensive. The emergence of resistant bacteria is an inevitable consequence of using antibiotics, and the root of the resistance problem is well established: the more antibiotics we use the more resistance grows.

Antibiotics are used appropriately to treat both sick humans and sick animals. However, a significant portion of U.S. antibiotics are given to healthy animals to prevent illness or to promote growth, practices classified as nontherapeutic use. Today's animal agricultural industry produces more meat than at any point in history and has been able to do so by raising more animals in less space. This high density production, while allowing for more and cheaper meat, increases the risk of disease spread between animals and reduces their natural immune functions. To mitigate these impacts, animals are given antibiotics nontherapeutically in low doses over much of their lifetimes.

The Preservation of Antibiotics for Medical Treatment Act of 2011 (PAMTA, H.R. 965) addresses increasing antibiotic resistance by strengthening the safety standards regulating the nontherapeutic use of antibiotics in food-animal production. Strengthening these regulations is an important and necessary step to mitigating antibiotic resistance but will require a significant change in current farming practices. Animal agriculture accounts for 6% of U.S. GDP and the transition away from widespread antibiotic use will require new farming practices, veterinary technology, and incentive programs.

This report outlines a program designed to implement the mandatory requirements of the Act affecting drug approval and consists of four components: 1) enhancing safety standards, 2) transition support, 3) surveillance and monitoring, and 4) enforcement. The transition support is intended to help farmers shift away from extensive nontherapeutic use of antibiotics and to encourage research and development of new antibiotics and antibiotic alternatives. Expanded surveillance and monitoring will also be important for tracking antibiotic resistance. Finally, the enforcement component is intended to ensure that antibiotics are being used appropriately and in ways that will not pose a significant threat to public health.

Overall, the goal of this program is twofold: to reduce antibiotic use in animal agriculture and to reduce antibiotic resistance. While action to address antibiotic resistance is essential, it should be noted that neither the Preservation of Antibiotics for Medical Treatment Act nor the program recommended in this report are quick-fix solutions. The potential of either to adequately reduce bacterial antibiotic resistance is unknown because antibiotic resistance is pervasive and difficult to eliminate once it has been established. However, there is clear evidence that increases in antibiotic use have driven the development of resistance. A program to reduce resistance will require many components, and an obvious starting point is to stop increasing resistance by managing our antibiotic arsenal properly. The enormity of this challenge demands action as antibiotic resistance has serious consequences for everyone—producers, consumers, and the general public. We believe that the program outlined in this report is a positive step in balancing agricultural production with public health.

# INTRODUCTION



# INTRODUCTION

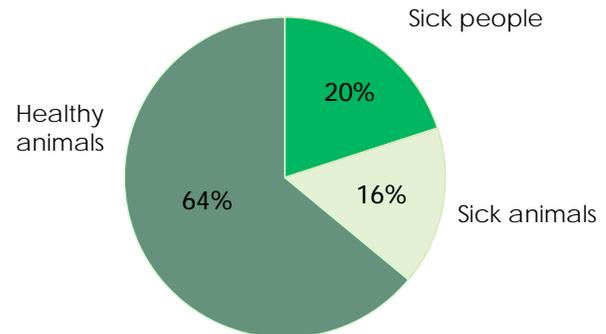
Since the development of penicillin in the 1940s, humans have depended on antibiotics to treat illness caused by bacterial infections. However, these antibiotics are becoming progressively less effective due to the evolution of resistance within pathogens, creating a considerable public health concern (Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine, 1969; Scott, 2005; Kummerer, 2009; Baquero and Garau, 2010). Antibiotic-resistant infections are estimated to cost the U.S. healthcare system over 20 billion dollars annually (Roberts et al, 2009; PRNewswire, 2009). These costs, along with the erosion of antibiotic effectiveness, present a substantial threat to our safety and security.

Resistance to antibiotics increases as their use increases, so any efforts to address resistance must target the amount of antibiotics applied and the capacity in which they are used (Jansen et al, 2006). As of 2009, 80% of antibiotics used in the United States were used in industrial animal agriculture with 64% of the total used at chronic low doses on healthy animals (FDA, 2009; Figure 1). This practice, called nontherapeutic use, is intended to prevent disease and promote faster growth (FDA, 2009). Modern animal agriculture depends on this nontherapeutic use of antibiotics to produce large amounts of meat at relatively low prices with industrial efficiency achieved through very high densities of farm animals. However, this increased meat supply comes at a cost to public health by contributing to the prevalence of antibiotic resistance (Scott, 2005).

The Preservation of Antibiotics for Medical Treatment Act of 2011 (H.R. 965) is motivated to reduce this public health burden and aims to do so by addressing antibiotic use in animal agriculture. The Act mandates enhanced safety standards for the approval of antibiotics for use in animals and effectively bans the nontherapeutic

use of any antibiotic for which use will lead to resistance. In this report, we develop a program to implement these enhanced safety standards and manage some of the impacts of the legislation on the meat and pharmaceutical industries. The non-mandatory components of the program design address transitioning away from the current reliance on antibiotics in animal agriculture and improving the management of antibiotics through surveillance, monitoring, and enforcement. While the complete program design is outlined and discussed within this report, staffing, budgeting, and timelines are presented only for the first year of implementation.

## ANNUAL ALLOCATION OF ANTIBIOTICS IN THE UNITED STATES



**Figure 1:** Annual allocation of antibiotics in the United States. The Preservation of Antibiotics for Medical Treatment Act will enhance drug safety standards to reduce the health risks associated with the widespread administration of antibiotics to healthy animals (adapted from FDA, 2009).

## The Science Behind Antibiotic Resistance

The development of antibiotic resistance, while mechanistically complex, is an environmental problem for which cause and effect are well established. We know that as the use of

antibiotics increases, bacterial resistance to those antibiotics increases (Jansen et al., 2006; Figure 2). Awareness of this relationship has existed since the middle of the twentieth century when widespread resistance to several antibiotics was first noted (Scott, 2005).

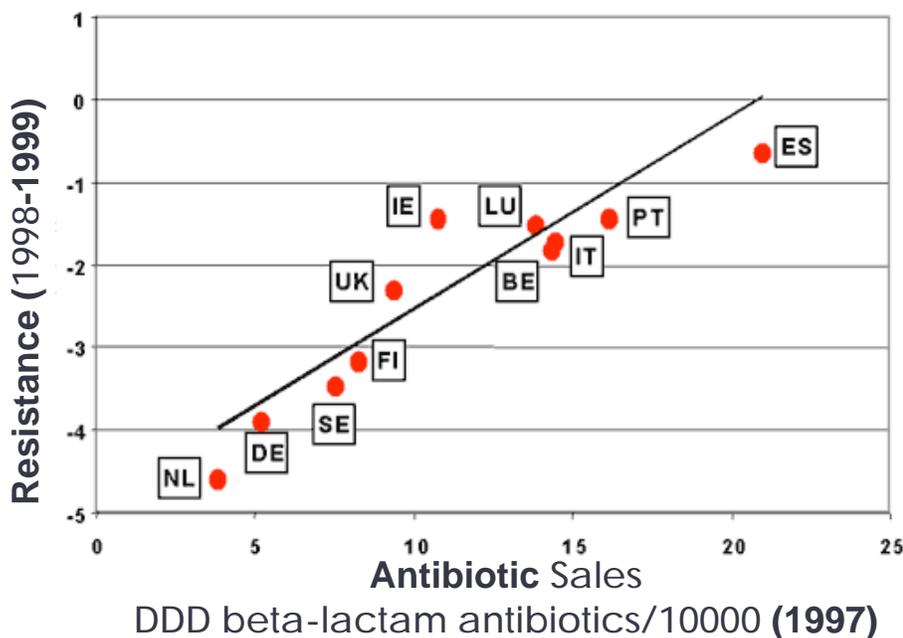
While increased use of antibiotics leads to increased resistance, antibiotic-resistance genes initially appear as a result of spontaneous mutation of DNA. These resistant genes can then increase as bacteria multiply or spread to other bacteria through a variety of complex genetic mechanisms including horizontal gene transfer, gene linkages, and transformation (Andersson, 2003; Scott, 2005).

Resistance to an antibiotic is a function of a pathogen's genetic makeup—to be resistant, a bacterium must possess genes that limit the physiological effects of the antibiotic. These

genetic variations emerge by spontaneous mutation that occurs at a rate ranging from one in a million to one in a billion gene duplications ( $10^6$  to  $10^9$ ; Scott, 2005). Though these rates appear low, when put into the context of microbial life cycles and population numbers, the occurrence of new mutations is quite common. Up to 10 quadrillion ( $10^{16}$ ) bacteria per liter live within the fluid in a cow's rumen, meaning there can be over 10 billion bacteria with spontaneous new mutations at a given time (Brooker et al., 2008). The vast majority of these mutations will have neutral or deleterious effects on the bacteria, which will die out, but the few bacteria whose mutations confer an advantage will thrive.

Resistance originates from random spontaneous genetic mutation, but the chronic presence of antibiotics in industrial agriculture exacerbates the spread of resistance genes within bacterial populations (Walsh, 2000; Hogberg et al.,

**PROLIFERATION OF ANTIBIOTIC RESISTANCE IN EUROPEAN UNION COUNTRIES**



**Figure 2:** Proliferation of Antibiotic Resistance in European Union Countries. This graph compares the amount of antibiotics sold to the resistance of *Streptococcus pneumoniae* to penicillin in eleven countries in the European Union. Resistance is measured as the log-odds ratio of resistance among invasive isolates of *Streptococcus pneumoniae* ( $\ln(R/[1-R])$ ) and is regressed against outpatient sales of beta-lactam antibiotics (Defined daily dose/1000); antimicrobial resistance data are from 1998 to 1999 and antibiotic sales data are from 1997. BE = Belgium; DE = Germany; FI = Finland; IE = Ireland; IT = Italy; LU = Luxembourg; NL = the Netherlands; PT = Portugal; ES = Spain; SE = Sweden; UK = United Kingdom (adapted from Brownzawer et al., 2002).

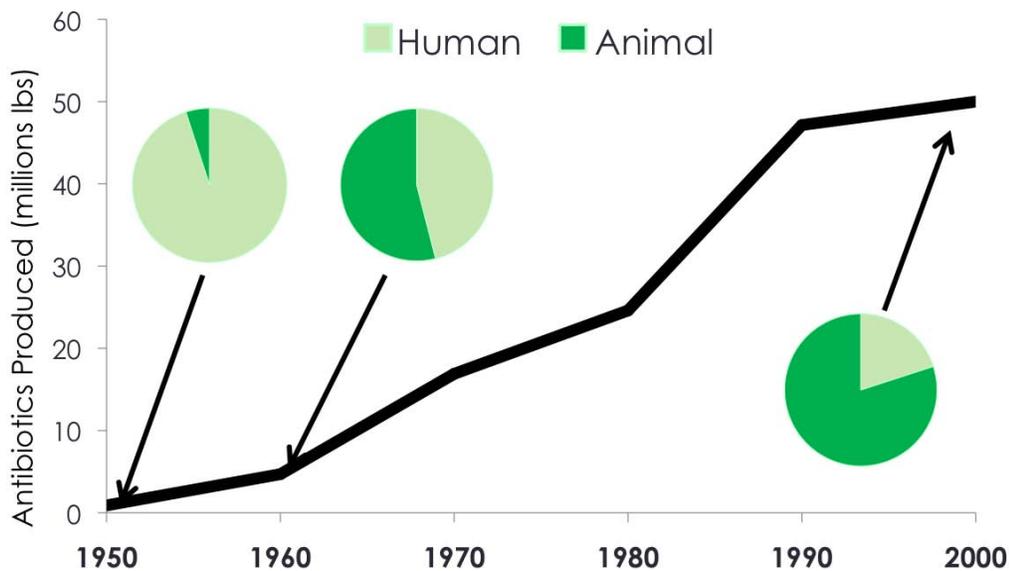
2010). Resistance genes affect the physiology of bacteria in a way that can put them at a general disadvantage, but this cost becomes a benefit in the presence of antibiotics (Levin et al., 2000; Andersson, 2003; Jansen et al., 2006; Summers, 2006; Hogberg et al., 2010). When antibiotics are applied, susceptible bacteria are killed, leaving behind those that are resistant. This resistance is then spread through direct inheritance. Bacteria can divide every 15 minutes to an hour, meaning that one resistant bacterium could potentially produce 281 trillion ( $2.81 \times 10^{14}$ ) genetically identical bacteria within 24 hours (Todar, 2008). Genes can also spread through complex genetic interactions including horizontal gene transfer, gene linkages, and transformations. The consistent use of antibiotics increases all of these possibilities by creating an environment that favors the spread of resistance; therefore

increased antibiotic use leads to increased resistance (Walsh, 2000; Hogberg et al., 2010).

## Antibiotic Resistance and Animal Agriculture

In the 1940s, 5% of the antibiotics produced in the United States annually—45 thousand pounds—were given to animals; by 2009, 80% of the total antibiotics produced annually—29 million pounds—went to livestock and poultry (Jukes, 1972; Smart and Marstrand, 1972; UCS, 2001; FDA, 2009; Figure 3). This increased use of antibiotics allowed for a drastic intensification of animal production such that between 1978 and 1994 the average number of swine per operation increased 2.8 times while the average number

### ANTIBIOTIC PRODUCTION AND DISTRIBUTION WITHIN THE UNITED STATES

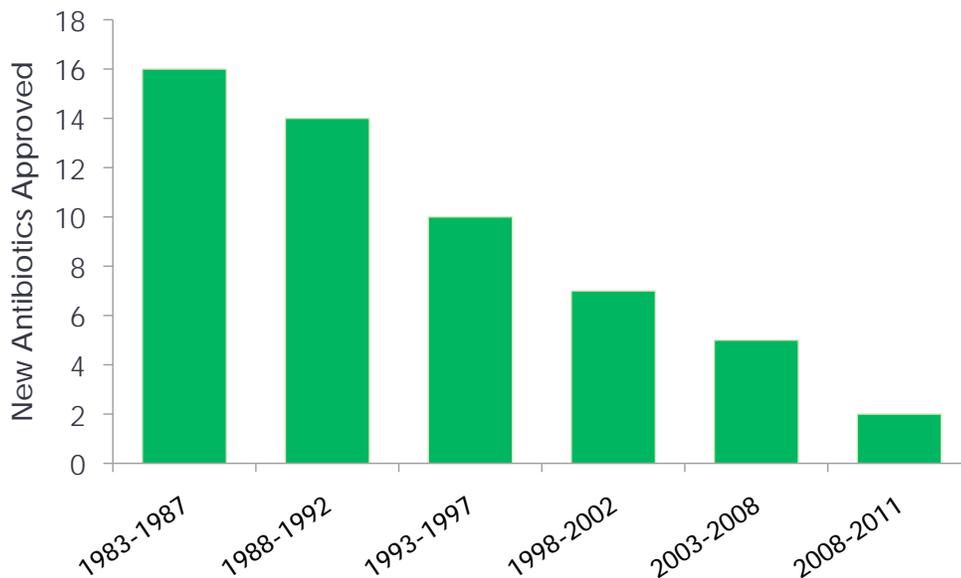


**Figure 3:** Antibiotic production and distribution within the United States. (adapted from UCS, 2011 and Smart and Marstrand, 1972).

of cattle per operation increased 1.6 times (Tilman et al., 2002). Similar changes took place within the poultry industry, which experienced a compounded annual growth rate of 3.9% between 1945 and 1999, increasing production from 5 million to 40 million pounds (McEwen and Fedorka-Cray, 2002). Animal crowding, poor sanitation, and insufficient temperature and ventilation control are all characteristics of the confined animal feeding operations that account for the majority of meat production in the United States (McEwen and Fedorka-Cray, 2002). To combat the negative health effects these conditions can have on animals, antibiotics are administered in low doses over long periods of time to animals that are not sick (i.e., nontherapeutically) to prevent the spread of disease. Antibiotics given in this manner also act as growth promoters. As of 2002, more than 83% of feedlots administered at least one antibiotic through feed or water for prophylaxis or growth promotion (McEwen and Fedorka-Cray, 2002).

The antibiotic resistance that develops in animal agriculture is problematic for two reasons: humans and animals share antibiotics, and antibiotic-resistant bacteria can spread. According to the Union of Concerned Scientists, 55% of drugs used for growth promotion and disease prevention in animals are also used to treat disease in humans (UCS, 2001). These drugs, including penicillin, erythromycin, and amoxicillin, are used therapeutically in humans to treat illnesses such as strep throat, pneumonia, and a number of sexually transmitted diseases (UCS, 2001). The likelihood of resistance emerging in the bacteria that cause these illnesses increases with the use of antibiotics in food-producing animals because resistance can transfer between types of bacteria (Campagnolo et al., 2002). Resistant bacteria emerging on farms can then spread to human populations via farm workers and those living in close proximity to farms through the handling and consumption of meat products and through environmental pathways (Levy et al., 1976; Hummel et al.,

**NUMBER OF ANTIBIOTICS APPROVED BY THE US FDA BETWEEN 1983 AND 2011**

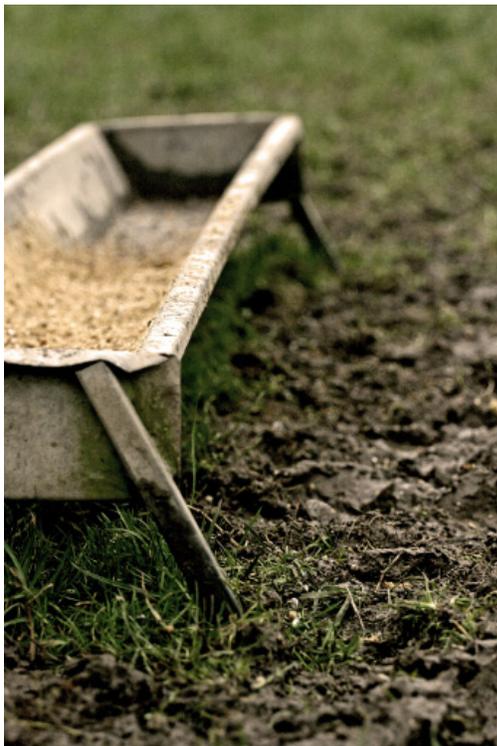


**Figure 4:** Approvals of new antibiotic drugs by the US FDA between 1983 and 2011 (adapted from *Infections Diseases Society of America*, 2011).

1986; McEwen and Fedorka-Cray, 2002).

The decreased effectiveness of existing drugs due to antibiotic resistance could potentially be offset by the development of new antibiotics. If resistance to an antibiotic develops, one option is to simply replace that antibiotic. The rate of approvals of new antibiotics, however, is diminishing. Over the past 30 years the number of antibiotics approved each year by the U.S. Food and Drug Administration (FDA) has steadily decreased, with only two approved since 2008 (Infectious Disease Society of America, 2011; Figure 4). Since new antibiotics are not being developed at a rate that allows us to simply replace ineffective antibiotics, combating resistance must entail managing the use of the antibiotics we already have.

*“The antibiotic resistance that develops in animal agriculture is problematic for two reasons: humans and animals share antibiotics, and antibiotic-resistant bacteria can spread.”*



## Proposed Legislative Solution

Awareness of these public health risks has existed for some time: the first congressional hearing on antibiotic resistance was held in 1977. That hearing and several since have focused on bacterial resistance to specific antibiotics in relation to their use in animal feed as well as the connection between antibiotic use in food-producing animals and the transmission of resistant bacteria to human populations (Antibiotics in Animal Feeds, 1977; Antibiotic Resistance, 1984). While the relationship between antibiotic resistance and antibiotic use in animal agriculture has been known for several decades, the federal government has not passed comprehensive legislation on non-therapeutic antibiotic use in food production. The Preservation of Medical Treatment Act of 2011 (H.R. 965) is the fifth version of the bill to be introduced in Congress since 2003. While many bills addressing antibiotic resistance have been proposed since 1999, none has ever progressed past committee review.

The goal of the Preservation of Antibiotics for Medical Treatment Act is to regulate the use of antibiotics in animal agriculture in order to reduce the presence of resistant bacteria everywhere (Figure 5). It does so by amending the Federal Food, Drug, and Cosmetic Act to define “critical antimicrobial drug” and “nontherapeutic use” as well as to modify the approval process of antibiotic drugs through the following changes:

### 1. Applications for New Drugs:

The Secretary of Health and Human Services is required to deny an application for any critical antimicrobial animal drug unless the applicant demonstrates that there is reasonable certainty of no harm to human health due to the development of antimicrobial resistance attributable to the nontherapeutic use of the drug (H.R. 965).

## 2. Retroactive Review:

The Secretary will withdraw approval for nontherapeutic antibiotics approved prior to enactment unless the holder proves within a two-year period that nontherapeutic use does not lead to microbial resistance detrimental to humans, as explained above (H.R. 965).

### MANDATORY COMPONENTS OF THE ACT

#### Definitions

- Critically important antimicrobial drugs
- Nontherapeutic use

#### Enhanced Safety Review

- Additional criteria for review of new drugs
- Retroactive review of approved drugs

**Figure 5:** *Mandatory components of the Preservation of Antibiotics for Medical Treatment Act.* The mandatory components of the Act begin with standardizing two definitions. The first is ‘critically important antimicrobial drug,’ which refers to any antimicrobial that is in the same drug class as those used in people. The second is ‘nontherapeutic use,’ which refers to the administration of antibiotics to healthy animals to prevent disease and/or promote growth. The Act also adds new safety criteria to the drug approval process such that new drugs must be proven to cause no harm to human health due to increasing resistance. In addition, the Act imposes a two-year retroactive review period by the end of which all previously-approved drugs must meet the new safety standards or be recalled from the market.

## Politics of the Issue

Support for the Act and its goals is broad, with primary backing coming from the health and environmental sectors and portions of the agricultural sector. As of April 2011, three hundred seventy-eight organizations had formally endorsed the legislation, including the Union of Concerned Scientists, Organic Trade Association, The American Livestock Breeds Conservancy, American Medical Association,

American Nurses Association, Animal Welfare Institute, Environmental Defense Fund, Sierra Club, and United States Environmental Watch (UCS, 2011). These organizations recognize the documented link between the prevalence of antibiotic resistance in humans and the widespread nontherapeutic use of antibiotics in food-animal production. They are also concerned with the socioeconomic, environmental, and public health issues associated with antibiotic resistance, from rising domestic healthcare costs to consequences for international trade.

Concern over rising health care costs and increasing tension with trade partners that have strong food safety laws are at their root economic considerations of antibiotic resistance. Extended hospital stays due to antibiotic-resistant infections are estimated to cost approximately \$18,588 to \$29,069 more per patient, which amounts to billions in additional national healthcare costs each year (Roberts et al., 2009). Rather than continuing to spend billions of dollars to treat drug-resistant infections, advocates promote preventing these infections through the management of resistance. Similarly, decreased international markets for U.S. meat could have severe economic consequences. Many U.S. trade partners including New Zealand, South Korea, and the European Union have institutionalized legal restrictions on antibiotics in food production. Should the U.S. not begin to make similar changes to restrict the use of antibiotic drugs in animal agriculture, the country’s position in foreign livestock and poultry markets could suffer (Johnson, 2011).

Animal agriculture within the United States is an immense industry that is integral to the national economy. The meat and poultry packing and processing industries are some of the largest and most widely interconnected sectors of the U.S. economy (US Department of Commerce, 2008; AMI, 2011). The meat and poultry industries are estimated to generate over \$850 billion annually, which represents about 6% of U.S. GDP (AMI,

2011). In 2009 these industries directly employed over 500,000 people, and the broader industry including suppliers, distributors, retailers, and ancillary industries employed 6.2 million people (AMI, 2011). Substantial reductions in antibiotic use due to increased safety regulations would lead to significant economic impacts on the industry.

Unsurprisingly, meat producers are largely opposed to increased regulation of the industry's use of antibiotics. Organized opposition has come from the National Cattlemen's Beef Association, National Pork Producers Council, National Turkey Federation, National Chicken Council, National Milk Producers Federation, American Meat Institute, and National Meat Association (Moscovitch, 2010). These groups oppose antibiotic regulations on a number of grounds including the suggestion that the cost of meat production will increase, leading to increased prices for consumers (National Pork Producer's Council, 2009). These industries have also raised concerns about the evidence linking antibiotic use in animal agriculture to increases in resistant infections in humans. Their position is that existing guidelines and regulations are sufficient to ensure appropriate use of antibiotics in animal agriculture (National Pork Producers Council, 2009; National Cattlemen's Beef Association, 2011).

*“The meat and poultry industries are estimated to generate over \$850 billion annually, which represents about 6% of U.S. GDP.”*

The pharmaceutical industry is also opposed to increased regulation. Pharmaceutical companies share the position of meat producers that existing guidelines and regulations regarding drug approval and antibiotic use in farming are sufficient (Animal Health Institute, 2011a). A number of pharmaceutical companies including Bayer, Novartis, Pfizer, and Eli Lilly and Company

are members of the Animal Health Institute, which lobbies against legislation to restrict antibiotic use (Loglisci, 2010; Animal Health Institute, 2011b). The total lobbying expenditures of the Animal Health Institute over the past ten years range from \$30,000 to \$200,000 per annum (Opensecrets.org). While it is difficult to quantify political power, many of the groups opposing the legislation have significant financial resources to apply towards their interests regarding the use of antibiotics in food production in the United States.

Pharmaceutical companies are important to addressing antibiotic resistance outside of their stance and influence on related legislation. The development of new antibiotics by these companies could mitigate the threat of antibiotic resistance, but antibiotic research and development is an expensive process that takes many years (Figure 4). Determining the cost of drug development is complicated by transparency limitations and proprietary information, but the costs are estimated to be between \$92 and 883.6 million, or between \$161 million and 1.8 billion when including the cost of capital (Morgan et al., 2011). On average, drug development takes 12 years, and only 5 in 5,000 (0.1%) of the drugs that begin preclinical testing make it to human testing, and only 1 of those 5 drugs (0.02% of the 5,000) that began preclinical testing is approved for human use (California Biomedical Research Association, n.d.).

New antibiotic development is not a feasible quick-fix solution to address increasing antibiotic resistance. Multiple strategies are needed to mitigate this public health threat, including enforcing appropriate application of antibiotics in farm animals, addressing the farming practices that are dependent upon the nontherapeutic use of antibiotics, and creating a robust database to better understand trends in antibiotic resistance. These strategies are incorporated into the recommended program design for the implementation of the Preservation of Antibiotics for Medical Treatment Act of 2011.



# PROGRAM DESIGN

# PROGRAM DESIGN

The program design outlined in this report develops an implementation plan for the mandatory components described in the Preservation of Antibiotics for Medical Treatment Act of 2011 and also recommends additional components to address the effects of new regulations on food-animal production, supply, and cost. As the current animal agriculture system relies on extensive nontherapeutic use of antibiotics, new regulations affecting that use are expected to have immediate and significant effects on this production system. Considering the likelihood of significant changes in food-animal production due to enhanced drug safety standards, this program design includes activities aimed at mitigating potential adverse consequences.

These two components—enhancing safety standards and transition support—are outlined with staffing and budgeting plans for the first year of implementation. A surveillance and monitoring component is designed to collect the data needed to accurately track antibiotic resistance by building on the capacity of existing systems in different federal agencies. An enforcement component is intended to support the regulations by ensuring the appropriate use of antibiotics. Because the Act establishes a two-year period before antibiotics in current use come up for retroactive review, and some time is needed to establish the new safety standards, these last two components are inherently delayed in their operations.

Because the program is complex and involves multiple federal agencies, particularly with the inclusion of the surveillance and monitoring component, the program design includes the establishment of a multiagency coordination office. The responsibility of this office will be to coordinate the components of the program and ensure communication among

these interconnected initiatives. This role will be contracted out to a consulting agency through a call for bids of up to \$250,000. This agency will report to the head of the Center for Veterinary Medicine in the FDA. The contract will be up for review after three years.

The following sections of this report provide further detail on each of the program components. These sections include expected budgets, recommended staff additions, benchmarks for performance management, and timelines for the first year of implementation. Further detail on the overall program budget and staffing plans are provided in Appendices I, II, and III.

## [ Program Design ]



## Enhancing Drug Safety Standards

**Goal:** Amend standards for the approval of antibiotics intended for use in food-producing animals

**Total Budget:** \$416,098

**Added Staff:**

*Associate Director of New Drug Review*  
- Office of New Animal Drug Evaluation,  
Center for Veterinary Medicine, Food  
and Drug Administration

**Benchmarks:**

- Hire Associate Director of New Drug Review
- Convene Assembly of Experts
- Draft new standards for safety review
- Receive comments on draft standards from stakeholders
- Publish new standards

Enhancing the safety standards against which drugs are evaluated is the foundation of this program design. To carry out these enhancements, Congress will amend Sections 201 and 512 of the Federal Food, Drug, and Cosmetic Act. Changes to Section 201 will include establishing definitions of ‘critical antimicrobial animal drugs’ and ‘nontherapeutic use’ of antibiotics, along with changes to Section 512 (‘New Animal Drugs’) to establish a phased elimination of nontherapeutic use of antimicrobial drugs important for human health. The implementation of these mandates will be managed by the Center for Veterinary Medicine (CVM), a division of the Food and Drug Administration (FDA).

The Center for Veterinary Medicine is the unit within the FDA that regulates the manufacture and distribution of food additives and drugs given to animals (FDA, 2011a). The Office of New Animal Drug Evaluation (ONADE) is responsible for reviewing information submitted by drug sponsors seeking approval to manufacture and

market new animal drugs (FDA, 2010). ONADE evaluates the safety and efficacy of each animal drug as well as its potential effects on the environment. It also coordinates the development and implementation of regulations and policies pertaining to the new drug intended for animal use. As a result, any new statutory requirements for changing the new animal drug approval process will be realized through ONADE.

Developing new safety standards requires collaboration among a variety of stakeholders—government officials, scientific experts, and industries—as well as efficient administrative efforts. To implement these new standards, we recommend that the Office of New Animal Drug Evaluation expand its staff by hiring an Associate Director for New Drug Review. (For organizational charts, see Appendix III.) During the hiring process, existing ONADE staff will begin contacting experts, including pharmacologists, veterinarians, and public health scientists. These experts will be charged with creating reasonable safeguards for antibiotic effectiveness by determining the criteria necessary to establish the “reasonable certainty of no harm to human health due to antibiotic resistance” called for in the legislation (H.R. 965). This assembly of scientific and policy experts will convene for a three-day meeting in April, and during this working conference they will draft recommendations for the new approval standards.

Following this assembly, CVM staff will process the expert recommendations and release a draft set of safety standards. Once the draft standards are published, the CVM will hold public meetings and webcasts open to public discussion for a sixty-day comment period from July to August 2012. From August to September the Associate Director of New Drug Review will consult pharmaceutical companies to discuss any concerns with the draft safety standards. After comments from the public and industry are incorporated, revised standards will be published for another 30-day comment

period in November. After processing comments from the second period, CVM staff will make revisions and publish final new safety standards by the end of 2012. At this point, the Center for Veterinary Medicine will begin applying these standards to applications for approval of new antibiotics. Retroactive review of antibiotics previously approved for use in animal agriculture will also begin at this time, and sponsors will have two years to reapply for approval before the products must be taken off the market.

The nature of the period following the implementation of enhanced safety standards will largely be determined by the standards themselves and the definitions established by the legislation. The burden of proof required by the new safety standards and the number of antibiotics able to meet them will impact the scope of the other program components. If pharmaceutical companies determine that the nontherapeutic use of certain antibiotics will not meet the new safety standards, they may choose not to pursue reapproval and will remove them from the market at the end of the two year period. If the definition of ‘critical antimicrobial drugs’ is very broad, it will affect a larger portion of the drug marketplace than if the term is defined more narrowly. The impacts of the new safety standards also extend to other components of the program. The number of antibiotics available for use after the reapproval process will determine the extent to which farming practices will need to change. Likewise, the safety standards will shape the monitoring and enforcement of appropriate use of antibiotics in animal agriculture. In light of these uncertainties, staffing and budgeting plans for 2013 and beyond must be flexible.

### **Indicators for Performance Management**

The following indicators will be used to assess the effectiveness of the enhanced drug safety standards component. The one-time indicators are activities that will happen once with either

a yes or no outcome. These one-time indicators include hiring the Associate Director of New Drug Review in the CVM, convening the assembly of experts to determine the new safety standards, and amending the FDA drug approval process. Ongoing indicators are those that will occur more than once, here including the number of new approval and reapproval applications submitted as well as the number of new antibiotics approved. Because the new safety standards will not be finalized until the end of the first year, we expect that there will be zero applications submitted under this program during the first year. There will also be zero new antibiotics approved within the first year as the approval process will be suspended until the new standards are finalized. Approvals and reapprovals will begin following the adoption of new standards in 2013.

<b>Indicators</b>	<b>First Year Outcome</b>
<b>One-time Indicators</b>	
Hiring of Associate Director of New Drug Review	Yes/No
Assembly of experts convened	Yes/No
Amended FDA process for drug approval	Yes/No
<b>Ongoing Indicators</b>	
Number of new drug approval applications	0
Number of drug reapproval applications	0
Number of new antibiotics approved	0

## BOX 1: HOW DOES A DRUG GET APPROVED FOR ANIMAL USE?

All new animal drugs must submit an application to the Office of New Animal Drug Evaluation (ONADE) within the Center of Veterinary Medicine (CVM), which is a part of the Food and Drug Administration (FDA). ONADE's major responsibility is to review information provided by drug sponsors who wish to manufacture and market animal drugs (FDA, 2010a). Before a new drug intended for use in a food-producing animal receives FDA approval, it must be clinically tested for effectiveness and safety in the target animal as well as in human consumers, and the edible animal products must be free of unsafe drug residues. ONADE evaluates the safety and efficacy of each animal drug as well as its potential effects on the environment. It is the responsibility of the drug sponsor, the individual or firm seeking FDA approval of the drug, to develop analytical methods and conduct the tests to detect and measure drug residues in edible animal products. If the information shows the drug is safe and effective, ONADE provides a recommendation to the Center Director that the drug should be approved. If the Director agrees, he/she approves the application, a notice of approval is published in the Federal Register, and the drug can be marketed for approved uses.

### *Fees for Animal Drug Approval Applications*

The Animal Drug User Fee Act (ADUFA) of 2003 amended the Federal Food, Drug, and Cosmetic Act (FFDCA) to authorize the FDA to collect fees for some animal drug applications and for the establishments (i.e. pharmaceutical companies), products (i.e. each drug), and sponsors associated with these and previously approved drugs (FDA, 2011c). This authorization, which generates additional revenue, is intended to support the FDA's review of animal drugs. In fiscal year 2010, the FDA collected \$15.8 million in animal drug user fees and spent \$16.6 million in user fees to process reviews. Under the ADUFA, any fees collected, appropriated, and not obligated at the end of a fiscal year remain available to the FDA for future use. For fiscal year 2012, the fee for each animal drug application will be \$372,100 (FDA, 2011d).

The Preservation of Antibiotics for Medical Treatment Act (PAMTA) mandates enhanced drug safety standards by requiring that to be approved for animal use a critical antimicrobial must demonstrate reasonable certainty of no harm to human health due to the development of antimicrobial resistance. After these safety standards have been augmented, new drug applications will be reviewed through a process similar to the FDA's current review process. PAMTA also requires that a retroactive review take place for all drugs currently on the market for use in animal agriculture and that these drugs undergo retesting. All new and renewal drug applications will require fees from sponsors which will be set during the first year by the FDA such that the fees will cover the expenses associated with the review process. Should these fees be unable to cover review expenses due to the number of drug sponsors applying for reapproval, the FDA would need another source of revenue such as a Congressional appropriation or additional user fees.

## Transition Support

**Goal:** Help farmers reduce their reliance on nontherapeutic antibiotic use.

**Total Budget, Added Staff, and First-Year Benchmarks:** See components below

Once the new safety standards are enacted, these new regulations will likely have significant impacts on animal agriculture within the United States. Therefore, we propose a transition support program to assist the animal agriculture industry in adjusting to a system in which nontherapeutic use of antibiotics is more strictly regulated. As explained previously, the current farming system that provides a large supply of low-cost meat relies on an industrial model of production that maximizes the amount of meat produced per farm. The high animal densities and close quarters associated with this model stress animals' immune systems, increasing the rate of spread and magnitude of impacts from disease (UCS, 2006; Casewell, 2003). A likely outcome of stricter safety regulations for antibiotics is a reduction in the number of the antibiotics available and an overall decrease in the nontherapeutic use of antibiotics. This reduction in antibiotic use will likely force at least a partial shift away from the high-density industrial model of animal agriculture that depends on antibiotics to maintain production.

The Preservation of Antibiotics for Medical Treatment Act of 2011 only calls for the revision of the safety standards for drugs that will be used nontherapeutically in food producing animals. But the current dependence of the meat industry on extensive nontherapeutic antibiotic use demands that the implementation of this legislation addresses the inevitable changes in animal agriculture practices. The transition support component of the program

is intended to mitigate the effects of the stricter standards by helping farmers improve their practices through better husbandry techniques and the use of antibiotic alternatives such as probiotics and vaccines. In order to find the best ways to incentivize these practices as well as to incentivize the research and development of new antibiotics and antibiotic alternatives by the pharmaceutical industry, the USDA and the FDA will compile reports detailing incentive options for these sectors.

The likelihood that these transitional activities will have positive effects on the industry's adjustment to new standards for antibiotics is promising if we consider a historical precedent. In 1998, the Danish government banned the use of antibiotic growth promoters during the finishing stage of pork production. In 1999, it banned all antibiotic growth promoters, and later that year the entire European Union banned the nontherapeutic use of several antibiotics used as growth promoters in animals (Hayes and Jensen, 2003). A recent report from the PEW Charitable Trusts found that while this ban was focused on antibiotics for growth promotion, overall antibiotic use in swine decreased by over 50% without any significant long-term effects on swine health (PEW Campaign, 2011). Danish industry representatives judge the changes in animal husbandry practices, such as improved ventilation and increased space for animals, along with adjustments to feed quality and additives to be effective in replacing the routine use of antibiotics (PEW Campaign, 2011).

The remainder of this section details the four transition support initiatives included in the program design: 1) education and outreach grants, 2) a farmer incentives report, 3) a grant program at the National Institute of Food and Agriculture, and 4) a pharmaceutical industry incentives report. The first two initiatives will assist farmers as they adapt to increased antibiotic restrictions, while the second two initiatives will encourage the research and

development of new husbandry techniques and of new antibiotics and antibiotic alternatives.

## SUPPORTING FARMERS

### *Education and Outreach*

**Total Budget:** \$2,825,000

**Added Staff:** None

**Benchmarks:**

- Deliver best practices report
- Disburse grant funds to Land Grant Universities
- Commence farmer training programs

This part of the program establishes initiatives to support farmers and enhance their capacity to transition away from the extensive use of antibiotics. Educational and outreach activities will connect farmers to appropriate methods to both replace antibiotics and change the practices that make extensive nontherapeutic use of antibiotics necessary. These educational activities will be founded upon a best practices report commissioned from the National Research Council and will utilize the Cooperative Extension Services partnership between the federal government and Land Grant Universities in each state. The National Institute of Food and Agriculture (NIFA) within the United States Department of Agriculture (USDA) will be responsible for managing these initiatives.

During the first year of implementation, USDA staff within the Research, Education, and Economics division will contact the National Research Council (NRC) in January of 2012 and commission the Council to write a report detailing best husbandry practices without the use of nontherapeutic antibiotics. The expected cost of preparing this report will be \$250,000, which is in line with fees for other NRC reports. That

report will be completed by the end of November so that USDA staff can begin distribution to Land Grant Universities, Cooperative Extension Services, and farmers by the end of 2012.

Within the first year, USDA staff will also be responsible for distributing grants to support reduced-antibiotic farming practices to the Land Grant Universities' Cooperative Extension Services in each state. The Cooperative Extension Services are funded by the USDA to reach out to, support, and educate farmers in each state (USDA, 2011a). Our program design calls for the distribution of \$50,000 to each state's Cooperative Extension Service so that the Services can design and implement an outreach program for farmers about raising animals with decreased antibiotic use. Since we expect the NRC report on best practices to form the foundation of these education programs, we do not expect to see specific training programs implemented until after this report is distributed. Therefore, the USDA will distribute these funds during December 2012 for use in 2013 and beyond.

### *Indicators for Performance Management*

To assess the effectiveness and accomplishments of the education and outreach programs we have designed several indicators. A one-time indicator within the first year is receiving the best practices guide from the NRC. Within the first year, the USDA will distribute \$2.5 million to the Land Grant Universities and this will continue annually. During the first year no training programs are expected as they must first be developed by the Cooperative Extension Services, but in subsequent years the number of training programs completed will be a measure of how effectively the grant funds are being used. A third ongoing indicator will be to measure farmer awareness of both the existence of these educational opportunities and the information being disseminated, such as better husbandry

techniques. The Congressional Research Service will measure this awareness via surveys, but since there will be no training programs within the first year, these surveys will not begin until year two.

Indicators	First Year Outcome
<b>One-time Indicators</b>	
NRC issue best practices guide	Yes/No
<b>Ongoing Indicators</b>	
Funding dispersed to universities by USDA	\$2.5 million dispersed
Training programs running	0
Annual surveys by the Congressional Research Service measuring increased farmer awareness	0

### *Farmer Incentives Report by the USDA Economic Research Service*

**Total Budget:** \$168,697  
**Added Staff:** None  
**Benchmarks:**

- Create a report outlining the options for farmer incentive programs to implement retrofits and best practices that lower their nontherapeutic application of antibiotics

To support farmers as they adjust to increased regulations on antibiotic use, we recommend federal action to incentivize farmers to implement practices and upgrade equipment that will allow them to maintain productivity while transitioning away from nontherapeutic antibiotic use. While the educational and research initiatives will provide valuable information to farmers on best practices, we recommend that there be federal initiatives to incentivize farmers to implement these changes. To determine the optimal way for federal agencies to implement

such initiatives, the USDA will create a report outlining the most effective actions agencies can take to improve husbandry practices as well as increase farm retrofits and the use of antibiotic alternatives such as probiotics and vaccines.

The Market and Trade Economics Division within the USDA's Economic Research Service will be responsible for producing the Farmer Incentives Report. This division conducts research and analysis on the impacts of both global and national economic policies on agricultural markets, and this research is used to inform public policy and program decisions (USDA, 2011b). A current staff member within the Animal Products and Cost of Production branch will be appointed as supervisor for this report, which is expected to be completed within one year. To assist with this assignment, the supervisor will hire two short term researchers to help compile the report (Appendix III).

### ENCOURAGING RESEARCH AND DEVELOPMENT

#### *Research Grant Program at the National Institute of Food and Agriculture (NIFA)*

**Total Budget:** \$100,000,000  
**Added Staff:** None  
**Benchmarks:**

- Allocate additional \$100 million to NIFA's budget for a new grant program
- Establish research grant program and award grants

The goal of the research grant program is to change farming practices to reduce reliance on nontherapeutic antibiotic use. Addressing antibiotic resistance is the primary goal of the Preservation of Antibiotics of Medical Treatment Act of 2011, but the implementation program includes a substantial grant program because

maintaining a safe and affordable meat supply is also an important consideration. In order to maintain that supply in light of new regulations, farming practices will change and the findings from research funded via this grant program will allow for that change to be more efficient and less costly to farmers. The research from this grant program will also tie into the overall program’s educational initiatives as new findings can be incorporated into farmer training through the Cooperative Extension Services.

The mission of the USDA’s National Institute of Food and Agriculture (NIFA) is to “advance knowledge for agriculture, human health and well-being, and communities” (NIFA, 2011). NIFA does not perform or supervise research itself, but instead funds research at the state and local levels through national program leadership and provision of federal assistance to researchers and institutions (NIFA, 2011). Based on the average amount of money allocated to NIFA grants and the estimated need for research into husbandry without nontherapeutic antibiotic use, NIFA will be allocated an additional \$100 million annually by the Committee of Appropriations to establish a competitive grant program specifically funding research focused on developing agricultural practices that reduce reliance on nontherapeutic antibiotic use. The Division of Animal Systems in the Institute of Food Production and Sustainability within NIFA will administer the program. The program will be established by June 2012, at which point NIFA will begin publicizing the competition for funding and accepting proposals for evaluation.

The 100 million dollars allocated to NIFA is intended to also cover the administrative costs associated with actually developing and running the grant program. As NIFA already has a process in place for doing so, NIFA leadership will decide what administrative actions and expenses are necessary to establish and manage the program; these expenses, however, must not exceed \$250,000 of the \$100,000,000 allocated annually.

Expenses may include staff hires or reallocations, grant advertising and communication, processing and reviewing applications, and the collecting and compiling of research updates from funded projects into an annual report.

### *Indicators for Performance Management*

Within the first year, a one-time indicator will be the establishment of the grant program run by NIFA focused on husbandry techniques not dependent on the nontherapeutic use of antibiotics. The ongoing indicators include the annual allocation of \$100 million to NIFA and the awarding of grant money to selected research applicants. A third ongoing indicator will be an expected annual report compiled by NIFA on the outcomes of the research projects funded by this grant. Within the first year no report is expected as the grants will have only just been distributed by the end of the year.

<b>Indicators</b>	<b>First Year Outcome</b>
<i>One-time Indicators</i>	
Grant Program Established	Yes/No
<i>Ongoing Indicators</i>	
Allocation of \$100 million to NIFA	Annual Yes/No
Grants Awarded	Annual amount awarded
Annual NIFA project report on research outcomes	No report during the first year

## BOX 2: WHO CARRIES WEIGHT IN THE PORK INDUSTRY?

In 2008 the Center on Globalization, Governance & Competitiveness at Duke University prepared a report for the Corporate Partnerships Program of the Environmental Defense Fund detailing the value chain of the pork industry with the aim of identifying key players that have the capacity to effect changes across the industry. The report was prepared with a focus on the use of antibiotics in pork product production and divided the industry into four components: inputs, production, processing and distribution, and marketing (Lowe and Gereffi, 2008). Within each of the four components, the report identifies those companies with the most leverage.

The report finds that the number of key players in the pork industry is relatively small, with a handful of large companies touching almost every segment of the value chain from production to processing to sales. These large companies, such as Tyson Foods and Smithfield Foods, will be highly relevant in the implementation of an industry response to the enhanced safety standards mandated by the Preservation of Antibiotics for Medical Treatment Act (PAMTA). The only firms with direct control over antibiotic management are hog farms, but these farms are often in contract with large nationwide pork and pork product distributors, such as Tyson and Smithfield, that own the animals.

The transition support initiative in the implementation program for PAMTA will demand consideration of these large industry players. In particular, the report to be completed by the USDA's Economic Research Service recommending best incentives for transitioning away from nontherapeutic antibiotic use will entail considerable communication and interaction with these firms. Because the pork industry is condensed into a small number of entities, there is promise for a large reduction in antibiotic use should appropriate incentives be established to assist these companies. Meeting with representatives from these companies will provide insight into multiple points along the supply chain and could yield ideas for appropriate incentives across the meat industry, including beef and poultry firms.



## *Industry Incentives Report by the Food and Drug Administration*

**Total Budget:** \$168,697

**Added Staff:** None

**Benchmarks:**

- Create a report outlining options to encourage the pharmaceutical industry to invest in research and development of new antibiotics and antibiotic alternatives.

As discussed previously, drug research and development is a lengthy and expensive process, and the number of new antibiotic approvals has steadily decreased over the past twenty-five years (IDSA, 2011). The lack of new antibiotics to replace the increasingly less effective drugs in the existing antibiotic supply is a serious concern. To preserve the current arsenal of antibiotics, we must modify the capacity in which we use them, particularly in food production. The development of new antibiotic alternatives for use in food-producing animals will play an important role in transitioning away from the nontherapeutic use of antibiotics. Federal action to incentivize the development of alternatives such as probiotics and vaccines is crucial to facilitating this transition in farming practices. Therefore, we recommend that the Science and Research arm of the FDA create an industry incentives report outlining ways the federal government could promote the development of new antibiotics and antibiotic alternatives.

The Science and Research arm of the FDA undertakes various research initiatives. One of these initiatives, the Critical Path Initiative, is intended to understand how market forces and considerations impact medical product development (FDA, 2011b). This Initiative will be responsible for creating the Industry Incentives Report outlining the best options for incentivizing the development of new antibiotics

as well as new antibiotic alternatives for food producing animals. A current staff member within the Initiative will be appointed as supervisor for this report, which will be completed within one year. To assist with this assignment, the supervisor will hire two short term researchers to help compile the report (Appendix III).

## Surveillance and Monitoring

**Goal:** To confirm that antibiotics are being used in accordance with the new safety standards and collect data on antibiotic resistance.

### IMPROVING DATA ON ANTIBIOTIC RESISTANCE

The program design includes a component focused on antimicrobial surveillance and monitoring, which is critical for identifying emerging problems, tracking resistance patterns, and evaluating prevention and control measures. Currently, the U.S. lacks a coordinated national program for antimicrobial surveillance and has no system in place that tracks the amount of antibiotics used in animal agriculture or the purposes for which those drugs are applied. There are, however, a number of government organizations concerned with researching, monitoring, and communicating about antimicrobial resistance in the U.S. This program design requires expanding existing measures to more thoroughly track antibiotic usage and trends in antimicrobial resistance. The goal of enhancing monitoring is to establish more comprehensive information on antimicrobial resistance and antibiotic usage. These activities will require collaboration between different government agencies but will be carried out primarily by the National Antimicrobial Resistance Monitoring System (NARMS).

## *The National Antimicrobial Resistance Monitoring System*

In 1996, the FDA, USDA, and Center for Disease Control and Prevention (CDC) founded NARMS (Torrence, 2001), and it is the primary organization responsible for the monitoring of antimicrobial resistance patterns among human and animal populations in the United States. Bacterial resistance data under the animal component of the organization is collected by the USDA from slaughter and meat processing facilities. Participating CDC laboratories, the Center for Veterinary Medicine (CVM), and the Foodborne Diseases Active Surveillance Network (FoodNet) are responsible for the retail meat component, which tests meat samples for resistant microbes (NARMS, 2010). At present, NARMS screens primarily for the presence of three prominent bacteria: *Salmonella*, *Escherichia coli*, and *Campylobacter*. The bacteria are then tested for resistance to seventeen antimicrobials. Each sample is then classified as ‘susceptible’, ‘intermediate’, or ‘resistant’ to the drug (Torrence, 2001; NARMS, 2010). In a separate branch of the organization, the human component of NARMS is dependent on participating FoodNet sites, public-health laboratory reporting of confirmed cases of antimicrobial resistant food-borne illness, and state-level health

departments (NARMS, 2008; NARMS, 2010).

### EXPANDING CURRENT PROGRAMS

Since existing surveillance and monitoring programs are not comprehensive, many gaps remain in the information collected by the Department of Health and Human Services and USDA on antibiotic use in food animals as well as on resistant bacteria in animals and animal products (GAO, 2011). Since 2004, the FDA has collected data from pharmaceutical companies on antibiotics sold for food animal use, but this data does not specify whether the products were used therapeutically or nontherapeutically or to which species they were administered (GAO, 2011). The current monitoring network is largely restricted to specific regions and does not provide a national perspective on the problem of antimicrobial resistance. Expanding the scope of existing programs to incorporate samples from more geographic regions and from a wider variety of animals and animal products will improve the quality of data collected. These improvements will be achieved by expanding the CDC’s FoodNet program, which currently only surveys foodborne diseases in ten states, into a nationwide initiative. Additionally, more strains



of bacteria and resistance to more antibiotics will be incorporated into data collection.

## MANDATORY MONITORING OF DRUGS

### POST-APPROVAL

There are post-approval programs currently in place at the FDA that are designed to collect information related to the antimicrobial susceptibility of foodborne pathogens found in animals. These data are unique in that they track antimicrobial resistance that may develop under actual growth conditions for the farm animals. These data-collection and reporting programs, currently voluntary, will be made mandatory. The responsibility of monitoring resistance to each antimicrobial will be placed on the drug sponsor, with ultimate evaluation and review by CVM's Office of Surveillance and Compliance (OS&C).

The CVM's OS&C, in cooperation with FDA Field Offices, the Environmental Protection Agency (EPA), Department of Agriculture (USDA), and other federal and state agencies, monitors marketed animal drugs and food additives to assure their safety and effectiveness. This office has primary responsibility for three of CVM's four core functions: compliance-related actions, post-approval monitoring, and animal feed safety. Composed of several offices, OS&C has numerous target functions that include overseeing medicated animal feeds, monitoring drugs used in food and non-food animals, monitoring antibiotic resistance in animal-derived foods, monitoring compliance of the industry, and pursuing regulatory actions if warranted (FDA, 2011e). The Office's Bioresearch Monitoring Team oversees inspections of both nonclinical (laboratory) and clinical studies to provide assurance of the integrity of data submitted in support of animal drug applications. The Office also coordinates the Center's administrative actions involving approved drugs, such as

actions to withdraw drug approvals. In order to maintain the safety and effectiveness of human antimicrobials, CVM/OS&C has requested drug sponsors to provide information, in the form of Post-Approval Monitoring Programs (PAMPs), during the marketing period for new animal drugs that are of public health concern. We recommend that this activity be expanded.

## Enforcement

**Goal:** To ensure compliance with the new standards for antibiotic use in animal agriculture.

The fourth component of the program design is the enforcement of the new safety standards to ensure that antibiotics are only administered as approved. Enforcement is critical to raising and maintaining standards, as it upholds the law by demonstrating that action will be taken against offenders (World Animal Net, 2011). Currently, the USDA's Investigative and Enforcement Services (IES) department, which operates under the Animal and Plant Health Inspection Service (APHIS), assists the animal agriculture sector in complying with federal regulations (USDA, 2010). The IES department investigates alleged violations of federal laws and regulations and gathers and shares information on violators and violations (USDA, 2010). The IES, along with the CVM's OS&C, will work to ensure that antibiotics are used in compliance with regulations. The OS&C ensures industry compliance by evaluating and coordinating legal cases brought against violators by the FDA. When warranted, the OS&C withdraws drugs and food additives from the market and develops and implements policies that affect marketed products. It is through this last role that regulatory action will be taken under the Act to ensure the continued safety and efficacy of drugs on the market.

The National Animal Health Monitoring System (NAHMS) currently studies the animal health and management practices of the U.S. livestock and poultry industries. NAHMS collects information on how antibiotics are administered (e.g., in water, feed), the number of animals treated, and situations in which antibiotics are used (GAO, 2011). To gather this information, APHIS staff members visit farms multiple times over a period of three to six months and survey management practices (GAO, 2011). However, NAHMS is limited in scope, as surveys typically occur every five to seven years for each species (GAO, 2011). Additionally, NAHMS relies on the voluntary participation of food animal producers and collects only qualitative information on antibiotic usage (GAO, 2011). To improve the quality of this audit process, APHIS and NAHMS will be given the resources necessary to visit farms and collect more detailed quantitative data on antibiotic usage. Additionally, participation in NAHMS will become mandatory, allowing comprehensive enforcement of new regulations and a more effective means to identify individuals who misuse antibiotics. Noncompliance will be discouraged by establishing a system of warnings followed by fines for continued abuses.

## LONG-TERM PERSPECTIVE ON THE PROGRAM DESIGN

### *Enhancing Drug Safety Standards*

Drug applications will essentially be suspended until the new safety standards are established and the approval process is updated and released. Once the new standards are published, the staff in the Office of New Animal Drug Evaluation within the CVM can begin to review applications, and this process will continue indefinitely. The rigor and extent of the new standards and application process will likely affect the number of antibiotics that enter the new application and retroactive review

process. As of 2006, there were 20 antibiotics approved for use as feed additives in the United States (Sharma et al., 2006 as cited in PEW Commission, 2011). As it is well established that nontherapeutic antibiotic use leads to resistance, some companies may find the safety standards impossible to meet for some nontherapeutic antibiotics and not apply for reapproval. The pharmaceutical industry's reaction to the new safety standards will play a large part in determining the number of applications the CVM will need to process in the coming years.

### *Transition Support*

In the years immediately following implementation, the Cooperative Extension Services should continue to provide educational outreach to farmers across the country. Research grants for investigating better husbandry practices as awarded through NIFA will be annual awards, and the latest findings would ideally be incorporated into the Cooperative Extension Services' outreach programs. Because the nature of the transition from nontherapeutic antibiotic use to solely therapeutic use is likely to take a number of years, it is expected that these transition programs will continue for at least five years. After that point, their efficiency and results will be evaluated through performance management indicators and reports.

### *Surveillance and Monitoring*

The initial tasks of this component are staff hires and the establishment of agency responsibilities and protocols for data collection and reporting. Once data collection begins in year two, there will be baseline data on antibiotic resistance that can be used to assess changing levels of resistance within animals and people. In time this data can be used to investigate whether or not the implementation of the program has reduced levels of antibiotic resistance and, as such, this component will

function as a performance management tool to assess the effectiveness of this legislation.

### *Enforcement*

After enforcement staff are hired they will establish enforcement procedures and penalties for misuse of antibiotics. As drug approvals and rejections begin based on the new safety standards, enforcement will ensure that antibiotics are being used appropriately in food-animal production.



## ADDRESSING ANTIBIOTIC RESISTANCE BEYOND THE SCOPE OF THE PRESERVATION OF ANTIBIOTICS FOR MEDICAL TREATMENT ACT OF 2011

While the program detailed in this report is designed to implement a specific act of legislation, it is also designed to address the problem of increasing antibiotic resistance as a whole. In this regard, it must be considered that reducing future applications of antibiotics in animal agriculture may not be sufficient to reduce overall antibiotic resistance and the associated public health threats. The partial ban on antibiotics for growth promotion enacted in Denmark led to improved farming practices and a better quality of life for food-producing animals; however, it did not clearly impact levels of resistant bacteria in either animals or humans. Findings from several government agencies and studies across antimicrobial classes and animal species do not show significant changes in resistance after reductions in antibiotic use in Denmark (Hayes and Jensen, 2003; Danish Veterinary and Food Administration et al., 2009). For example, overall resistance levels of *Escherichia coli* towards seven different classes of antibiotics observed in cattle and pigs have neither increased nor declined significantly since restrictions began in Denmark (DANMAP, 2009). It is important to note, however, that Denmark adopted only a partial ban on antibiotic use. The Preservation of Antibiotics for Medical Treatment Act of 2011 calls for restrictions that go beyond those in Denmark as the Act restricts the use of antibiotics for not only growth promotion, but also disease prevention. However, the legislation does not address the therapeutic use of antibiotics in the treatment of sick animals, and it is possible that because significant levels of resistance have already been established, reducing only nontherapeutic antibiotic use will have little impact on reducing overall resistance within these bacterial populations.

There is also evidence suggesting that a complete ban of antibiotics in animal agriculture may be an important part of the solution. Organic farms as defined by the USDA's National Organic Program are not allowed to use antibiotics on either healthy or sick animals (USDA, 2010). Bacterial resistance to antibiotics has been found to be significantly lower on organic poultry farms than on conventional poultry farms for two different types of bacteria - *Enterococcus faecalis* and *Enterococcus faecium* (Sapkota et al., 2011). These results suggest that it is possible to reduce antibiotic resistance in farm animals by completely halting the use of antibiotics.

Notably, the organic farms used in the study had all recently converted from conventional poultry practices and were producing their first organic flocks (Sapkota et al., 2011). The study did not provide the rates of resistance on the organic farms before their conversions, so it is possible that the converted farms may have already been applying better husbandry practices and using relatively few antibiotics even before their certifications. However, these results do suggest that completely removing antibiotics from animal agriculture could effectively reduce resistance if the Preservation of Antibiotics for Medical Treatment Act of 2011 does not lead to measurable decreases in antibiotic resistance.



# CONCLUSION

# CONCLUSION

Antibiotic resistance is a public health threat with a documented link to the increased use of antibiotics in animal agriculture. While the industrialization of food-animal production has increased the amount of meat available to consumers at low prices, these farming practices have also substantially contributed to the increase of antibiotic resistance. The Preservation of Antibiotics for Medical Treatment Act of 2011 addresses this problem by establishing new safety standards for the approval of drugs intended for animal use. The program designed to implement the Act is founded upon the enhancement of these safety standards while considering the possible consequences of these increased regulations for the animal agricultural sector.

The program outlined in this report is wide-ranging in many regards—in the variety of initiatives from education to data collection, in the geographic scope of all fifty states, and in the scope of the government agencies involved. Antibiotic resistance is a problem with vast social, health, economic, and environmental consequences; therefore, any attempt to mitigate antibiotic resistance must be comprehensive.



## APPENDIX I - FIRST YEAR CALENDAR

	Enhancing Safety Standards	Transition Support		
		NIFA Grant Program	Education and Outreach	Incentive Reports
<b>January</b>		\$100 million dispersed to NIFA	NRC report commission	
<b>February</b>				
<b>March</b>	Assembly of experts established			Short-term researchers hired at USDA and FDA
<b>April</b>	Meeting of experts convened			
<b>May</b>		Grant program established and advertised		
<b>June</b>	Associate Director of New Drug Review at CVM hired; Safety standards drafted			
<b>July</b>				
<b>August</b>	Public comment period 1 completed			
<b>September</b>	Meeting with industry completed			
<b>October</b>	Public and industry feedback reviewed			
<b>November</b>	Public comment period 2 completed	All proposals collected	NRC report delivered	
<b>December</b>	Standards reviewed and published	Grant money awarded	NRC report distributed and grants awarded to Land-Grant Universities	Farmer industry incentives reports completed (USDA); Industry incentives report completed (FDA)

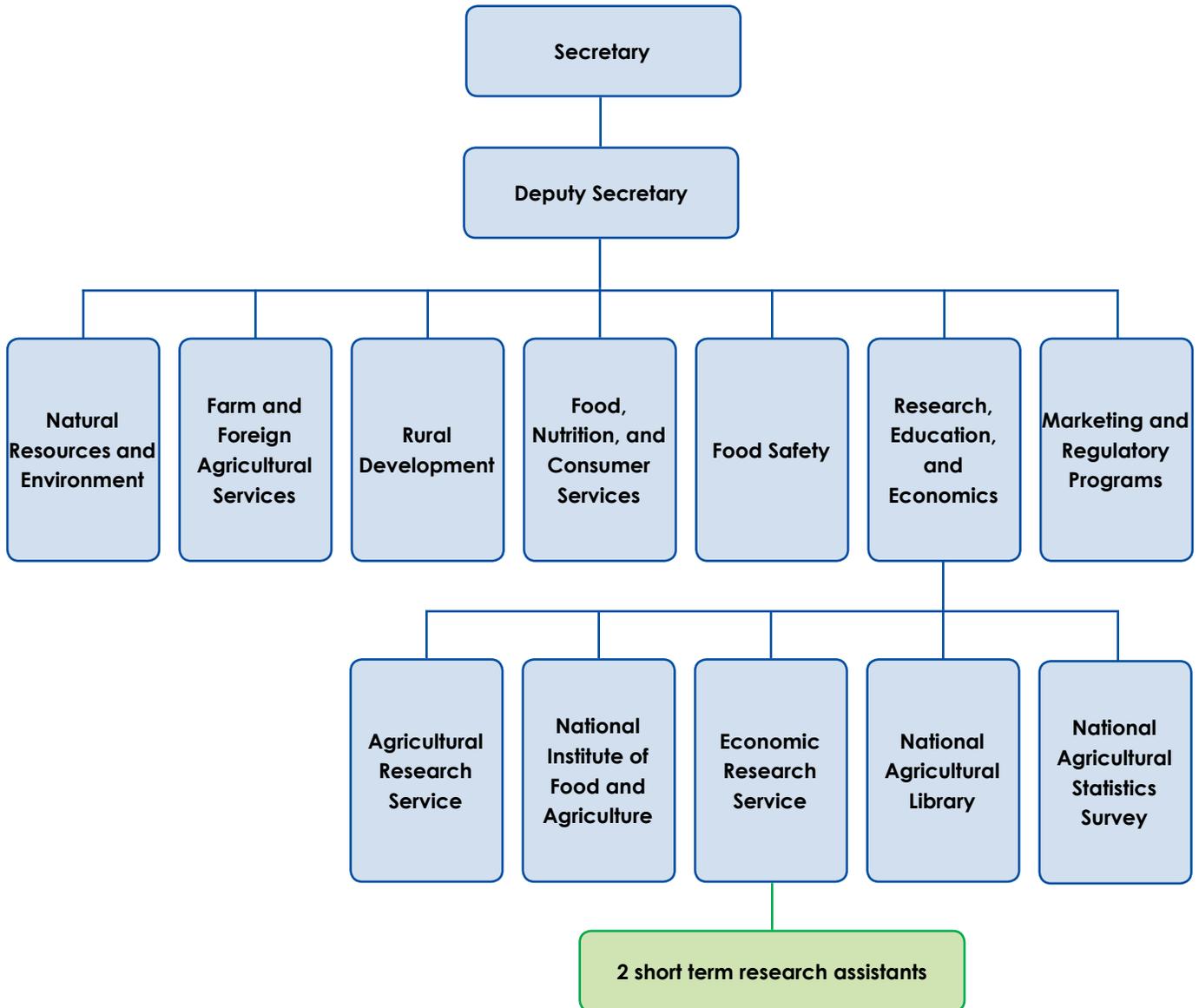
## APPENDIX II - FIRST YEAR PROGRAM BUDGET

	Transition Assistance				
	Administrative	Enhancing Safety Standards	Land Grant Universities	NIFA Grant Program	Incentives Reports
<b>Revenue</b>					
Government	-	-	-	-	-
Earned	-	-	-	-	-
Other	-	-	-	-	-
	\$0	\$0	\$0	\$0	\$0
<b>Expenses</b>					
<b>PS</b>					
Salaries	-	\$181,398	-	-	\$109,724
Benefits	-	\$27,210	-	-	\$16,459
Taxes	-	\$18,140	-	-	\$10,972
	\$0	\$226,748			\$137,155
<b>OTPS</b>					
Office Rental and Utilities	-	\$11,963	-	-	-
Office Equipment and Supplies	-	\$25,119	-	-	\$50,238
Communications	-	\$1,469	-	-	-
Travel and Transportation	-	\$23,890	-	-	-
Town Halls	-	\$2,000	-	-	-
Meetings and Conferences	-	\$7,800	-	-	-
Consulting	\$250,000	-	-	-	-
Printing	-	\$75,000	\$75,000	-	\$150,000
Contracting (A/V, Experts)	-	\$4,000	-	-	-
Annual Conference	-	\$38,110	-	-	-
Grants	-	-	\$2,500,000	\$100,000,000	-
National Resource Council Contract	-	-	\$250,000	-	-
Other	-	-	-	-	-
	\$250,000	\$189,351	\$2,825,000	\$100,000,000	\$200,238
	\$250,000	\$189,351	\$2,825,000	\$100,000,000	\$200,238
Revenue	\$0	\$0	\$0	\$0	\$0
Expenses	\$250,000	\$416,098	\$2,825,000	\$100,000,000	\$337,393
<b>Net</b>	<b>-\$250,000</b>	<b>-\$416,098</b>	<b>-\$2,825,000</b>	<b>-\$100,000,000</b>	<b>-\$337,393</b>

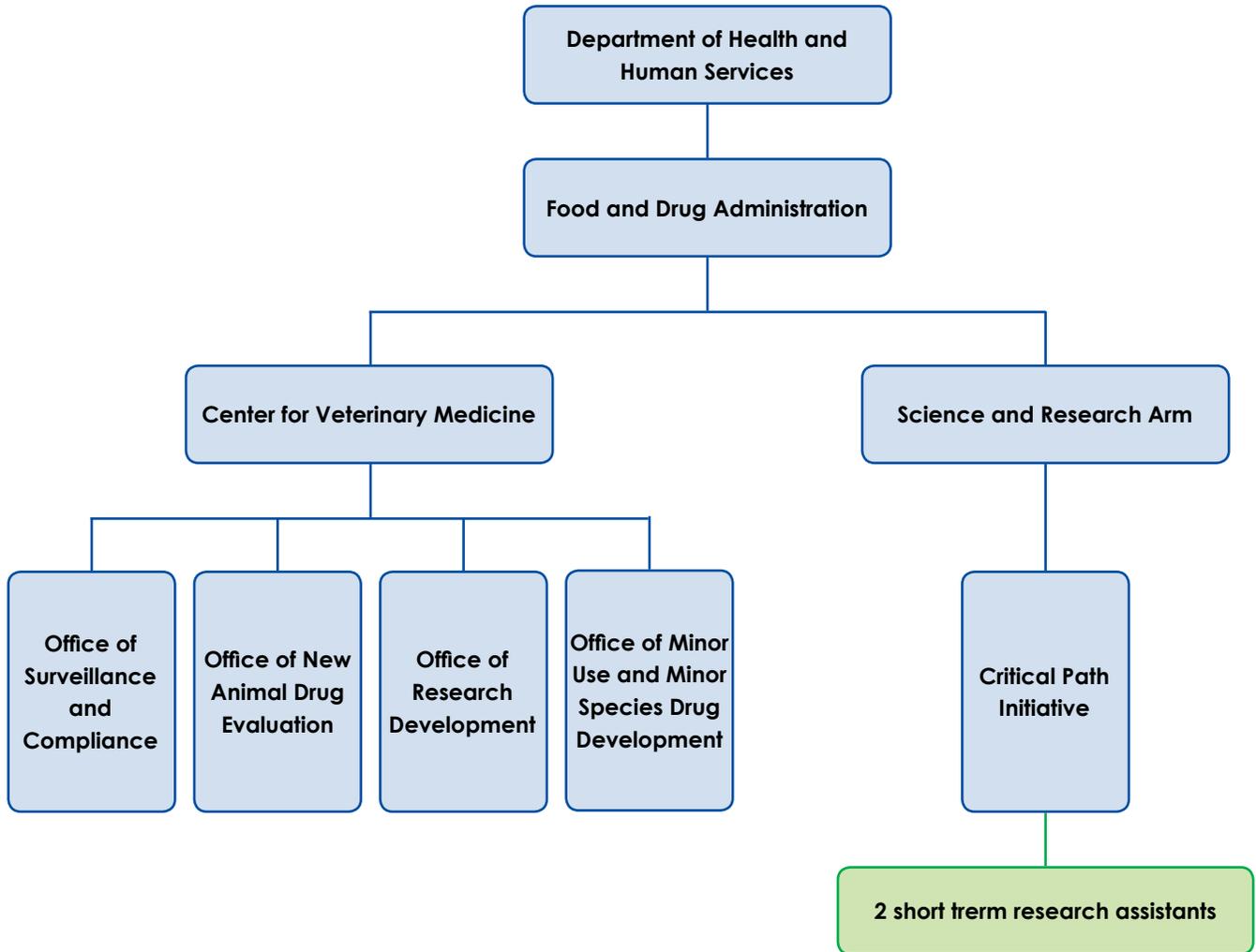
**TOTAL FIRST YEAR EXPENSES = \$103,828,491**

## APPENDIX III - FIRST YEAR STAFFING ADDITIONS

United States Department of Agriculture (USDA)



United States Food and Drug Administration (USFDA)



# IMAGE SOURCES

Cover Page: Cow. 1 December, 2011. <http://www.flickr.com/photos/11741671@N03/4318888102/>

Page 5: Chicken. 1 December, 2011. <http://www.flickr.com/photos/rockyweeds/2413154243>

Page 7: Pills. 1 December, 2011. <http://www.flickr.com/photos/27384147@N02/5042725247/>

Page 12: Trough. 1 December, 2011. <http://www.flickr.com/photos/davemont/3276537890/sizes/l/in/photostream/>

Page 15: Pig. 1 December, 2011. [http://www.flickr.com/photos/denial\\_land/5998216150](http://www.flickr.com/photos/denial_land/5998216150)

Page 24: Pigs. 1 December, 2011. [http://www.flickr.com/photos/\\_belial/346616404](http://www.flickr.com/photos/_belial/346616404)

Page 26: Old Barn. 1 December, 2011. <http://www.flickr.com/photos/andyrobe/1041593297>

Page 29: Chicken on grass. 1 December, 2011. <http://www.oakwoodfarmservices.co.uk/img/bg3.jpg>

Page 31: Cow on hill. 1 December, 2011. <http://www.flickr.com/photos/willj/3538595019>

Page 32: Cow near barn. 1 December, 2011. <http://www.flickr.com/photos/brainware3000/42670662/>

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