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REVIEW PAPER

Antibiotic Resistance Due to Modern Agricultural Practices: An Ethical Perspective

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Abstract The use of subtherapeutic doses of antibiotics in food-producing animals has been linked to antibiotic resistant infections in humans. Although this practice has been banned in Europe, the U.S. regulatory authorities have been slow to act. This paper discusses the regulatory hurdles and ethical dilemmas of banning this practice within the context of the risk analysis model (risk assessment, risk management, and risk communication). Specific issues include unethical use of scientific uncertainty during the risk assessment phase, the rejection of the precautionary principle leading to ineffective risk management, and the criticality of risk communication to build consensus and force action. The underlying root cause is a conflict of values (Type I ethical problem) among key stakeholders, which is examined in depth along with an ethical analysis using public health ethical values.

Keywords Antibiotic resistance · Feeding of antibiotics to farm animals · Growth promotion agents · Risk management · Ethical analysis · Type I and type II errors

Introduction

Beginning with the discovery of penicillin in the 1940's, antibiotics have been a critical tool in our war against communicable diseases such as tuberculosis, dysentery, pneumonia, and sepsis. During the "Golden Age" of antibiotic development, multiple families of therapeutic drugs were developed to combat a host of infectious agents. The effective use of these drugs, along with other public health measures such as improved sanitation, vaccinations, nutrition, and housing, resulted in a precipitous drop in morbidity and mortality rates and increased in life expectancy. This is one of the great public health success stories of the 20th century.

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However, the use of antibiotics as growth promotion agents in animal feed has contributed to the development of antibiotic resistant pathogens. The negative impact on national and global health outcomes is a real and present danger that will only increase with time unless strong action is taken to limit this practice. In the U.S., both government organizations (e.g., FDA and Congress) and advocacy organizations (e.g., Keep Antibiotics Working, Union of Concerned Scientists, The Pew Campaign on Human Health and Industrial Farming) have proposed limiting the use of antibiotics in livestock management in the U.S., but no definitive actions have been taken to date. This is in stark contrast to the European Union (EU) approach where antibiotic usage for growth promotion is prohibited in agriculture (European Medicines Agency 2009) with no significant financial impact to industry (World Health Organization 2003). This is due to a difference in the risk analysis philosophies and systems as well as the divergence in stakeholder ethical systems.

There are three components of risk analysis as defined by the Joint FAO/WHO Expert Consultation (Joint FAO/OIE/WHO Expert Workshop 2003):

- Risk Assessment is "the scientific evaluation of known or potential adverse health effects resulting from human exposure to food borne hazards" (p. 6).
- Risk Management is "the process of weighing policy alternatives to accept, minimize or reduce assessed risks and to select and implement options" (p. 6). Interestingly, risk management begins even before risk assessment with identifying the public health problem, establishing a risk profile, prioritizing the hazard, committing resources and commissioning the risk assessment work (Joint FAO/OIE/WHO Consultation 1997)
- Risk Communication is "an interactive process of exchange of information and opinion on risk among risk assessors, risk managers, and other interested parties" (p. 6).

Risk assessment should use an objective, scientific process that produces data and evidence with a clear conclusion that is presumably evidenced based without political influence. However, an assessment is often done in an uncertain environment, based on broad assumptions and therefore, as Simon states, "utilizes scientific information, but it is not science. The struggle for honest regulators is knowing how well the predictions of a risk assessment, with all their inherent uncertainty, can serve as an appropriate basis for the setting of environmental standards" (Simon 2011. p. 801). The basic risk related questions for this issue are:

- Does the use of antibiotics in subtherapeutic doses for growth promotion in feedlot animals lead to the development of antibiotic resistant pathogens?
- Are these pathogens transferred to humans, resulting in infections which cannot be treated with a standard course of antibiotics?

The first question can be answered with a great degree of scientific certainty but the second one is much more difficult and this allows the agricultural and pharmaceutical industries to challenge the validity of the risk assessment. Another point to explore is the objectivity of the studies and the assessments. Can this risk really be assessed with absolute objectivity and in the absence of a value judgment?

Risk management is a political and administrative phase where the risk managers evaluate the risks and benefits of a proposed course of action, judge the impact to society, and decide on what actions to take. If there is uncertainty in the data presented, then the risk manager's attitude towards risk is critical. For historical and cultural reasons, European regulators apply the precautionary principle whereas the U.S. relies on proving scientific certainty. According to the WHO Regional Office for Europe, the precautionary principle states "that in the case of serious or irreversible threats to the health of humans or the ecosystem, acknowledged scientific uncertainty should not be used as a reason to postpone preventive measures" (Botti et al. 2004).

Effective risk management requires that stakeholders share a core set of values to facilitate consensus and closure of their decisions. The major participants in this process hold conflicting values, resulting in a Type I ethical problem. Type I problems "arise when different individuals have conflicting values or ethical perspectives, especially when they involve contradictory evaluations of relevant social benefits and costs and contrary perspectives on individual rights and duties that are germane to the ethical problem in question" (James 2003). This is a major impediment to effectively addressing this risk (Table 1).

Successful risk communication requires an honest and transparent dialogue among all stakeholders throughout the risk analysis and management processes including both risk managers and risk assessors within the scope of their responsibilities. It is questionable whether this is occurring in this situation. Additionally, it is also questionable whether the public fully understands how critical and serious the consequences of this public health crisis could be. Effective communication of public health issues requires that the risk managers identify the target audiences, which are often diverse in nature, and then tailor the messages accordingly in order to build consensus around the decision. The audiences here include the agricultural community, the veterinary and medical communities, and the general U.S. population. Perhaps the most critical communication is to the general public in order to motivate congressional leaders to take legislative action.

Once society has reached consensus, then all stakeholders have an ethical obligation to comply with the required actions. An FDA guidance document, "The Judicious Use of Medically Important Antimicrbial Drugs in Food-Producing Animals" (U.S. Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine 2010), has been drafted, but there

Table 1 Definition and Example of Ethical Problem Types I and II

Type	Definition	Example
I	There is no consensus as to what is ethical due to conflicting values	Lack of agreement on use of antibiotics as growth promotion agents in U.S. This has delayed the issuance of FDA's guidance on the use of these agents.
II	There is a consensus, but incentives exist for individuals to violate the ethical agreement or norm	Potential for agricultural interests to disregard the guidance based on cost of compliance.

are concerns that the agricultural industry may not comply. This could lead to a Type II ethical problem where "individuals have an incentive to violate established or recognized ethical or legal norms of behavior" (James 2003).

The objectives of this paper are to:

- Review the development and impact of antibiotics and antibiotic resistance and the role that modern livestock production practices plays in fostering antibiotic resistance,
- Discuss the impact of scientific uncertainty and conflict of ethical principles and practices among major stakeholders on the resolution of this issue.
- Analyze the ethical issues from a public health perspective and explore options and recommendations to resolve this impasse.

History of Antibiotics and Antibiotic Resistance

In the last century there has been a dramatic drop in mortality rates caused by infectious diseases. From 1900 to 1937, the annual rate decreased by 2.8% per year primarily driven by improvements in sanitation, nutrition, housing and health care (Armstrong et al. 1999). From 1937 to 1952, the mortality rate decreased by 8.2% per year driven by the decline in pneumonia/influenza and tuberculosis (Armstrong et al. 1999). It was during this period that antibiotics were introduced and used extensively for treating infections. The 1950's through the 1960's was the "Golden Age" of antibiotic development when pharmaceutical companies developed and commercialized as many as 20 classes of these drugs, having 10 major targets of action such as attacking cell walls and membranes, and interfering with the synthesis of critical molecules (Khachatourians 1998). By 1997, the Global Burden of Disease Study estimated that infectious diseases were responsible for only 4.2% of disability-adjusted life years (a measure of the burden of disease and injuries) as opposed to 81.0% accounted for by chronic and neoplastic diseases (Murray and Lopez 1997).

This shift in the morbidity and mortality rates (Murray and Lopez 1997) encouraged pharmaceutical companies to refocus their efforts toward finding cures for chronic, non-infectious diseases such as cancer and coronary disease (Cohen 2000). These chronic diseases require long term treatments and commiserate cash flows to recoup the research investments whereas antibiotics are used for shorter periods of time and do not generate the same magnitude of profits. This has resulted in a 75% decrease in the FDA approval of systemic antibiotics between 1987 and 2007 (Boucher et al. 2009). This makes the effort to slow down the acquisition of resistance even more critical.

Resistance is a natural genetic response where bacteria adapt to survive in a hostile environment. It is beyond the scope of this paper to fully detail the mechanism of genetic adaptation, but there are two critical conditions for resistance to emerge as a problem. First, the bacteria must be in contact with the antibiotic and then the resistance needs to develop along with a way for the bacteria to pass this genetic resistance code to other cells. This genetic transfer occurs either through

normal cell division or through the lateral transfer of extrachromosomal materials known as plasmids. The transfer of plasmids between bacterial species is very efficient mechanism for bacterial survival (Khachatourians 1998).

The emergence of antibiotic resistance is due to the misuse of antibiotics in both human and animal treatments as well as zootechnical use. Antibiotics are used at subtherapeutic levels to promote growth of feedlot animals and to prophylactically and meta-phylactically prevent disease in the extremely crowded conditions that food animals (feedlot cattle, slaughter pigs, broilers, and battery hens/layers) are raised in. Laura Sayre (2009) has compared this confined environment to hospitals ''where everyone is given antibiotics, patients lie in unchanged beds, hygiene is nonexistent, infections and re-infections are rife, waste is thrown out the window, and visitors enter and leave at will''(p. 78). Although there is common agreement that antibiotics promote animal growth by changing the intestinal flora, the exact mechanism of action has not been proven (Neiwold 2007). There is ample evidence that good husbandry techniques such as all in all out, biosecurity, heat treatment of feed and vaccination, could reduce or eliminate the use of antimicrobials (Khachatourians 1998).

It is estimated that at least 70% of antibiotics consumed in the U.S. is for non-therapeutic livestock use compared to 9% for human therapeutic use (Union of Concerned Scientist 2008). By contrast, the estimated non-therapeutic livestock use in the EU is 15% with 52% used to treat humans (European Commission Health and Consumer Protection Directorate General 1999). To treat disease, antibiotics are dispensed directly to the animal at a therapeutic dose. For growth promotion, they are added to feed or water at a lower level where it is difficult to control the dosing. Exposure to low doses over a long time favors the development of antibiotic resistance. In this environment, the antibiotic selects for resistant bacteria and these bacteria may or may not cause disease in the animal, however, these resistant strains are transferred to humans via several routes including contamination of farm workers and food processers and consumer consumption of contaminated meat. Also, animal waste from feedlots is used as fertilizer and can contaminate produce crops and ground water systems (United States Government Accountability Office (GAO) 2004). Once in the human body, these bacteria as well as pathogens exchange their antibiotic resistant genes with human commensal bacteria (Gorbach 2001).

Risk Assessment

Scientific Certainty vs. Uncertainty

FDA issued a Draft Guidance on "The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals (U.S. Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine 2010)" that lists 14 reports from various governmental and non-governmental organizations assessing the scientific evidence on development of antibiotic resistant bacteria in animal production facilities and the transference of these

organisms to humans. These reports summarize the scientific evidence known at the time of publication and provide a chronological timeline of the scientific evidence to answer the risk assessment questions posed above.

In 1969, the Swann report established that the use of antibiotics in growth promotion resulted in a significant increase of "enteric bacteria of animal origin which show resistance to one or more antibiotics" (Swann et al. 1969). However, the link to human infection was not fully established as the report noted, "There is ample and incontrovertible evidence to show that man *may* [emphasis added] commonly ingest enteric bacteria of animal origin" (Swann et al. 1969). In 1980, this direct link continued to be elusive as evidenced by a statement in the National Academy of Sciences Report (1980), "The lack of data linking human illness with subtherapuetic levels of antimicrobials must not be equated with proof that the proposed hazards do not exist. The research necessary to establish and measure a definitive risk has not been conducted and, indeed, may not be possible." The National Research Council (1999) also confirmed the difficulty in tracking and documenting this link but noted that human disease does result from exposure to animal pathogens through the food chain where the potential for transmission to humans is large as compared to other paths such as direct animal contact. It is, therefore, a rational assumption that humans can also be infected by antibiotic resistant pathogens from the food chain. Given the increasing sophistication in accessible databases and microbiological and genetic techniques, it would be a matter of time before the link could be empirically evaluated.

In 2003, a Joint FAO/OIE/WHO report stated that "there is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials" (Joint FAO/OIE/WHO Expert Workshop 2003. In 2004, the United States Government Accountability Office (GAO) issued a report to Congress that concluded, "Antibiotic-resistant bacteria have been transferred from animals to humans, and many of the studies we reviewed found that this transference poses significant risks for human health." However, this same report noted that researchers still disagreed about the significance of the risk to human health and "a small number of studies contend that the health risks of the transference are minimal" (United States Government Accountability Office (GAO 2004).

Scientific Objectivity—A Question of Ethics

Although there is now scientific consensus in the U.S. linking the use of growth promotion antibiotics in livestock to human infections, there is still some dissension among the stakeholders (Marshall and Levy 2011). One factor in the delay reaching this consensus was the lag in scientific capability to collect and analyze the data. But perhaps a larger factor is how ethics and values are used in the scientific approach. In his paper, "Ethics, Science, and Antimicrobial Resistance," Bernard Rollin (2001) claims that science should not be value-free and that ethics must be a part of the scientific process. Scientists are traditionally trained to be totally objective and to make conclusions based on data without applying an ethical or value driven framework. This type of thinking led to transgressions such as Tuskegee and subsequently to the establishment of the Belmont report (Department of Health,

Education, and Welfare 1979) and other protocols to protect research subjects. Rollin (2001) contends that the drive for absolute scientific proof or certainty ignores that the decision is ultimately a "value judgment, and research will only give us more *facts.* The issue is not that we need more facts or more detailed explanations of mechanisms, but rather that what we need *is a rational, social consensus moral position to accommodate the facts we already know!*" (p. 31).

The current dissension in the scientific community about the link of antibiotic resistant pathogens from feedlots to human disease may also be due to an ethical problem in that some of these dissenters are aligned with the agricultural business that has a large financial interest in using antibiotics as growth promoters. This is analogous to the tobacco industry efforts in claiming that the causal link between smoking and cancer was not established even with the preponderance of circumstantial evidence (Rollin 2001). In their extensive review, "Food animals and antimicrobials: Impacts on human health," Marshal and Levy (2011) establish evidence that satisfies many of Hill's (1965) criteria for causality including strength of association and consistency of findings.

These scenarios beg the question of whether the overlay of a value or ethic framework that is arrived at through social consensus should be applied during the risk assessment process or later on in the risk management process. Given that risk managers are responsible for commissioning the risk assessment and setting the key parameters, it is appropriate for them to decide how to apply the precautionary principle and the ethical framework. Public consensus should provide the political will to do so. This leads to the risk management phase of risk analysis where the precautionary principle as well as the conflicting value systems among the major stakeholders is considered.

Risk Management

The Precautionary Principle in Regulatory Actions—Europe vs. United States

In Europe and the U.S., review of the studies mentioned above has resulted in different outcomes. Europe has banned the use of antibiotics for growth promotion since 1999 (European Commission Health and Consumer Protection Directorate General 1999) while the U.S. issued draft voluntary guidance for the use of antibiotics in animals which was still in the comment phase as of 2010 (U.S. Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine 2010). This disparity appears to be driven by differences in the use of scientific data and political influence.

The U.S. assesses risk using specific, quantitative data on safety, efficacy, and environmental impact. Europe takes a more qualitative, holistic approach based on these traditional criteria while also considering the potential impact and cost to society. In fact, European government ministers have the final say in approval, which further accentuates the social impact criteria and the political nature of the decision (Buttel 2003). Additionally, Europe embraces the precautionary principle, which states that in the absence of scientific certainty, if an action or policy has a

risk of causing harm to the public, then the burden of proof that it is *not* harmful falls on those taking the action (Buttel 2003). The U.S. operates under the principle of "substantial equivalence" where if a new substance is found to be substantially equivalent to an existing entity, then safety is presumed to be equivalent. In effect, the two regulatory bodies viewed the scientific uncertainty connecting antibiotic use in animals to antibiotic resistant infections in humans through different lenses. European authorities saw the potential link (antibiotic resistant animal isolates) to a real world risk (increase in antibiotic resistant infections) and applied the precautionary principle to ban the practice. The U.S. called for more studies to scientifically prove the link and then issued a voluntary guidance document.

Draft Guidance #209 states "FDA has reviewed the recommendations provided by the various published reports and, based on this review, believes the overall weight of evidence available to data supports the conclusion that using medically important drugs for production purposes is not in the interest of protecting and promoting the public health" (p. 13). The following principles are advised to combat the development of antibiotic resistant organisms (U.S. Department of Health and Human Services, Food and Drug Administration Center for Veterinary Medicine 2010, pp. 16–17):

- "The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health."
  - Antibiotics should not be used for production purposes such as growth promotion.
  - Antibiotics should be used for treatment and prevention of specific diseases and these agents can be administered via feed and water.
- "The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation."
  - FDA to phase in measures to limit use of medically important antibiotics.
  - Promote more veterinary oversight in the use of these drugs.

Both industry and public health advocates have voiced strong and opposing concerns. Industry is focused on the economic impact of a decision that they claim is based on scientific uncertainty and public health organizations are concerned that these voluntary steps are not sufficient in scope and will not be followed. Examples of these positions can be found in the comments on the Draft Guidelines Comments. An excerpt from the National Grain and Feed Association (2010) illustrates the agricultural industry position:

> Although FDA states in its draft guidance that it "believes the overall weight of evidence available to date supports the conclusion that using medically important antimicrobial drugs for production purposes is not in the interest of protecting and promoting the public health," it is clear that there are other scientific experts and bodies involved in the fields of veterinary medicine and

> epidemiology that hold strong and dissenting opinions. Again, we urge FDA to actively engage all stakeholders—including the full scientific community—so that its future decisions related to this matter are based on validated, scientific evidence.

Stuart Levy's (president of the Alliance for the Prudent Use of Antibiotics) (Levy 2010) comments represent the public health concern:

> That FDA has taken an initiative regarding antibiotic use in food-producing animals is indicative of its foresight in carrying out its mission to safeguard both animal and public health. However, even if finalized-the guidance is purely voluntary, and I fear, will exact no compliance from the agricultural industry to eliminate inappropriate use of antibiotics. Without mandating the termination of injudicious use and establishing a system to monitor compliance, I believe that the new FDA guidance will be to no avail: agribusiness will continue its practice of feeding animals antibiotics non-therapeutically.

As of today, we are in the midst of "regulatory paralysis" (Cranor 2003) where adverse health data supports regulatory action but pharmaceutical and agricultural concerns continue to raise questions about the validity of the data and to lobby and litigate to block any ban on non-therapeutic use of antibiotics in food-producing animals. These different viewpoints follow from a conflict in values.

Shared Values Matter

To fully understand this conflict in values requires an exploration of stakeholder ethic systems:

- Public Health Ethics—FDA/regulatory bodies/public health advocacy groups
- Business Ethics—Agricultural/pharmaceutical businesses
- Agricultural Ethics—Agriculturists

Public Health Ethics

Public Health ethical frameworks are well developed as compared to other professions including business and agriculture. Bioethics provided a strong base from which public health evolved with the biggest difference stemming from the emphasis on autonomy in bioethics and justice in public health (Baum et al. 2007). This reflects the focus of bioethics on individual health and safety while public health is concerned with community or global health objectives. In addition to justice and autonomy, public health ethics value beneficence and non-maleficence. The American Public Health Association (APHA) issued "The Public Health Code of Ethics" (Public Health Leadership Society 2002), which expands these basic values into 12 actionable principles. Two principles that are germane to this issue are:

- Public health should address principally the fundamental causes of disease and requirements for health, aiming to prevent adverse health conditions.
- Public health should seek the information needed to implement effective policies and programs that protect and promote health.

Ethical evaluation is generally done within the context of two major theories, the utilitarian theory, which focuses on the consequences of the activity and looks to maximize the benefits across society and the deontological theory, that focuses on the validity of the process or means of accomplishing the goal. Additionally, there are several frameworks that also include cost/benefit analysis, political feasibility, accountability, and other practicalities to facilitate analysis and program implementation (Baum et al. 2007; Kass 2001).

Business Ethics

Business codes of conduct are currently a much debated topic due to recent unethical business practices resulting in financial, environmental and public health failures. Although there is no universally accepted system, there are numerous code and guideline proposals developed by business and non-business organizations. Lynne Paine et al. (2005) analyzed a select group of these codes to establish the "Global Business Standards Codex" for use as a world class benchmark code of conduct. The authors reviewed 23 sources including multiparty codes, individual company codes, and legal and regulatory documents, including the Sarbanes–Oxley Act. Not surprisingly, codes written by the business sector emphasize responsibility to investors, economic health, and the employee responsibility to the corporation. The non-business authored codes emphasize employee rights, human rights, and environmental protection.

Overall, these codes indentified six separate corporate stakeholders including the public and eight overarching principles: Fiduciary, Property, Reliability, Transparency, Dignity, Fairness, Citizenship, and Responsiveness. The principles and standards relating to this analysis are (Paine et al. 2005)

Transparency (p. 127)

- "Be honest and respect truth in all activities."
- "Communicate and consult with communities affected by environmental, health, and safety impacts of the enterprise."

Dignity (p. 128)

- "Protect human health and safety."

Citizenship (p. 130)

- "Do not use lack of scientific certainty as a reason to postpone cost-effective measures to address threats of serious damage to the environment." [*note: it would be appropriate to apply this standard to public health cases also*]
- "Recognize government's obligation and jurisdiction concerning society at large; avoid improper involvement in political activities and campaigns."

If these ethical principles and standards were applied as written, then the public health and business positions would be closer together. However, this is not the case. For example, the National Pork Producers Council made the following statement upon the release of the FDA Guidelines, "Guidance on the use of antibiotics in livestock and poultry production issued today by the U.S. Food and Drug Administration could lead to the elimination or costly review of previously approved animal health products. The National Pork Producers Council said there appears to be no science on which FDA based the guidance." (National Pork Producers Council 2010). The statement ignores all the studies cited in the FDA document and uses scientific uncertainty as a reason to reject the FDA guidance.

The basic conflict involves social justice where public health believes that benefits and burdens should be shared by all. Business focuses on maximizing shareholder profit (benefits) while minimizing costs (burdens) often by shifting costs to others. This is not to say that corporations do not respect the basic tenets of human dignity and justice but their decisions and actions are a balance between profits and adhering to social norms. Although balance is acceptable, sometimes these scales will tip in a way that overly benefits the business at the expense of the general public.

Agricultural Ethics

Agriculturists consider themselves to be innately ethical and moral because they feed the world with safe, nutritious food at a low cost (Dundon 2003). They are also businessmen who embrace economics with its emphasis on market and production efficiencies. Traditional agricultural ethics is an informal utilitarian system where the end (sufficient food) justifies the means (e.g., use of antibiotics). However, as Dundon (2003) states, "Immunity from ethical scrutiny is not granted to agriculture because of the unquestioned necessity and nobility of its end products, because profound human values may be impacted by the choice of means of production" (p. 427). This is a classic conflict between the deontological and utilitarian theories that leads to Type I ethical problems (James 2003).

Agricultural ethics reflect the conflict between public health and business values. This tension has significantly increased over the past several decades with the advent of factory farming, which stresses profitability and the concurrent evolution of the environmental movement with its focus on social justice and sustainability, which is essentially justice across generations. In this case, negative externality occurs where society pays the cost of the resultant infections.

Agricultural ethicists are developing a variety of models, values, and frameworks many of which are based on public health models, a logical extension as food safety is a public health objective. Some examples of these are:

- Inclusion of a deontological framework to foster normative evaluation of processes as well as end products (Dundon 2003).
- Greater emphasis of justice as a value where burdens and benefits are equally shared across society and across generations (sustainability) (Dundon 2003).

- Expansion of the harm principle to "protect the rights of individual producers and consumers by preventing people from acting in ways that harm others" (Anomaly 2009).
- Incorporation of normative values and the precautionary principle in the risk management phase especially where scientific uncertainty exists for major technological advance (Sperling 2010).

This conflict in values within agricultural ethics has given rise to a situation where agricultural production has a high societal cost in terms of health care costs and mortality rates. These costs are "external" to the farmers so they are not accounted for in the agricultural cost structures (Buttel 2003). The burden is borne by the public health care systems, which mean the taxpayers pay the cost, a violation of the justice principle.

Risk Communication

Vose et al. (2001) states that one of the goals of risk communication is "to promote consistency and transparency in arriving at and implementing risk management decisions" (p. 818). The FDA review and comment process fosters open communication where FDA acts as an "impartial and independent arbitrator by welcoming a variety of guest and public speakers to present their criticisms" (Dean and Scott 2005, p. 483). The issue lies in the transparency of some of the participants especially outside of the formal process. Dean and Scott (2005) found that opponents of limiting the use of antibiotics challenged the risk assessment methodology and data within these formal meetings but went even further outside the meetings, challenging FDA's motivations. In conversations with pharmaceutical executives, the authors were told, "that public interest groups, the FDA, and the CDC are more motivated by a desire to eliminate industrial animal agriculture than by legitimately (read scientifically) based concerns about resistance arising in animal agriculture" (p. 485). This implies an attempt by industry to attack the morality of the FDA and sway the public consensus.

Public awareness of this issue is growing especially after a CBS Evening News broadcast in February of 2010 and ongoing Congressional hearings led by Congresswoman Louise Slaughter (D-N.Y.) who has authored the Preservation of Antibiotics for Medical Treatment Act (PAMTA) which would ban the use of subtherapeutic use of antibiotics in food-producing animals (Couric 2010). However, this type of risk is difficult to communicate effectively as it is probabilistic (not entirely certain that if one farmer uses growth promoters, it will lead to sickness and death) and the potential harm is diffuse (consequences can occur across geographies and time) (Anomaly 2009). It is not a direct and politically sensationally perceived harm such as bioterrorism, which has generated a tremendous amount of public attention.

Various governmental and public health organizations are communicating the risk associated with this practice but is not clear if the public perceives this issue as harmful in the broader sense due to the latent nature of the harmful effect. Risk

communication is essential to motivating the public sector into pressing the government into action to ban the use of antibiotics as growth promoters.

Ethical Analysis

The development of antibiotic resistant pathogens in food-producing animals is a critical public health issue; therefore an ethical analysis should be done using public health values and frameworks. The impact of this issue can be categorized in terms of the four core principles: autonomy, beneficence, non-malificence, and justice.

From the agriculturist's point of view, autonomy is a major factor as farmers value individualism and independence. Removing an established production technique could be seen as an issue of autonomy. However, when an action causes harm to others and this harm is a predictable consequence of the action and is done without consent from the victim, then autonomy can be revoked per the harm principle. Prevention of harm trumps autonomy and there is a global consensus that this practice is harmful.

Another aspect of autonomy is that farmers are economically constrained to use antibiotic growth promoters via the "Prisoner's dilemma" (Anomaly 2009). Although a producer might want to stop using these agents, he would give up a competitive advantage and lose money. Additionally, most farmers are under contracts to large corporations that require the use of these agents.

Beneficence requires us to do good and non-malicifence refers to "do no harm." Although these are distinct actions, they are related and can form the basis of cost/benefit analysis. The cost/benefit analysis for the use of antibiotics in agriculture is complex due to the uncertainty and variation in data, including food production and health care costs, as well as the indirect, diffuse nature of the impact (Anomaly 2009). These resistant pathogens develop in many settings (including hospitals), proliferate at a high rate, and disperse rapidly across geographies and from generation to generation. Therefore, it is difficult to assess the true cost to society of this specific practice, however, here are some general considerations:

- Infections that do not respond to antibiotics are extremely difficult to treat, resulting in increased hospital stays and mortality rates which drive up health care costs. In 2005, it was estimated that MRSA alone caused 18,600 deaths in the U.S., surpassing the mortality rate for HIV/AIDs (Klevens et al. 2007) Infected individuals experience higher levels of pain and distress. There are estimated costs for treating antibiotic resistant infections in general, but not specifically for animal derived organisms. These estimates range from $17 B to $26B per year (Gallagher 2009; Roberts et al. 2009). Also, how do you cost out the pain and death caused by these infections?
- Eliminating antibiotic growth promoters will initially result in increased production costs leading to higher prices for meat. However, the National Research Council (1999) estimated that the total cost to the livestock industry would be $1.2 to $2.5 billion per year which translates to a per capita annual consumer cost increase of $4.82 to $9.92, not a significant amount from an

individual consumer point of view. This may even be less given the potential savings on export subsidies.

- There is some conjecture that antibiotics may reduce the prevalence of food-borne pathogens in animal carcasses which is a major food safety issue (Callaway et al. 2003). However, even if antibiotics do reduce these pathogens, potential contamination can be managed through good husbandry techniques and infections from non-resistant pathogens are easier and less costly to treat.
- There is a potential trade issue as the EU now bans subtherapeutic antibiotics and may ban the import of meat products using growth promoters. (United States Government Accountability Office (GAO) 2004)
- Pharmaceutical profits would be negatively impacted and this could further reduce their spending on developing new antibiotics.

Again, the monetary costs are difficult to ascertain but the present and future cost in terms of human morbidity and mortality is significant. This practice provides the greatest benefits to the pharmaceutical and agricultural industries with the burden passing to the public in terms of reduced health outcomes and increased health care costs.

This disparity in benefits and burdens is not the only issue concerning social justice. Antibiotic resistant organisms are particularly dangerous to certain vulnerable populations such as immuno-compromised individuals and the elderly as it is more difficult to treat antibiotic resistant infections, leading to a higher mortality rate (Klevens et al. 2007). Additionally, the cost of fighting these infections are particularly onerous for lower socio-economic groups who are less likely to have health insurance and will often delay treatment which increases the mortality rate. Another vulnerable population is the farm and food processing workers because they are regularly exposed to these pathogens, which then enter the body through cuts and abrasions. The justice principle also requires us to look at the impact across generations (sustainability). Antibiotic resistance may not be completely reversible and therefore the problem will persist over time. This burden will actually increase in scope if we do not develop new antibiotics or infection control strategies.

Per the utilitarian theory (the greatest good for the greatest number of people), the practice of feeding subtherapeutic doses of antibiotics to animals should be banned. It appears that the harm to public health for this and future generations far outweigh the benefits to the current members of the agricultural and pharmaceutical industries. Application of the deontological theory (the validity of the process or means of accomplishing the goal) brings us to the same conclusion. The discontinuation of subtherapeutic antibiotic use will require farmers to adopt different procedures and may result in higher food costs, but it appears that the impact will be minimal compared to potential infection rates of superbugs.

Conclusions and Recommendations

Antibiotic resistance is one of the most serious public health crises that we face today. Discontinuing the use of subtherapeutic antibiotics in livestock is a critical

"must do" given the current body of evidence. The roadblocks discussed above include:

- The inherent difficulty in dealing with scientific uncertainty in assessing the risk and the propensity of industry to take advantage of this uncertainty.
- The lack of adherence to the precautionary principle by the risk managers in protecting the public health.
- The inability of the risk communicators to break through the political noise and energize the public into consensus and action.

The root cause lies in the conflict of values among key stakeholders and the inability to raise a broad, value- oriented public response. Strong public consensus and advocacy is required to force government to regulate and industry to comply. James (2003) states that Type I ethical problems are "resolved when parties reach some form of agreement or consensus as to what the solution or ethical norm ought to be or when the general public is convinced of the soundness and validity of one side over the other" (p. 443). Given the recent comments from industry on the voluntary guidelines, it is doubtful that agreement will be forthcoming without the weight of public opinion. Winning this public relations campaign requires defining and targeting the audience. An assessment is needed on the current level of understanding and awareness, the values held regarding this issue, and who should lead the communication (who is the most trusted voice). Although facts and details are important and must be provided in a transparent manner, care must be taken that they are not used to confuse the issue. This is a persuasive ethical argument. To paraphrase Caplan (2009), Antibiotic resistance "is not in the details," antibiotic resistance "is in the ethics" (p. 2862).

Assuming that the public consensus battle is won, the war is not over. The focus now shifts from a Type I problem to a Type II problem where conformance to the social consensus or law becomes the issue. "In order to resolve Type II ethical problems, effort must be placed on changing the incentives people face to violate the ethical or legal norms, perhaps by creating rewards to compliance with the ethical principle or by creating sanctions that will result if the ethical norm is violated" (James 2003, p.12). For example:

- Boycotting antibiotic fed meat at the retail and consumer levels. The Environmental Defense Fund (2009) worked with McDonald's to implement purchasing policies with clear guideline on appropriate antibiotic use. They estimate an annual reduction of over 220,000 pounds of antibiotics from this initiative.
- Designing farming subsidies to reward good husbandry practices that reduce antibiotic usage instead of rewarding concentrated animal feeding operations.
- Passing the Preservation of Antibiotics for Medical Treatment Act as this will have the force of law and alleviate the concern with the voluntary guidance approach.

For the health and welfare of our present society and future generations, failure is not an option.

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