

Cost of Antibiotics in Society and Economic Approach

Jayshree D. Patel and Reza Fadaei

(School of Business Management, National University, USA)

Abstract: Antibiotics make a significant worldwide contribution by saving thousands of lives annually. After the discovery of antibiotics, rapid emergences of antibiotic-resistant bacteria are threatening this extraordinary achievement. Antibiotic-resistant infections place a substantial economic burden on the global health care system. The crisis is highly accepted by policy makers and scientists, as well as civil society organizations including: the World Health Organization (WHO), the Food and Drug Administration (FDA), the Center for Disease Control (CDC), and the Dutch Presidency of the European Union (EU). It reflects the worldwide overuse of antibiotics and the lack of newly developed drugs by pharmaceutical companies to address the challenges. Coordinated effort to implement new policies, renew research efforts, and pursue steps to manage this crisis is highly needed. This paper reviews facts associated with antibiotics, necessities for developing new antibiotics in public health, the economic burden of new diseases on society, and possible solutions through a proposed antibiotic development model. Efforts are made to prove that antibiotics are financial assets in society. Suggestions are made on a proposed antibiotic development model with respect to economic importance.

Keywords: society, antibiotics, antibiotic-resistance, economics, infection, statistic

I. Introduction

Antibiotics are medicines that treat diseases caused by bacteria. They are useful for humans, animals, and agricultural crops. The discovery of Penicillin by Alexander Fleming in 1942 was the breakthrough, which opened the door to combating many diseases caused by bacterial infections; it has also saved thousands of lives. Unfortunately, soon after this discovery, the effectiveness of antibiotics was reduced due to drug-resistant superbugs. Poultry, cattle, and swine raised with antibiotic treatment possess antibiotic-resistant bacteria, which is transmitted to humans through consumption of meat, eggs, and milk. Antibiotics used in agriculture and aquaculture add a global burden to antibiotic-resistance in both animals and humans. A national survey of infectious disease specialists found that 60% of approved systemic antibiotics have become useless against resistant bacterial infections. Spellberg, Bartlett, Wunderink, and Gilbert [1] reviewed that bacterial resistance towards existing antibiotics made various treatments ineffective, which often results in hospitalization due to sepsis and multi-organ system failure. The lack of new antibiotic drugs and insufficient investment in conservation are primary questions for economic incentives. Currently, antibiotics developed by pharmaceutical companies is not a profit driven business. The review provides statistical analyses and adjustment of the net present value of the company, which helps management make decisions investing in antibiotics. This paper explains facts about antibiotics, the necessity of antibiotics for society to combat the emergence of antibiotic-resistant bacteria, the economic burden due to public health, and a possible resolution using a proposed economic model.

II. Economic Burden on Society

Surveys show that antibiotics are saving 77,000 lives per year. Yet many diseases emerged in the last decade which are incurable. Antibiotic-resistant bacteria are responsible for over 700,000 deaths annually around the world, which is predicted to exponentially rise to above 10 million deaths per year by 2050 [2]. The global economic burden of such rise in mortality and morbidity is estimated to be \$100 trillion. In the U.S., antibiotic-resistance causes 99,000 deaths per year that cost \$21-34 billion per year. The 25,000 deaths in E.U. costs approximately €1.5 billion annually and 600 million days of lost productivity [3]. The Middle East and North Africa reported 38% patient's deaths are from antibiotic-resistance. The death rate of antibiotic-resistant bacteria infected children is double than other diseases. In Asia, antibiotic-resistant bacteria went from being resistant to 7 drugs to being resistant to 21 drugs within four years. Antibiotic consumption in humans increased globally during the last decade, which has greatly affected human health in every country. Based on the data collected from 71 countries, total global antibiotic consumption grew by 30 percent in the last decade [4]. Antibiotic consumption per person in the United States (U.S.) is very high compared to other countries. Growing economic prosperity, rising incomes, and expanding insurance coverage assisted in the increase and consumption of antibiotics. However, antibiotic usage in humans is less than the amount used for animal consumption. At least 63,200 tons of antibiotics were consumed by livestock annually as of 2010. This figure is

projected to rise by two-thirds, to 105,600 tons, by 2030 [4]. U.S. Food and Drug Administration (FDA) also supported that the average antibiotics consumption for animals are 14.6 million kg, which is four times more than human consumption (3.29 million kg) per year. This consumption is forecasted to increase by 67% by 2030 [5]. The statistic shows that antibiotic requirements and consumption will increase in the future.

Antibacterial-resistant infections are an economic and substantial health burden to the global healthcare system. The WHO produced a report on the worldwide economic burden of healthcare associated infections in high, middle, and low-income countries. The findings highlighted that prevalence of surgical site infections in developing country is one-third (nine times) higher than in developed countries, whereas in high-income countries 30% of patients are affected by healthcare-associated infections [6]. In the U.S., a single infection that requires antibiotic treatment costs around \$11,285 per case, which equals to the astonishing \$1.51 billion increase in annual cost to the American healthcare system [4]. The U.S. pays an indefinite amount of money behind the treatment of infections caused by antibiotic-resistant threats. Simultaneously, future rates of antibiotic-resistant superbugs are not predictable. Therefore, planning for new antibiotic development is necessary in order to find an economic solution for society as well as government.

Only five new antibiotics have been marketed since the year 2000, none of which are successful in targeting highly resistant bacteria. The total number of submitted antibiotic patents has declined by 34.8% between 2007 and 2012 [2]. Currently, only 57 antibiotics are in clinical development phase globally. Historical evidence shows that 1 in 5 antibiotics will receive approval from Food and Drug Administration. Therefore, a development timeline for these drugs is unknown. The public funding of antibiotic research and development (R&D) demonstrates that global venture capital has declined from over \$2 billion to less than \$1.5 billion (-33%). R&D investment for main subcategories within infectious disease have experienced 74% drop from \$785 million down to just \$202 million [7]. The raised funding for cancer (24%), neurology (12%), and cardiovascular (6%) may be the reason for the decline in response to antibiotic development. Investment in alternative medicines such as anti-cancer, anti-depressants, or cardiovascular health generates high return on capital to the drug development companies.

III. Economic Model of Antibiotic Development Process

Drug discovery and development is an essentially systematic program for pharmaceutical companies. Each company follows five main stages in their drug development model. Figure 1 represents the diagrammatic logical plan of pharmaceutical companies. This five-stage business model introduces activities from starting discovery stage to ending manufacturing. Some reformation in drug approval policy is desirable in the current situation because the traditional model of the drug development process and current drug approval strategy brings pharmaceutical companies an unsuccessful business model. This section explains successful possibilities to fight against bacterial threats within society. Every new generation of antibiotic is more expensive than its predecessors. Pharmaceutical companies spend \$5 billion in research and testing for each new drug they bring in the market. Unfortunately, 80 percent of drugs emerged from labs fail in safety or efficacy trials. The new antibiotic Sivextro by Cubist pharmaceutical, launched in June 2014 has spent more than 5 years and \$400 million in the discovery and development stage antibiotics [8]. Many pharmaceutical companies are not taking risks in spending massive amounts of money and time because antibiotic discovery and development is not a profit driven business. Furthermore, the slow progress of new antibiotics is the outcome of reduced and ambiguous commercial markets. The licensing process for antibiotics has become slow and inconsistent and causes a large increase in both time and cost [9]. The FDA approved only 2 systemic antibiotics in the last five years, which is 88 % lower than the mid-1980's [10]. Tough registration and approval processes declined company's interest in new antibiotic development programs.

IV. Target Plans and Future Prospects

Antibiotic resistant bacteria are a complex, multi-factorial problem that requires a global solution to support or replace current antibiotics. The main reasons for the antibiotic resistance crises are overuse and misuse of these medications, as well as a lack of drug development by pharmaceutical industries due to challenging regulatory requirements and economic incentives. Furthermore, pharmaceutical companies are facing many challenges in every stage of the drug development process. As a result of the slow approval process, companies cannot introduce the final product in the market. The estimated cost incurred by the pharmaceutical company to discover and develop a new drug is \$2.6 billion, and the total time required to complete this process is 12-15 years [11]. The pipeline of the development of new antibiotics has failed the global fight against antibiotic resistance. U.S. and British officials announced a collaborative program to accelerate discovery and development of new antibiotics in the fight against antibiotic resistance. The U.S has invested \$260 million in public funding for R&D of new antibiotics in 2015 which is expected to grow up to \$413 million in 2016 [2]. Table 1 shows that one antibiotic development process takes 12 to 15 years and costs at least \$1 billion, including marketing costs. From the government's perspective, the proposed price is very

high, because it does not include those antibiotics which fail in any phase, but it could provide a 100 percent return. If researchers generate just one new antibiotic class per year, the \$1-billion-per-year payment would be a reasonable investment because the U.S. pays \$35 billion annually for bacterial infections. Statistically, antibiotic development is profit driven business. Focusing on the statistical and cost-utility analysis with the evidence of dominated antibiotics, pharmacists will achieve the solution to solve current scenarios of antibiotic-resistant bacterial infection by developing new antibiotics. The global problems to spark antibiotic development in the market will resolve by applying R&D strategies, which include increasing access to scientific resources, providing research grants, offering tax incentives, and establishing partnerships for dividing R&D costs. Some pull mechanisms such as rewarding pharmaceutical companies by increasing or ensuring future revenue, monetary prizes, and patent buyouts will help encourage R&D.

Pharmaceutical companies need to be encouraged with an accelerated drug assessment pathway, market exclusivity extensions, anti-trust reforms, and value-based reimbursement. Unlocking the value of pipeline to support the overall approval process will increase pharma economic value to meet future demand. Exclusive marketing rights granted by the FDA upon approval of a drug will promote balance between generic drug competitions. The FDA has legal authority to speed the availability of drugs to treat serious disease. Accelerated drug assessment pathways such as Fast Track (FT), Accelerated Approval (AA), and Priority Review (PR) offered in the U.S. will help drug development companies to gain similar advantages to focus on unmet medical needs.

V. Figures and Tables

Table 1. Typical antibiotic development phases and process model

Development Stage	Time required	Typical cost of development	Possibility of Success
Preclinical	5 years 6 months	\$ 10,688,946	9.3%
Phase one	11 months	\$ 10,072,048	33.0%
Phase two	1 year 1 and a half months	\$ 26,312,760	75.0%
Phase three	1 year 10 months	\$ 96,295,600	85.7%
Approval	9 months	\$ 3,676,466	75.0%
Post-Approval trials	3 years	\$ 146,295,599	

Figure 1, Drug discovery and development logical plan

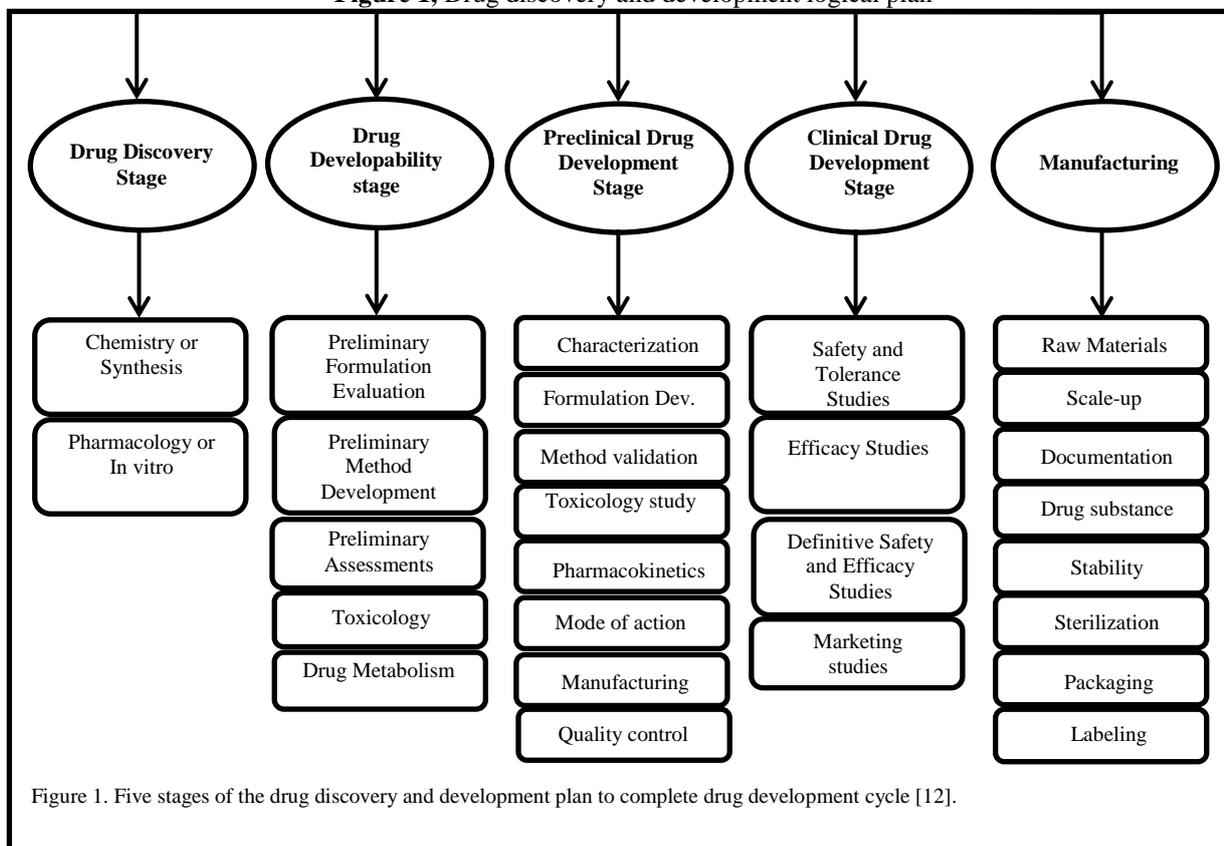


Figure 1. Five stages of the drug discovery and development plan to complete drug development cycle [12].

VI. Conclusion

Antibiotics are essential in maintaining worldwide public health. The public health concern is an economic issue around the world because of direct and indirect effects on the economy. The direct effects are due to treatment costs and indirect effects due to lost productivities. The issue is important because it includes the health economic value of an antibiotic, or the value that is deteriorated as a result of antibiotic resistance. Strategic planning to discover and develop new antibiotics in continuous basis will protect the world economy. In the future, society will pay a high price, if the current scenario of antibiotic-resistant superbugs is not controlled by improved antibiotic development programs.

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