



**Deteriorating human and environmental health is forcing us to change how we understand the life cycle of pharmaceuticals and personal care products.**

## Ecological Economics and the Drug Life Cycle: The True Cost of Medicine

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*Ecological economics recognizes that humans and their economies are parts of larger natural ecosystems and coevolve with those natural systems. . . Some concept of value is required for rational activities of human economies within their natural systems.*<sup>1</sup>

After 15 years, 10,000 compounds, and \$8 million, a new drug is born.<sup>2</sup> The life cycle of a drug is typically thought to encompass its journey from conception, design, and manufacture, to its introduction into the marketplace. Now, however, overwhelming evidence of deteriorating human and environmental health is forcing us to change how we understand the life cycle of pharmaceuticals and personal care products (PPCPs).

Forward-thinking individuals in the pharmaceutical industry—and those who use their products—realize that we must embrace “product stewardship,” which means becoming accountable for the *entire* life cycle of a medicine, from conception through drug recycling and disposal. A product-centered approach to environmental protection requires industry participants—manufacturers, retailers, users, and disposers—to share responsibility for reducing the environmental impacts of products.<sup>3</sup> In a stewardship model, pharmaceutical manufacturers, doctors, nurses, and consumers are all educated about ecological and social impacts of the life cycle of a drug.

True cost of pharmaceutical drug development is complex to evaluate. The path from understanding an illness to providing a treatment is lengthy, difficult, and expensive. Drug clinical trials involve complex processes of rigorous testing to determine efficacy and toxicity. To ensure the safety and well-being of future patients, such testing proceeds with the precaution and diligence necessary for offering effective medical care. However, this diligence comes at a high price, negatively affecting land, natural resources, and local communities on ecological, social, and spiritual levels. From initial idea conception to drug delivery, the medical industry can benefit by utilizing principles of ecological economics.



**Ecological Economics values a product or service according to its ability to enhance human wellbeing while supporting sustainable societies and ecosystems.**

The primary principles of ecological economics are social, human, built, and natural capital. This emerging economic perspective values a product or service according to its ability to enhance human well-being while supporting sustainable societies and ecosystems.<sup>4</sup>

**Social Capital** refers to the web of interpersonal connections, institutional arrangements, rules, and norms that facilitate individual human interactions.

**Human Capital** includes both the physical labor of humans and the know-how stored in their brains.

**Built Capital** encompasses machines and other infrastructure such as buildings, roads, and factories that compose the human economy.

**Natural Capital** refers to land and the many natural resources it contains, including ecological systems, mineral deposits, and other features of the natural world.

As we begin to apply the principles of ecological economics seriously, we are forced to question whether or not modern medicine as it is currently practiced can truly provide sustainable means for healing our communities.

## How Ecological Economics Changes our Understanding of the Drug Life Cycle

### Pre-discovery

In the first or pre-discovery phase of the drug life cycle, scientists fully understand the disease of interest and begin pharmaceutical design. The first step in the research is target identification<sup>1</sup>—choosing a disease to target with a drug—and the final step is target validation<sup>1</sup>—testing the target and confirming its mechanism in the body. Worldwide, more than \$70 billion is spent annually on health research and development (R & D) by the public and private sectors.<sup>5</sup> The great interest in drug R & D shows commitment to improving health conditions, but we must ask ourselves, who are these drugs being made for? Of the 1,393 new pharmaceuticals marketed between 1975 and 1999, only 13 were for “neglected” diseases.<sup>6</sup> Neglected diseases include illnesses such as Human African trypanosomiasis (HAT), V. Leishmaniasis, Malaria, and Chagas. Neglected diseases typically occur in developing countries whose patients are too deeply impoverished to constitute a market that can attract investment in drug R & D.<sup>7</sup> Only an estimated 10% of worldwide medical investments are used for research into 90% of the world’s health problems.<sup>8</sup> This is what is called “the 10/90 gap.”<sup>5</sup> The consequences of that profound imbalance are evident around the world.

In addition to this blatant disregard for social capital, pharmaceutical companies fail to consider the consequences of not valuing human relationships and interactions. For a moment, consider what an economic system would look like if it took the principle of valuing social capital seriously. Physicians might be more likely to accept uninsured, impoverished patients. Employers might be more inclined to provide better coverage to employees. Various sectors of the health care system, such as physicians and hospitals, might more efficiently coordinate care, and patients



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might be willing to absorb higher out-of-pocket costs because they trusted and valued the quality of their health care organizations.<sup>9</sup> Integrating the value of social capital into medical economics improves the health and economy of so-called “developing” nations. For example, the World Health Organization estimates Africa’s gross domestic product (GDP) would be up to \$100 billion greater annually if malaria had been the focus of pharmaceutical research years ago.<sup>10</sup> The complete integration of social capital into all stages of the pharmaceutical industry would undoubtedly serve to fulfill a vision of high quality health care for all.

### Drug Discovery

Drug discovery, the next phase of developing a drug, a candidate, or a “lead compound”<sup>2</sup> is identified. The sources for lead compounds vary and change considerably over the course of time. Nature is a primary source for drug discovery. Scientists and public health experts traditionally have paid little attention to either the relationship between human health and the health of other species, or the value of natural capital; neither have these topics been addressed in the education of health care professionals.<sup>11</sup> Take, for example, Taxol. During the 1960s, a potent anti-cancer compound, known as Taxol, was discovered on the bark of the Pacific Yew tree. Following considerable depletion of these valuable trees and additional research, scientists found that each patient would need 60 pounds of Yew bark to produce enough Taxol to sustain the course of their treatment. The problem was that one tree provided only 20 pounds, and over 40,000 women needed the remedy.<sup>12</sup> Due to the impact of this resource depletion on the local ecosystem and communities, scientists developed a synthetic and more powerful form of this groundbreaking cancer drug from the leaves of the Pacific Yew.

As pharmaceutical companies worldwide are becoming more aware of the need to conserve biodiversity and natural capital, some are developing local biodiversity action plans (BAPs) aimed at conserving natural resources, and where possible, increasing local diversity on and around the company’s land. For example, Glasko-Smith Kline is creating or maintaining refuges and “green corridors” for flora and fauna and reintroducing indigenous species. Some pharmaceutical manufacturing operations are now requiring sites to evaluate its impact on the environment:<sup>13</sup>

- identify and assess potential impacts of their activities on local habitats
- minimize adverse effects of their activities on important habitats
- enhance biodiversity where feasible
- monitor impacts to ensure action remains effective in protecting and enhancing local biodiversity

Prioritizing sustainability is a respectable step towards resource conservation, but it is only the beginning of actions the medical industry must take.

While the natural world is a primary source for drug discovery, scientists also develop medicine *de novo*, creating molecules from scratch using advanced computer modeling. A recent survey found that 30% of new drugs were completely synthetic in origin. The other 70% were derived from or were similar to chemicals found in nature.<sup>13</sup> But whether the compounds are synthetic or natural, the pharmaceutical industry’s efficiency rate relative to use of raw materials is abysmal. Typically, about 100 kg of material raw material is used for every 1 kg of active pharmaceutical

## Top 20 Prescriptions for 2006

- 1 Lipitor – Cholesterol lowering agent
- 2 Toprol XL – Antihypertensive
- 3 Norvasc – Antihypertensive
- 4 Synthroid – Thyroid hormone
- 5 Lexapro – Antidepressant
- 6 Nexium – Gastrointestinal
- 7 Singulair – asthma prophylaxis
- 8 Prevacid – Gastrintestinal
- 9 Ambien – Sedative
- 10 Zoloft - Antidepressant
- 11 Advair Diskus – Corticosteroid
- 12 Zyrtec – Antihistamine
- 13 Effexor XR – Antidepressant
- 14 Fosamax – Bisphosphonate
- 15 Plavix – Anticoagulant
- 16 Protonix – Proton pump inhibitor
- 17 Vytorin – Cholesterol lowering agent
- 18 Zocor – Cholesterol lowering agent
- 19 Diovan – Angiotensin blocker
- 20 Lotrel – Calcium channel blocker

Source: Drug Topics. Top 200 Brand-Name Drugs by Units in 2006. [www.drugtopics.com](http://www.drugtopics.com)

ingredient produced<sup>13</sup>—a miserable 1% material efficiency, compared to the production of fine chemicals (20%) and bulk chemicals (50%). This inefficient process, which wastes valuable resources and has negative environmental and financial consequences, demonstrates the industry's lack of regard for the worth of natural capital.

The brighter side is that the industry is initiating a variety of conservation methods to extend the life of raw materials and reduce the impact drug development on the environment. High throughput screening is currently the most common form of drug development.<sup>2</sup> Using robotics and computational power, researchers test hundreds of thousands of compounds in a relatively efficient manner. In addition, scientists are using biotechnology to genetically engineer living systems to produce the disease-fighting compounds in medicine.

## Pre-clinical and Clinical Phases, and Approval

Following discovery, drugs undergo extensive lab and animal testing in the pre-clinical phase to determine safety and efficacy for human testing.<sup>2</sup> In this stage, the pharmaceutical manufacturer submits an Investigational New Drug Application (IND) to obtain FDA approval to test on human subjects. This testing may reveal unanticipated weaknesses of the medicinal compound. The number of potential medicinal compounds is drastically reduced from 10,000 to 5 or fewer in this phase.<sup>2</sup> Problems can arise when the need to determine a potential drug's safety and efficacy overrides the welfare of living animals; because of concerns about abuse and maltreatment of animals, testing gets strong scrutiny from the public. Integrating the value of natural capital in the pharmaceutical industry would advance sophisticated technology development and replace harmful testing protocols.

In the next phase of drug development, which can last up to 6 or 7 years, researchers conduct clinical trials, or tests on humans, to determine if a drug is safe and effective. A clinical trials starts with Phase I tests on a small group of healthy volunteers and concludes with Phase 3 tests on a large group of patients. Some treatments may have unpleasant or even serious side effects. Often these are temporary and end when the treatment is stopped. Others, however, can be permanent. Side effects may appear during treatment, or not show up until after the study is over.<sup>14</sup>

Drug companies that are not committed to human capital fail to consider individual and community knowledge and may contribute to already deteriorating health conditions. In the previous decade or two, investigations by both public and private sectors have uncovered the fact that some researchers conduct unethical testing of impoverished peoples in the developing world. Without internal ethical review committees, such as research institutes or scientific panels, drugs continue to be tested without consent, on men, women, and children of developing nations. In 1996, Pfizer treated 100 Nigerian children with the antibiotic Trovan in order to determine the drug's effectiveness.<sup>15</sup> Eleven children in the trial died, and others suffered brain damage, were partly paralyzed, or became deaf.<sup>16</sup> Pharmaceutical industry researchers failed to acknowledge the inherent value of human life and became witnesses, and in some cases perpetrators of, unnecessary and unjustifiable deaths. It is imperative that the pharmaceutical industry reclaim its stance on human and social capital and insist on providing humane and effective care to all people, regardless of social or economic status.

Once clinical tests prove a drug to be effective, it goes through the approval phase. Once approved by the FDA, the drug goes into the manufacturing process. This phase is responsible for the majority of damage to natural capital within the drug development process.

## Drug Production and Natural Capital

In order to scale up production, pharmaceutical manufacturers rely on excessive use of the natural capital of energy, water, and toxic chemicals can be excessive, resulting in significant air, water, and land pollution.

### Energy

Perhaps the hottest topic right now among those concerned with sustainability is energy. Evidence that shows an increase in greenhouse gases, such as carbon dioxide, in the atmosphere is causing a rise in the Earth's temperature—global warming<sup>13</sup>—is spurring the search for alternative forms of energy production. The U.S. pharmaceutical industry consumes almost \$1 billion in energy annually.<sup>17</sup> In 2002, the industry generated over \$140 billion in output, up from \$108 billion in output in 1999.<sup>17</sup> In an attempt to curb energy usage, pharmaceutical companies have implemented a number of conservation methods, including solar-powered streetlights, wind turbines, and solar-heated water canteen and temperature control.

### Water

Water is the most abundant liquid on our planet, covering 70% of the Earth's surface and making up 60% of the human body. Of this, only 1% is freshwater. Freshwater is used in the drug development in manufacturing (for processes, products, cooling, and cleaning) and for general uses such as drinking, food services, and sanitation.<sup>2</sup> In 2005, the average pharmaceutical company used 22 million cubic meters of freshwater,<sup>17</sup> which is sourced mainly from municipal water supplies (59%) or wells or boreholes (40%),<sup>13</sup> with a small amount from other sources.

Many pharmaceutical manufacturing facilities are located in countries where water resources are classified as “highly stressed.”<sup>18</sup> Beyond excessive resource consumption, threats to water include the unknown effects associated with active ingredients in the drugs being produced on nontarget species.<sup>2</sup> In addition, environmental pressures on water negatively impact the surrounding society's access to food and drinking water and lessen the opportunities for those in the affected areas to build sustainable communities.

Conservation measures the pharmaceutical industry has taken to date include rainwater collection for sanitary purposes and recycling up to 90% effluent process water for landscaping, with an eventual goal of zero-wastewater (no discharge to water bodies or municipal sewers).

**Ecological economics poses the question, Is modern medicine as it is currently practiced a truly just and sustainable way to truly heal our communities?**



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## Air

Clean air is essential for overall well-being and good health. The heavy use of solvents in drug research, development, and manufacturing results in the emission of Hazardous Air Pollutants (HAPs), such as volatile organic compounds (VOCs). The emissions of VOCs can give rise to ground level ozone in the presence of UV light, which has adverse effects on human and plant life. Some VOCs are also greenhouse gases and may contribute to climate change.<sup>19</sup> In order to curb air pollution, pharmaceutical industries are increasing the reuse and recycling of solvents during drug manufacturing and installing VOC abatement equipment. A reduction in the manufacture and prescription of CFC-driven inhalers could further decrease the release of ozone-depleting substances.<sup>20</sup>

## Solid Waste

More than 80% of the hazardous waste in drug development consists of solvents that are used in production processes,<sup>13</sup> and a daunting number of regulations guide and restrict the way hazardous waste is handled. Regulations vary widely around the world, and the primary disposal option is incineration. In 2005, GlaxoSmithKline disposed of 68 million kg of hazardous waste (excluding demolition and construction waste): 44% of this was incinerated with energy recovery, and 54% was incinerated without energy recovery. During that year, the company recycled 72% of the total waste it generated, an increase of 2% since 2004. This is far from reaching its seemingly simple goal of 10% increase in the proportion of waste recycled since 2001.<sup>13</sup> In 2003, Roche incinerated 23% of its general waste, and the rest (77%) was sent to landfill.<sup>17</sup>

Packaging is a significant source of solid waste in the drug life cycle. Conservation initiatives include increasing the amount of recycled and renewable material used in packaging, and eliminating the presence of harmful products such as PVCs associated with plastics. For example, companies in Japan are replacing PVC packaging material with polypropylene (PP) blister packaging and optimizing blister packaging, which will eliminate approximately 20 tons of cardboard and 5 tons of aluminum bags.<sup>13</sup>

The latest research on the life cycle of pharmaceuticals and personal care products exposes the serious environmental consequences associated with pharmaceutical use and improper disposal (See Pharmaceutical Pollution on p.5). Solid waste conservation efforts include waste minimization and recycling initiatives. Ecological economics would prioritize and require recycling of solvents.

## Land

Land is an increasingly scarce resource due to population increase, urban sprawl, and the impact of modern society on land productivity. In order to sustain future generations, every industry's use of land should be analyzed. For many pharmaceutical manufacturers, operations at processing sites have taken place for nearly 100 years.<sup>19</sup> Often manufacturers need to build a new facility or reconstruct old ones, since every drug has different and varying needs.<sup>2</sup> Inefficient building construction and poor management of solid waste, water, and energy at these facilities harm the land on which operations take place.

## 12 Principles of Green Chemistry

1. Prevent waste
2. Design safer chemicals and products
3. Design less hazardous chemical syntheses
4. Use renewable feedstock
5. Use catalysts, not stoichiometric reagents to minimize waste
6. Avoid chemical derivatives
7. Maximize atom economy
8. Use safer solvents and reaction conditions
9. Increase energy efficiency
10. Design chemicals and products to degrade after use
11. Analyze in real time to prevent pollution
12. Minimize the potential for accidents

Increasing concern about environmental sustainability is prompting some manufacturers to minimize environmental impact and promote sound land management policies as they construct or select new facilities. During project planning, soil surveys inform decisions about facility construction and appropriate disposal methods for surplus soil resulting from construction.

### Transportation

Once developed, a drug must reach appropriate dispensaries. In 2005, Glasko-Smith Kline products were transported a total of 195 million kilometers, the majority (82%) by air freight. Business-related travel accounts for a great majority of CO<sub>2</sub> emissions and include plane (232 million kg), employee plane travel (112 million kg of CO<sub>2</sub>), and global sales fleet by car (102 million kg of CO<sub>2</sub>).<sup>13</sup> In addition to business travel, manufacturers also transport products from manufacturing plants to distributors.

Efforts to advance sustainability in regards to transportation include “green travel plans”, encouraging employees to carpool, drive fuel efficient vehicles, and provide showers for cyclists.<sup>13</sup> In addition, teleconferencing is made available to employees to reduce travel.

### Summary

If the pharmaceutical industry integrates and addresses the true cost of drug development, a healthier world and more sustainable way of living can and will emerge. The four principles of value of the ecological economics model—social, human, built, and natural capital—offer an integral perspective for drug development and administration. If we inform our economic analyses, strategies, and policies with an understanding of the interdependency of these four types of capital, we can better meet our goals of sustainable human health and contentment.<sup>4</sup>

The emerging field of green chemistry and environmentally sound improvements in hazardous waste management suggest that the gate to environmental sustainability is open wider than ever before. Two important steps the pharmaceutical industry can take are committing to environmental protection and advocacy, and implementing a cradle-to-cradle approach to the life cycle of drugs. To reach true sustainability, however, the industry—and all of us—will need to expand our understanding of product stewardship to value the social, human, built, and natural capital outlined in ecological economics model. We have a great opportunity.

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### **What Pharmacists and Providers Can Do**

- Do not prescribe more medications than can be used
- Prescribe starter packs and refill packs
- Review and regularly reassess the patient's total consumption of medication
- Consider environmental impact when prescribing medications
- Learn more about which drugs have large environmental impacts
- Educate consumers about the importance of proper disposal of pharmaceutical waste