

The difficult marriage of the pharmaceutical industry and the sustainable development goals

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Abstract

Biopharma succeeds in tackling devastating diseases and generating innovative medicines globally in record time. Nevertheless, it has not adapted its procedures to contribute overcoming global challenges such as fighting poverty, climate change, and protecting ecosystems and biodiversity.

To develop, produce, and commercialize drugs in a sustainable manner, making them accessible to the world population, policies should aim at 1. sharing risks and rewards more equitable between governments and industry, 2. promoting drug repurposing and licensing of shelved drugs, and 3. shifting from traditional chemistry to natural products for the identification and production of novel active pharmaceutical ingredients.

Biotechnological industries drive sustainable development in areas such as fighting hunger and poverty, clean water and energy, climate change, and protection of ecosystems and biodiversity (1).

The area of biotechnology focused on developing medicines for the treatment of diseases, pharmaceutical industry, plays a critical role in saving lives and improving the quality of lives across the globe. It has shown impressive success in tackling devastating conditions such as infectious diseases and has a remarkable ability to generate highly innovative drugs for highly complex diseases such as cancer and neurodegenerative disorders. Most notably, the pharmaceutical industry has created a global ecosystem comprising all the different steps of the complex task of creating, producing, and distributing new drugs. The reactivity and resilience of this ecosystem gave the Covid-19 vaccines in a record time. Nevertheless, this industry has not adapted its procedures to contribute to overcoming other global challenges such as fighting poverty, climate change, and protecting ecosystems and biodiversity.

It can be argued that this is due to the complexity of this industry, in which companies are expected to deliver innovative, safe, and efficient treatments at a reasonable cost for patients. This outcome presupposes an equation in which science, market, regulatory agencies' requirements, financing, competition, and serendipity are aligned. Adding to this equation 1. carbon-neutral research and development, production, and distribution chains, and 2. a business model that allows access to highly innovative drugs at an affordable price at a global scale might be just too difficult to achieve.

To the best of my knowledge, the only policy to date aiming at improving the environmental impact of biopharma is the Securities and Exchange Commission's (SEC) Rules to Enhancement and Standardization of Climate-Related Disclosures, which would require registrants to the public stocks market to include climate-related disclosures in their registration statements and periodic reports, including information about climate-related risks and climate-related financial statement metrics, including disclosure of greenhouse gas emissions (2). The Biotechnology Innovation Organization (BIO), the world's largest life sciences trade association, has expressed its concerns that these rules will have disproportionately negative effects on existing small biotech companies and discourage the formation of new ones because small biotech companies will not be able to cover the costs of the implementation of these rules (3). To date, these rules have not been implemented.

The size of the problem

Studies claim the pharma industry emits more greenhouse gases than the automotive sector: the pharma market is 28% yet 13% more polluting than the automotive sector (4). Surprisingly, little attention researchers have paid to the industry's greenhouse gas emissions (5). More than 200 companies represent the global pharmaceutical market, yet only 25 consistently reported their direct and indirect greenhouse gas

emissions in the past five years. Of those, only 15 reported their emissions since 2012.

To comply with the reduction targets in the Paris Agreement, by 2025 the pharmaceutical sector would have to reduce its emissions by 59% from 2015 levels (4, 6).

Also, it is commonly argued that there is a misalignment between pharmaceutical innovation and global health needs, as indicated by the global

pharmaceutical research and development (R&D) investments and the global burden of disease. R&D investment has mainly targeted pharmacological areas associated with disease prevalence in Western Europe, North America, and Australasia, namely neoplasms and mental and behavioral disorders (7, 8). However, the majority of the world's population lives in developing countries, for whom the disease burden is still mostly caused by infectious diseases and neonatal conditions (7), in stark contrast to the observed pattern of pharmaceutical innovation. Previous studies have addressed the need for intervention in global R&D markets, in the form of better alignment between public and private sector R&D strategy and health needs, and the urgent need to redesign public policies to foster innovation in neglected disease areas in both developed and developing countries (9).

Path to improvement 1: Redefining the role of governments in the innovation ecosystem.

The common knowledge states that the role of the government is to provide the general conditions (infrastructure, services, tax policies, etc) that will allow entrepreneurs and innovators to unleash the power of science into technological breakthroughs. According to this view, governments fill the gap for what is not being done by the private sector, for instance, financing research. Following this line of thought, governments have a passive role in the creation of innovative solutions and, being the private stakeholders taking most of the risk, they are entitled to the rewards when things work well.

This vision of governments is being challenged: very large sums of public money are spent on health innovation and the private sector tends to invest after the state has made the high-risk investments (10). Nevertheless, simplistic views of who are the winners and losers, leading to slogans such as "while risks are socialized, profits are privatized", should be avoided.

Beyond the details on how the benefits of biomedical innovations should be distributed, governments should have a bigger share of that. Those resources should be used to implement public policies that will aim to correct or counterbalance the distortions of the current system, which is largely managed by pharmaceutical corporations. With these resources governments should:

1. Run their own drug development programs, focused on societal and not monetary benefit.

2. Implement prevention and early detection programs.
3. Invest in R&D programs on neglected diseases and sustainable ways to produce innovative drugs.

Path to improvement 2: Drug repurposing and licensing of shelved drugs.

Drug repurposing is the research of new indications for already approved, investigational, or discontinued drugs, potentially shortening development timelines for 6–7 years and lowering overall development costs to US\$300 million compared with an estimated \$2–3 billion for a new chemical entity (11). The potential of drug repurposing remains relatively untapped, mainly due to challenges in 1. patenting a new repurposed indication and enforcing patent rights and 2. lack of initiative from companies owning drugs with repurposing potential (focus on the original application and resistance to out-license).

Though pharmaceutical companies generally patent new drugs, when further research and development into them ceases they are shelved. It is considered that 90% of clinical drug developments are shelved (12) and that strategic business decisions are the second-most common reason for companies to suspend the development of experimental medicines (13). The companies owning these shelved assets are typically reluctant to out-license or to share them in collaborations, given the risk that a third party achieves what the originating company couldn't, damaging its finance and reputation.

Drug repurposing and reactivation of shelved assets represent significant opportunities to develop cheaper drugs. To stimulate these areas, policies should aim at:

1. Develop novel IP policies to ease the protection of repurposed drugs.
2. Create measures like the Orphan Drug Act for repurposed and shelved drugs.
3. Stimulate the out-licensing of shelved drugs via tax reductions or similar initiatives.
4. Creation of drug development programs (spin-offs or government) and of an investment ecosystem focused on repurposed and shelved drugs.

Path to improvement 3: Natural products.

Oil and coal processing for solvents and chemicals will likely be diminished in the future, so synthetic pharmaceuticals cannot be relied on long term. In

addition, active pharmaceutical ingredients (APIs) can also cause environmental impacts following patient use and downstream production sites (14).

A sustainable alternative to synthetic pharmaceuticals is natural products. They are chemical entities formed by naturally occurring living organisms; such as plants, algae, bacteria, and yeast; with pharmacological properties. Despite the environmental and chemical advantages and multiple successful drug discovery examples, pharmaceutical companies have reduced natural product-based drug discovery programs, mainly due to technical and intellectual property challenges specific to natural products (15). Sustainable approaches for the isolation and production at the industrial scale of natural products are in situ extraction with green solvents, such as glycerol or natural deep eutectic and ionic solvents (NADES) (16), and engineering of pathways in cells as factories enabling the production of complex natural products (17).

The benefits of natural products are shared with countries of origin of biological material from which natural products are obtained, framed in the United Nations 1992 Convention on Biological Diversity and the Nagoya Protocol (18). Despite the good intention of this initiative, from a drug development perspective, it is seen oftentimes as an additional hurdle given the legal, administrative, and financial complexities of its application.

Natural products as a source of new APIs are an opportunity for more sustainable and cheaper drugs, representing a strong rationale for the preservation of biodiversity and allowing countries to use it for wealth creation. To stimulate these areas, policies should aim at:

1. Develop novel IP policies to ease the protection of natural products.
2. Simply the Nagoya protocol.
3. Stimulate the creation of drug development programs (spin-offs or government) and of an investment ecosystem focused on natural products.

Looking ahead - The pharmaceutical industry goes sustainable and equitable.

When it comes to adapting industrial practices to achieve the sustainable development goals, the pharmaceutical industry has largely passed under the radar. This could be because of two specific features of this sector: 1. its market are diseases and 2. it is intrinsically a high risk/high reward business. This led this industry to claim that imposing more constraints would lead to a decrease in its profitability and therefore a decrease in its capacity to provide solutions to the global health challenges. The Covid-19 pandemic has shown the value of a dynamic and efficient pharmaceutical industry.

Nonetheless, alternative, complementary, ways of tackling global health challenges in a more sustainable and equitable manner have to be developed. Here I propose three avenues that I consider of particular interest, but they are far from being the only ones. At this stage, the first step is to showcase that alternative approaches 1. are realistic and 2. provide real value.

Governments and policy-making institutions must imagine, execute, and finance these initiatives, getting the profit from their successes.

These alternative approaches will have to be done to varying degrees in collaboration with the existing pharmaceutical industry. These partnerships will have to be built in an equitable, transparent, and constructive manner, leaving aside stereotypes and hidden agendas. A change of culture and mindset will be required from both sides, which is likely to be the biggest challenge of all.

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