A MODEL OF REGULATORY BURDEN IN TECHNOLOGY DIFFUSION: The Case of Plant-Derived Vaccines

Demand for Novel Vaccines

The need for vaccines in poor and developing countries has never been more pressing. The development of new, safe and affordable vaccines and new vaccine delivery technology for infectious diseases in developing countries is crucial for the survival of hundreds of millions of people, especially children. As ongoing economic disparities lead to growing inequalities in healthcare, innovative vaccine technologies are badly needed. Genomics and biotechnology may lead to new vaccines, but developing these technologies is only half the battle. An equal challenge for policymakers and immunization stakeholders is to overcome regulatory barriers that impede new technologies from reaching those who need them most.

Innovative Technology: Plant-Derived Vaccines

Plant-derived vaccines (PDV) are a novel method for producing and administering vaccines in which plants are grown, processed, and the final product is dosed for oral administration. This method departs significantly from traditional vaccines, which are costly to produce and are administered by injection. The benefits of PDVs over traditional methods include lower production costs, the potential for in situ production, and ease of distribution because they do not require temperature control for storage and distribution. Because they are orally administered, risks and costs associated with injections are eliminated. PDVs are a promising health technology that have the potential to increase vaccination and reduce infectious disease in developing countries. At present, they are a proven research concept with viable products in clinical trial; the remaining scientific and technological challenges associated with PDVs appear to be surmountable.

Three Models to Distribute PDVs

PDV technology is sufficiently advanced that attention should now focus on institutional and regulatory barriers that may slow the uptake of PDVs in developing countries. These barriers include: intellectual property laws, import and export regulations, and environmental and production regulations. Together, these regulatory barriers can undermine the commercialization and distribution of PDVs in developing countries. At the same time, the actual means by which such barriers work to impede the diffusion of new technology is poorly understood, and difficult to predict.

The International Expert Group on Biotechnology, Innovation and Intellectual Property has done case research using a system dynamics (SD) model in order to examine the market introduction of a new PDV vaccine in India against hepatitis B. The group generated a dynamic simulation model of technology diffusion for studying regulatory barriers in the diffusion of PDVs between the United States and India. The role of regulatory burden was evaluated for three scenarios in which plant-derived vaccines are produced and diffused. The key differences are the nationality and location of the production and distribution firms:

Scenario 1
PDVs are produced in the United States and distributed in India by a US firm.

Scenario 2
PDVs are produced in the United States by a US firm and distributed in India by an Indian firm.

Scenario 3
PDVs are produced and distributed in India by an Indian firm.

Scenarios 1 and 2 reflect the current state of affairs: the initiative to research and develop PDVs has been undertaken in an industrialized country and firms in that country are likely to be involved in future product development and distribution. Scenario 3 reflects the potential for production and distribution dynamics to change as biotechnology capacity in developing countries improves around the world.

The nationality and location of the firms producing and distributing the vaccine have implications for the regulatory burden and trade barriers encountered during commercialization, and for the degree to which intellectual property affects the commercialization process. The following table briefly describes these factors for each of the three scenarios.

SUMMARY OF THE THREE POSSIBLE SCENARIOS FOR PDV DIFFUSION

Scenario 1	PDVs are produced in the United States and distributed in India by a US firm. Production must meet US regulatory standards regarding containment and confinement practices. Finished product must meet US drug and biologic regulations. These regulations ensure product safety and efficacy, but are expensive. India is open to foreign investment, but firms must undertake due diligence to ensure intellectual property rights protection. Import tariffs must be reviewed, and the distribution firm may be subject to review by the Reserve Bank of India.
Scenario 2	PDVs are produced in the United States by a US firm but distributed in India by an Indian firm. US environmental regulations and regulations for the finished product safety and quality apply. The US firm would typically negotiate a license with the Indian firm that set out a variety of conditions, including those related to intellectual property, for the distribution of the final product. In this scenario, the burden of foreign investment barriers is traded for licenses and importation tariffs. Like Scenario 1, the burden of US regulation in US, and high cost of production must be considered.
Scenario 3	Scenario 3 involves the production and distribution of the PDV in India by an Indian firm, requiring compliance with Indian environmental and manufacturing standards, which may not be as stringent as in the US. Several Indian authorities have regulatory jurisdiction over the commercialization of biotechnology, making the regulatory pathway somewhat uncertain and slow. Biosafety is a concern, and appears in many regulations, including the Indian Patent Act. While the technology would be licensed, importation and tariff rules no longer apply.

Findings

The three scenarios were modeled and assessed using dynamic simulation techniques. The simulations revealed that time delays due to regulatory barriers influenced both the cost and the disease burden experienced by a population. Therefore, time to distribution is the most significant factor in achieving a reduction in the number of infections and deaths related to the hepatitis B virus. The simulation demonstrated that Scenario 2 is expected to yield the fastest time to distribution and thus the greatest health benefits.

The results support a policy choice that favours producing PDVs in the United States while placing control over their distribution in India.

Conclusions

1. This case study demonstrates the utility of the dynamic simulation modeling technique adopted by the International Expert Group on Biotechnology, Innovation and Intellectual Property in evaluating the effects of regulatory burden on the diffusion of innovative technology.

2. Time delays due to regulatory barriers influence both the cost and the disease burden experienced by a population.

3. Technology transfer mechanisms under consideration for a new technology need to consider the composite impact of regulatory factors.

Recommendations

1. Intellectual property has the potential to be a significant hurdle in deploying a technology, particularly when the technology is transferred from one jurisdiction to another. Moreover, delays, costs and uncertainties associated with IP combined with other factors, most notably regulatory costs, can jointly cause even more significant delays. In order to encourage and facilitate technology transfer, developing country decision-makers in government and industry should be conscious of this combination of regulatory factors impacting technology diffusion.

2. Systems dynamics modeling is an effective tool for assessing the impact of multiple aspects of the regulatory burden (e.g. trade law, environmental regulations) in an integrated way. The PDV case study demonstrates that systems dynamics models identify the interaction of key factors and are useful as decision-making tools for policy-makers. The World Health Organization and other international decision making bodies would benefit from employing the systems dynamics framework used by the International Expert Group on Biotechnology, Innovation and Intellectual Property.

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For further information please contact:

The Innovation Partnership
3800A St-Hubert, Montreal, Quebec H2L 4A5 Canada
www.theinnovationpartnership.org

Centre for Intellectual Property Policy
Faculty of Law - McGill University
3644 Peel Street, Montreal, Quebec H3A 1W9 Canada
www.cipp.mcgill.ca