Diagnostic Tests for Cervical Cancer: PATH

The public sector institution PATH aims to improve global health by advancing technologies, strengthening systems, and encouraging healthy behaviors through effective collaborations with the private sector. PATH tries to reduce risks for a commercial company developing products for resource-poor countries by identifying gaps in the market that existing technology can fill, demonstrating value, and partnering in development and sustainable supply. In addition, PATH adapts products to different markets, provides training, and engages in advocacy with WHO and other public bodies. PATH is both a recipient and a provider of funding.

As a nonprofit organization that creates and manages intellectual property in house, PATH recognizes that working with private companies requires sensitivity to and awareness of commercial incentives. PATH believes that intellectual property is just one element of the economic environment of the technology. Successful collaborations with private sector companies impact positively the availability, accessibility and affordability of products in public sector health programs in developing countries.

During product development and distribution, PATH works to change behavior and to open or improve communication. It worked with India's Ministry of Health to launch a hepatitis B vaccine on a project that involved community education and communication in preparation for the vaccination program. The program's success has ensured national expansion of the program.

Diagnostics is a large field with a number of disparate groupings of intellectual property generated by scientists around the world; it is common for multiple parties to hold key pieces of intellectual property. PATH routinely conducts market and industry feasibility studies to determine the type of industry partner to pursue, to determine which is best positioned to take PATH into the target segments it is interested in, and to identify IP issues. The public sector needs to recognize that securing the necessary IP rights for diagnostic products is imperative before moving ahead with development and commercialization.

Procurement in diagnostics is not as centralized as other public health products, such as vaccines and drugs. This makes it more difficult to plan for the global public health sector. Marketing is generally on a country-by-country basis, unlike family planning products, for example, that have regional or global distribution agencies for the public sector markets.

THE CERVICAL CANCER DIAGNOSTIC TEST PROJECT

PATH is engaged in ongoing work with industry partners to develop rapid diagnostic tests for cervical cancer for use in developing countries. In addition, two major institutes, in India and China, are screening 30,000 women for cervical cancer and will then conduct the clinical trials to validate the efficacy of these these simple and inexpensive tests. In addition, this work will generate useful information on viruses that have not yet been examined in detail in these countries.

Under the terms of the R&D agreements between PATH and the industry parnters, PATH's obligations include funding a portion of the industry partner's direct R&D costs, conducting market and industry assessments, developing an evaluation framework

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for public-health use of the new test, and conducting multicountry clinical evaluation of the new tests' performance for registration purposes. The industry partner is responsible for development of the products, management of the intellectual property (patenting costs and prosecuting infringement), manufacture and supply for clinical evaluations, and finalizing the product for registration and commercial supply.

PATH retains ownership of specimens, but data are either jointly or individually owned. A product-development committee was formed, and PATH only provides funding sufficient to reach the next agreed-upon milestone. During the R&D phase PATH can terminate, without cost, at key milestones, although industry partners terminate at a cost.

The commercialization period of the agreement runs for ten years from the first sale of a registered product. Both industry partners are required to provide preferential public sector pricing. If these specific products are sold in developed countries, PATH will earn a royalty, however PATH has forgone all royalties on developing country sales. Termination clauses covering one industry partner involve repayment of PATH's direct funding and the transfer of distribution and/or manufacturing to a third party; the other industry partner is only required to grant PATH a nonexclusive license to the product and underlying reagent.

Both companies are working on products that are different from those they will launch in the United States and Europe. Developing a product with PATH could potentially jeopardize products in other developed countries; it is therefore critical for participating industry partners to be able to segment markets.

PATH's success in being able to attract industry partners to collaborate in its effort to develop a diagnostic test for cervical cancer is an example of creating an overarching cervical cancer prevention initiative that made collaboration attractive and worthwhile—in this case, a program of cervical cancer screening including clinical work, advocacy, and policy issues. PATH does not expect to be providing the product in the future; its industry partners have the intellectual property, are developing it, and are responsible for its management.

This case study illustrates that intellectual property and technology transfer are not enough to create a broad and lasting health impact. PATH believes it is possible to attract top-tier industry partners, especially if there is a comprehensive public health initiative and not just a technology development project. Issues to consider in developing a public health initiative include determining the value of know-how, deciding whether to grant an exclusive or a nonexclusive license, dealing with key reagent IP holders, and influencing the final product price.

TYPES OF AGREEMENTS

Over the years of diagnostic-test development and commercialization, PATH has:

- in-licensed key diagnostic reagents to PATH from academic, government, and private company sources
- out-licensed diagnostic test and reagent production know-how from PATH to diagnostic manufacturers
- some with geographically defined exclusive territories
- some on global nonexclusive basis
- materials transfer agreements
- supply agreements
- confidentiality agreements
- codevelopment agreements

IP RIGHTS DECISIONS AND IP MANAGEMENT

PATH has faced key areas of IP rights decision making and strategic IP management issues including:

- managing freedom to practice risks associated with other parties' intellectual property for certain diagnostic platforms and reagents
- determining the value of know-how developed for efficient production of certain diagnostic reagents even when the know-how was not patentable
- determining whether to provide downstream licensees with a greater or lesser level of market exclusivity, or whether to license only on a nonexclusive basis
- dealing with holders of key intellectual property involving particular antigens or antibodies necessary to develop particular diagnostic tests
- deciding whether to patent incremental in-house innovations in the face of uncertain demand and usefulness
- considering how to achieve or at least positively influence final product pricing and access when third-party diagnostics importers/distributors (not the PATH-licensed diagnostic manufacturer) will be the party making the sales transaction to a developing country government

POLICY IMPLEMENTATION

On an overall policy basis PATH works under its Guiding Principles for Private Sector Collaboration, endorsed by the board of directors, which is most often relevant to PATH's intellectual property and licensing activities with diagnostics. To conform to key elements of these guiding principles, a license (and overall collaboration) between PATH and a commercial diagnostics producer must:

- exhibit a clear link to PATH's mission by improving the availability, accessibility, and affordability of important products for public health programs in developing countries
- recognize that the commercial partner must achieve commercial benefit to ensure their sustainable commitment to supplying the technology
- provide a clear definition of the roles, responsibilities, and expectations of both PATH and the commercial producer
- balance PATH's need for transparent collaboration with the commercial producer's need to protect proprietary information
- reflect a rigorous process of due diligence on PATH's part before executing an agreement

The IP elements, working relationships, and technology economics of every project or program can vary from one extreme to the other. Because of this, PATH has found it counterproductive, for the most part, to make broad institutional policies about specific individual elements of complex intellectual property and collaborative development agreements. For example, there is no PATH-wide policy that states "all licensed manufacturers must sell to public sector at cost plus 10%." In some cases that structure might be appropriate, in others it might prevent the technology from ever coming to market. In cases where PATH has developed significant technology that may have value in developed country markets, PATH maintains the flexibility to negotiate for a royalty on developed country market sales. PATH forgoes royalties on sales of licensed technologies for developing country public sector use.

EXTERNAL FACTORS THAT AFFECTED DECISION MAKING

The diagnostics arena has a number of characteristics that have historically influenced PATH's strategies and decision making. These include:

- extremely competitive nature of global diagnostic industry
- relative ease of entry into global diagnostics industry
- proprietary control (whether through formal patents or, simply, sole possession of key clones) of key diagnostic reagents by individual companies or institutions
- multilevel manufacturing and distribution channels typical for diagnostic products
- distributed nature of global public sector procurement of diagnostic reagents—no single, huge, vertical procurement mechanism as exists for vaccines and, to a degree, family planning products

KEY LESSONS LEARNED AND HEALTH ACCESS ISSUES

The proprietary control of a single key diagnostic test reagent can give some parties control and power seemingly disproportionate to their contributions to an overall diagnostic test development project. It is critical to have either IP access and/or reagent supply agreements in place early in the product-development cycle, so that access uncertainty is reduced and cost of access is fully understood. The private sector understands this well, while we (at PATH and in the broader public sector) have not always done our homework in this area.

Noncommercial development and/or stewardship of diagnostic platform intellectual property or key component intellectual property can create a positive impact. For example, PATH enhanced the local production of key rapid-test raw materials (nitrocellulose filters and colloidal gold signal reagents) in India, which created an impact beyond the transfer of technology for individual tests to specific companies. Materials suppliers are now serving additional emerging diagnostic producers.

Intellectual property and technology transfer alone are rarely enough to create a lasting impact on public health. We are all working on solutions to health problems that have fundamentally less promise as a "business opportunity," from a commercial manufacturer's standpoint, than do other health problems. To make a new diagnostic test that will deliver profit to the manufacturer and be beneficial and accessible to patients, there needs to be policy change, advocacy work, and extensive evaluations. The diagnostic manufacturer will rarely fund these types of activities, especially for price-sensitive public health markets, so it is critical to involve others who will undertake this work. Intellectual property and technology transfer are certainly important. However, for maximum lasting health impact they should be managed as components of a comprehensive public health initiative rather than as independent activities. ■

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