Asia-Pacific
Economic Cooperation

Pictor Limited
New Zealand

Making Diagnostics Accessible to the World (A)

Written by

Lee Mathias

Director
Lee Mathias Limited

The case was developed with the cooperation of Pictor Limited solely for educational purposes as a contribution to the project entitled "IPR Strategies for Emerging Enterprises – Capacity Building for Successful Entry to Global Supply Chain," conducted under the auspices of the Asia-Pacific Economic Cooperation (APEC). The case is neither designed nor intended to illustrate the correct or incorrect management of the situation or issues contained in the case.

With the new Pictorial method of diagnostic laboratory testing for human, animal and food immuno assays, Dr. Sarita Kumble was excited with the idea of contributing to the health of the developing world, which did not have access to laboratory testing. Before she could bring the product to the market, she needed to ensure that the technology was used correctly and also make it commercially viable. A small start-up company with a big task, she needed to make sure her steps were right so that the technology she and her husband, Dr Anand Kumble, developed would be safe, effective and make a contribution to the world.

Dr Sarita Kumble's challenge was to address a number of concerns: how to identify which part of her discovery needed to be protected, how the intellectual assets (IA) protection should be managed, and how the IA should be valued. Likewise, she also had to formulate the strategy for commercialization and market the plan to potential investors, so as to ensure the financial health of the project, as well as to protect their IA from being used by others.

By the latter part of 2009 progress with both the development of the Pictor system and the manufacturing process of the test panels had been made, thus allowing Dr Sarita Kumble to enter into commercial contract negotiations. She knew that she had to get her unique product to the market as soon as possible considering that diagnostics development was a very competitive sector.

In January 2010, and with contracts well into the negotiation stage, Dr Sarita Kumble had to make some key decisions: to prioritize product development, raise sufficient funds to take Pictor to a new level of manufacturing, and recognize that the raising of those funds was dependent on both forthcoming contracts and the intellectual asset (IA) valuation.

Company Profile

In the mid 2000s and in good Kiwi style, Dr Sarita Kumble laid linoleum on her suburban Auckland garage floor and set up a research laboratory to test her ideas on miniaturizing and multiplexing enzyme linked immunosorbent assay (ELISA) technology. After a year or so, her research results indicated that she had a product that she believed – based on her previous biotech start-up experience – could be commercially viable. In 2005, Drs Sarita and Anand Kumble formally established Pictor Limited. The name "Pictor" described the "pictorial" of the test result gained from a simple scan of the test membrane.

Dr Sarita Kumble took on the CEO responsibilities while Dr Anand Kumble took charge of business development. Pictor had a number of small shareholders including Dr Lee Mathias who was also a fellow director of the Drs Kumble. The company employed a specialist biomedical engineer and a scientist who both worked on the research and development of the products.

The product, the miniaturization of ELISA technology used existing technology in a form that suited the needs of communities with limited or no access to affordable laboratory tests in 2009. The technology could be used for human and animal pathology and the testing of food products. Because the technology was miniaturized and multiplexed, simultaneous measurements of multiple disease indicators, in multiple

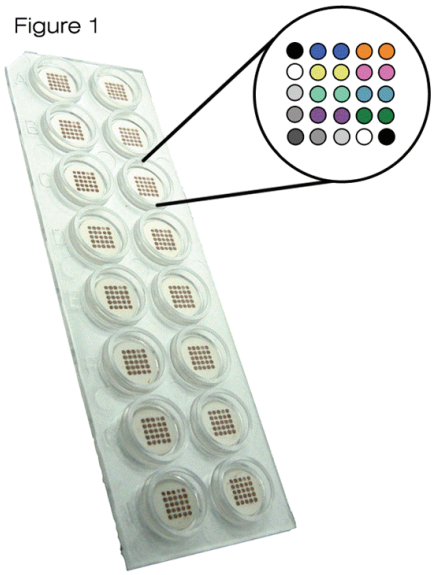
patient samples in parallel, could be undertaken. The result was volume throughput at speed.

Pictor Technology Point of Differentiation

In managing the IA protection process and its valuation, Dr Kumble's first job was to identify the point of differentiation of the company's product from other diagnostic products in the market.

Dr Kumble developed a method to stabilize dots of ELISA reagent into a membrane without the reagents "running" into each other. Pictor's products simultaneously conducted up to eight diagnostic tests in individual sample wells with only 50 micro litres (a drop of blood is 200 micro litres) of patient samples. The tests were based on the principle of "micro arrays" in which a pattern of clearly demarcated dots of reagents required for individual tests were printed on the bottom of individual wells in a 16 (or 96) -well device. In addition, self-validating tests were conducted with each sample to ensure that the prescribed tests had been correctly carried out. This feature could not be incorporated in conventional diagnostic tests. Figure 1 shows the layout of a typical test panel of eight pairs of tests, seven grayscale control dots and two dots which ensured correct alignment. All the reagents necessary for sample processing were provided in the test kit.

Figure 1



Another differentiation point of Pictor's products was the use of a standard flat-bed scanner to read the test endpoint thereby lowering setup costs significantly. The image data was analyzed using proprietary software providing an easy to read printout of the results within two minutes of test completion. In addition, Pictor's products could be used in laboratories with limited complex diagnostic equipment and minimum medical infrastructure.

Pictor initially targeted products for infectious and autoimmune diseases. Beta testing1 for these two panels had been completed by the end of 2009 resulting in the first negotiations for firm orders from customers.

Human Pathology Market Structure

The global IVD (*in vitro diagnostics* are tests using patient samples such as blood, urine and saliva) market was estimated to be US$42 billion in 2007 and projected to

[1] Beta testing is undertaken in the "real world" environment by those who are going to use the product. This phase follows Alpha testing which is designed to demonstrate that the product is feature complete and functional.

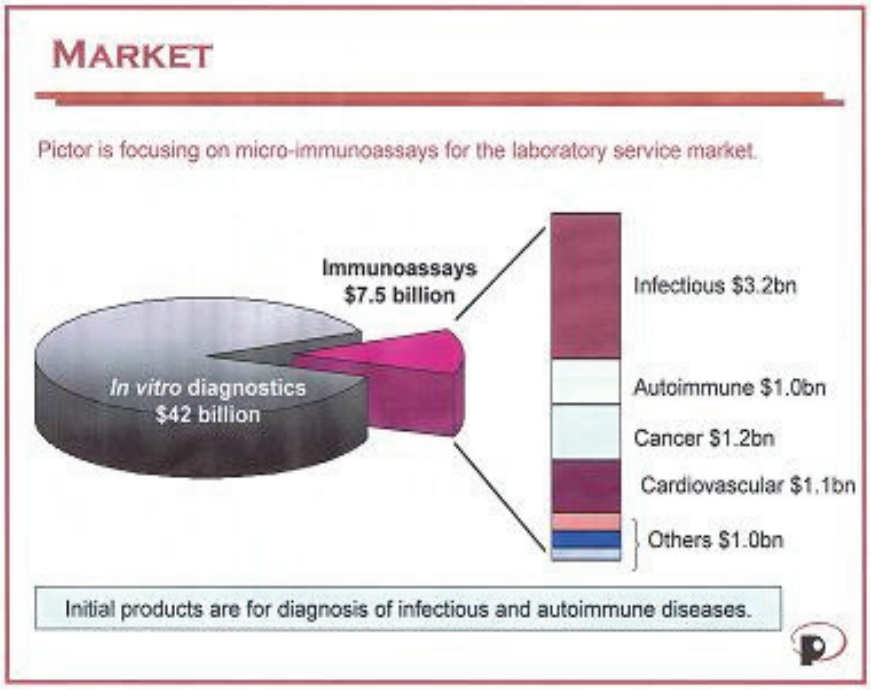
grow 6% annually until 2012. A significant portion of the total market growth was a result of increased test usage in emerging economies that were investing in healthcare infrastructure and insurance coverage for an increasingly affluent middle class. These markets were expected to experience 10% to 20% annual growth. Historically, third world economies did not have easy access to affordable diagnostics.

The IVD market was dominated by Abbott and Siemens which accounted for 60% while other major players, Roche and Beckman Coulter, had approximately 9% share each. Others like bioMerieux, Fujirebio and BioRad had strong presence but, like the dominant players, had high setup costs.

Diagnostic consumables were sold directly to pathology laboratories by the manufacturer or their agents mostly through the lease of an analyser provided at a low price. The laboratories however had to purchase compatible kits at market price.

Pictor was targeting the immunodiagnostic segment of the IVD market, which had the highest demand for innovative new products and an estimated value of US$7.5 billion in 2009 (Figure 2). Immunoassays were among the most widely used IVD tests, constituting 16% of the total diagnostic market (Marchant, 2006). The IVD market was driven by the need for cost-effective tests, with advances in genomic technologies making early stage diagnosis possible.

Figure 2. Estimated Worldwide Immunoassay Market by Clinical Segments (Marchant, 2006)



Segmented by end-user, the IVD market comprised:

- Private and hospital Diagnostic laboratory services
- Blood processing and screening
- Point-of-Care testing in hospitals and clinics
- Self-testing (over the counter tests)

Commercial clinical laboratories catered to 41% of this market, with hospital and physician-office laboratories making up 54% and 5%, respectively (IBIS, 2009). There were over 200,000 registered laboratories in the US alone.

By the beginning of 2010 the directors of Pictor had realized that they had to be more specific in their market share objectives. The Drs Kumble set their immediate goals for the company.

Initially, Pictor's strategy was to focus on the diagnostic laboratory service market and clinical laboratories in hospitals and clinics. These services were usually owned by large corporations with sophisticated distribution channels within their organizations.

An alternative strategy was to license the technology to existing manufacturers of IVDs. In 2009 and up to March 2010, Pictor had been working with a company specializing in the manufacture of autoimmune IVDs. This option was not disregarded although the Pictor directors considered the difficulty in establishing the value of royalty fees at this stage of the business cycle, the risks of the licensee owning the market and excluding Pictor, piracy of the technology and, in the longer term, the expiration of patents. However, Pictor had entered into an agreement to custom manufacture kits using the said company's reagents.

The Pictor directors also considered investigating whether there was a buyer for the technology. But without the manufacturing process being tried and tested at that time it was considered unlikely. By January 2010 the directors had confirmed the strategy to manufacture PictArray™ products in New Zealand, regardless of the source of reagents, to ensure quality control in the early stages of product development and to maintain the integrity of the product. It was also considered important to demonstrate to future investors that a semi automated manufacturing process was possible.

Pictor's Current Disease Areas Focus: Autoimmune Diseases

Autoimmune diseases included rheumatoid arthritis (RA), multiple sclerosis, juvenile diabetes and lupus among others. Typically, the testing of multiple disease markers was required for a definitive diagnosis of disease. The demand for these tests was growing with the 2007 market estimated at US$250 million; it was predicted to grow 10% annually and estimated to reach US$410 million in 2012. With the right pricing, it would be possible to tap into the much larger potential market.

Among autoimmune diseases, RA affected approximately one percent of the world's population. Pictor developed and validated a test panel that could screen patients for markers of RA and could also be used to follow treatment efficacy and disease progression. Table 1 shows the incidence and market size of RA in some of the regions Pictor wanted to target for its products. Pictor forecasts showed that it aimed to capture 1% of the autoimmune market in India and Europe by 2012.

Table 1. Incidence and Market Size for Autoimmune Diseases

Region	Incidence ('000)	Potential Market Size ($m)
United States	3,050	244
Europe	2,900	232
India	9,800	784
Australia	200	16
New Zealand	40	3.2

Source: The Autoimmune Outlook to 2013; Business Insights, 2009.

Infectious Diseases

In 2007, the World Health Organization (WHO) estimated that over 180 million people worldwide were infected with Hepatitis C virus (HCV), and a further 350 to 400 million people were chronically infected with the Hepatitis B virus (HBV), a virus 100 times more infectious than HIV. Pictor had developed and validated a test panel that, in addition to screening patients for active HBV infection, could also be used to follow markers that identified resolution of the infection and also tested for an early marker of liver cancer. Table 2 shows the worldwide market potential for hepatitis testing. Pictor forecasts showed that by 2012, its goal was to capture 1% of the market in India only.

Table 2. Potential Market Size for Hepatitis Testing

Region	Screening ($m)	Diagnostic ($m)
Africa	1,097	58
The Americas	1,324	70
Europe	1,312	69
Asia	2,462	130
Western Pacific	2,605	137
TOTAL	9,605	506

Source: Global Hepatitis Strategies; Kalorama Information, 2007.

Pictor's Value Proposition

Key benefits of the PictArray™ technology and process:
100-fold lower capital cost to set up
Could be used without special technical training
Proprietary software-driven rapid data analysis
Scalable from small clinics to mass screening centers
Single screening technology platform for multiple disease detection.

With these benefits in mind, the Drs Kumble had structured the pricing of their products based on the estimated value of the technology, the comparatively low manufacturing cost, the high distribution cost, and the high cost of IVDs in the world market.

For example, the manufacturing cost for a Rheumatoid Arthritis screening kit that could test sixteen samples was estimated to be $NZ80. The sales price would be

based on the volume of purchase ranging from $NZ120 to $NZ200 per kit. Increasing manufacturing efficiency and throughput could further reduce production costs, resulting in a cost per test of less than $NZ1.

Table 3 highlights the cost benefit of using Pictor's products compared with other multiplexed tests in all markets. These alternative technologies also required specialized training for system operation and data analysis.

Table 3. Comparative Setup Costs and Kit Costs of Multiplexed Tests (Unit: NZ$)

Company	Product	Setup Costs (Instrumentation)	Kit Costs (Price/test)
Pictor	PictArrays™	250	1.00
Luminex	xMAP Technology	120,000	1.30
BD	Cytometric Bead Array	125,000	4.60
MesoScale Discovery	Sector PR400 Imager	250,000	2.00
BioRad	BioPlex	500,000	0.90
Genesis Diagnostics	Genearrayt	30,000	1.10

Source: Individual company websites, marketing and sales documentation on behalf of Pictor.

One complication however was that at the beginning of 2010, the actual demand for the product in this format or for a similar product was still unknown; hence, all projections were based on the volume of tests using conventional technology. However, as a result of the positive beta testing results, the initial 1,000 autoimmune kits produced by Pictor had already been committed to a prospective customer, and up to 10,000 kits were expected to be sold in the first year. The first year forecasts placed the anticipated total kit sales at 13,800.

Intellectual Asset

Dr Kumble specified the IA to be protected as the "assay membrane and method of use thereof." Her decision focused on the technology's ability to hold the reagent dots to the membrane as well as on the process of analysis because the ELISA technology itself was already well established and being used in diagnostic systems.

The protection of Pictor's miniaturized and multiplexed (micro array) process was important as the ELISA for single tests was the most widely used format which had well-established protocols for the measurement of single proteins. Further, Pictor's micro array format meant that a small amount (50 microlitres) of serum was enough for testing to be undertaken. This would have major implications for screening, especially of babies and children.

Intellectual Property Strategy

By mid-2009, the Pictor directors had agreed that the IA to be owned by the company was the assay membrane and the process of use, including the copyright of the software developed for analyzing and reading the tests. This was because the directors were still not sure whether the company would have the capacity to increase its capital

to fund the potential manufacturing demand in the future. That is, while Pictor would own the science on which the technology was based, it might in the future, license others to manufacture and/or use the Pictor system.

Considering the importance of managing quality in the early stages of manufacture, by the end of 2009 the directors had agreed that Pictor would manufacture kits for human pathology in New Zealand Dr Kumble recognized that IA protection required the help of experts in the field. She worked with DLA Piper, a San Diego-based law firm specializing in biotechnology asset protection, and AJ Park in New Zealand to strategize the management of the intellectual property portfolio and patenting of Pictor innovations.

The Processes and Costs of Intellectual Asset Protection

A Patent Cooperation Treaty (PCT) application was filed in October 2007 with the United States PTO (International Patent Application Number PCT/US2007/082732) to protect the process for manufacturing arrays and testing samples using these arrays.

Under the PCT, the initial protection was to last for 18 months after which patents had to be filed in specific regions to continue the asset protection. The regional patents for Pictor technology were filed in key markets in July 2009 for protection in Australasia, Europe, India and the United States of America since these markets were considered the most receptive to the Pictor technology. Although Dr Kumble realized that it was risky not to adopt IA protection in other markets, the costs were considerable, hence her decision to limit the company's asset protection to the above-mentioned markets – a decision which the directors also supported.

A preliminary Freedom-to-Operate (FTO) [2] search gave Dr Kumble the confidence that the Pictor technology could be taken to market without infringing on the patent rights of others and therefore reduced the risk to Pictor directors and shareholders. At the same time, the company also considered adopting some strategies to protect Pictor should there be some infringement of the patent. However, given the financial constraints at that time no actual budget was allocated for this intervention. Instead, the directors opted for a strategy that would bring the product to the market as quickly as possible. In addition, Pictor filed for copyright protection of the data analysis software with the United States Patent Trademark Office (PTO) in March 2009.

A third aspect to asset protection arose in December 2009 as the manufacturing process became more refined. The biomedical technician had started working on the possibility of converting to a pneumatically powered system the manual punch and drag system for creating the dots. Likewise, the Drs Kumble started to focus their attention on the protection of the manufacturing system. They began preliminary work with DLA Piper in San Francisco and made arrangement to visit the patent attorney in May 2010 during their visit to the USA as part of their prize as finalist for the Health Focus Challenge sponsored by TECHNZ. These costs had not been estimated in March 2010.

[2] "Freedom to operate", abbreviated "FTO", is usually used to mean determining whether a particular action, such as testing or commercialising a product, can be done without infringing valid intellectual property rights of others. Source: www.patentlens.net.

As of March 2009, the total expenditure for the Pictor project amounted to $NZ 752,085. Costs of protecting the intellectual asset as at December 2009 was $NZ 270,000 with ongoing annual maintenance costs of $NZ 30,000.

Valuing the Asset

Identifying the value of the IA and the record of its protection created a further challenge for Dr Sarita Kumble. Dr Anand Kumble conducted a research on the global diagnostics market to determine the comparative prices of similar tests done by other companies. He used the data as the basis for the business plan presented to potential investors as part of an information memorandum. In that way, the approximate value of the company could be determined based on future potential sales. The directors however knew that using a financial formula would not give an accurate valuation of the IA, but given the financial constraints of the company, the value used in the information memorandum was a "best effort."

No matter how difficult, the valuation of the IA was paramount in establishing the company value and therefore the value of shares issued. There was a risk in undervaluing the technology, which took more than three years to get to the commercialization phase, as well as in overvaluing it since it could discourage investors. Thus, valuation of the company had to be balanced between what the technology might be worth and what the market could bear at a particular time. Pictor did not have a definitive valuation at December 2009 but Dr Kumble intended to prioritize the establishment of the IA value as soon as funds were available.

Decision Challenges for Pictor

The value proposition for investors was that Pictor technology changed the traditional paradigm for immunodiagnostic tests because of its ability to perform multiple tests and multiple disease detection, in parallel and with no major setup costs. Pictor technology required low to medium level of technological skill. It offered speed and simplicity, compatibility and also familiarity with traditional systems; it was scalable from small clinics to large diagnostic laboratories. These benefits would result in significant cost savings to clinical diagnostic laboratories.

On the other hand, the potential investors required Pictor to provide sufficient protection for its IA while bringing the concept to the market and to continue to provide the same protection even when the business had already been established.

At the end of 2009, Dr Kumble and her fellow Pictor directors assured the investors that the company's IA was protected and that what was important was the method of use of the Pictor process and the protection of the accompanying software rather than the basic science. Valuation of the IA was critical in determining the pricing structure of the kits as well as in setting the parameters for the future sale of the company. Investors wanted to be assured that the company had also planned its exit strategies.

The company was on track to meet its development objectives of having the first contracts for manufacturing kits by the end of 2009 and the first order filled by mid March 2010.

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