



*The Emerging Molecular Diagnostics Industry:  
Applera's Path to a Leadership Role*

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## 1. Introduction

For decades diagnostic labs have relied upon clinical chemistry and immunoassays to detect disease, but with the mapping of the human genome and advances in instrumentation technology, physicians of the future will have access to molecular diagnostic tools that will revolutionize the way medicine is practiced. Applied Biosystems, a division of Applera, is dominant in the life sciences industry market with respect to instruments and reagents, including nucleic acid detection and synthesis. Another division of Applera, Celera Genomics, has been securing intellectual property on gene expression patterns and single nucleotide polymorphisms (SNPs) faster than anyone in the industry today. With this combination of assets, Applera may be poised to capture the majority of the molecular diagnostics industry, the fastest growing segment of the \$22B *in vitro* diagnostics industry.

This paper will first review the current structure of the diagnostics industry; and in particular the nascent but fast-growing molecular diagnostics segment. Next, we will introduce Applera Corporation and its key subsidiaries, Applied Biosystems, Celera Genomics and Celera Diagnostics, a joint venture between Applied Biosystems and Celera Genomics. We will analyze Applera's intellectual property and complementary assets, key pieces to Applera's strategy within the molecular diagnostics industry. Using this understanding of the company's strategy we will assess the current commercialization environment and explain why Applera may not retain a majority of the value from its innovations. However, we will then consider a standard setting approach, which is an alternative that Applera can consider in efforts to increase the value it may obtain from its position in the molecular diagnostics industry. We will compare the strategy in this industry to the competitive structure of the computer industry, one that is dominated by standard setters such as IBM and Microsoft. Finally, strategic recommendations for achieving maximum growth and sustainability in this segment will be discussed.

## 2. Industry Overview

### 2.1. *In Vitro* Diagnostics

*In-vitro* diagnostic testing is the process of analyzing blood, urine and other specimens to screen for, diagnose and monitor diseases and other medical conditions or to determine the chemical and microbiological constituents of the specimens. Most of these tests require skilled technicians who must master numerous techniques and pieces of equipment provided by various vendors. No single technology or system has the monopoly in the *in vitro* diagnostics market, although big players, such as Abbott in the

clinical chemistry arena, have dominated various segments (Exhibit 1) . The largest segment of the \$22 billion *in-vitro* diagnostics market consists of clinical chemistry tests, followed by immunodiagnostics<sup>3</sup>. However, the most dynamic and promising product family, growing at five times the rate of the rest of the market, is molecular diagnostics (nucleic acid probe tests).

## ***2.2. Molecular Diagnostics***

The molecular diagnostic segment, while only about 4 percent of the total *in vitro* diagnostic market is the fastest growing segment due to new research into the genetics behind microorganisms, disease presence, prevalence, risk factors, and treatment plans. Molecular diagnostic revenues are currently only \$900 million a year but are expected to increase exponentially as more information about the relationship between these genes and disease become available. Today molecular diagnostics require sophisticated equipment and personnel and thus are slow to gain acceptance into the “old school” world of traditional diagnostics; where diagnosing disease is still guesswork. Genetic sequencers, machines that have automated the ability to identify a person’s human blueprint, have indeed helped the growth of molecular testing. These sequencers fueled the completion of the Human Genome Project (HGP) by rapidly sequencing the genomes of humans, bacteria, viruses and many other animals. Thus, this new genetic information has laid the groundwork for the development of clinical laboratory tests and therapies. Also helping the growth of molecular diagnostics has been the invention and mass utilization of polymerase chain reaction (PCR)<sup>4</sup>, a technique widely used to amplify DNA for accurate detection. PCR, a technology owned by Roche, and licensed to Applied Biosystems is the *de-facto* standard for amplification in the life sciences research market. PCR is beginning to make its way into the molecular diagnostics arena, and can be seen in both FDA approved tests as well as in “home brew” diagnostics tests<sup>5</sup>.

Today only 37 molecular diagnostics tests are FDA approved for used in the clinic, eight of them PCR-based (Exhibit 2). Most of these tests are for detection of infectious diseases such as sexually transmitted diseases and tuberculosis. In addition to infectious disease identification, the analysis of single nucleotide polymorphisms (SNPs), which are variations of nucleotide bases that can be related to disease

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<sup>3</sup> Medical & Healthcare Marketplace Guide

<sup>4</sup> Many consider the introduction and proliferation of polymerase chain reaction (PCR) technology to be one of the most significant innovations in recent science. PCR facilitates the diagnosis and characterization of disease by quickly and accurately replicating targeted sequences of genetic material.

<sup>5</sup> Home brew is a term used for diagnostics tests without FDA approval. By having the user add one ingredient that is not “packaged” in the test allows companies to sell a test (and clinicians to use it) as long as it is labeled “For research purposes only.”

<sup>8</sup> <http://www.applera.com/celeradiagnostics/corpinfo/corpinfo.html>

susceptibility, severity, progression, and responsiveness to therapy, are fast becoming an areas in which molecular tests are being developed. Genotyping for HIV and Hepatitis C Virus (HCV) accounts for approximately 90 percent of the genotyping performed today, and is expected to be applicable for a much broader range of disease states in the future. In addition to the expansion into infections disease testing and genotyping, growth is also expected in areas such as cancer diagnostic and prognostics. This oncology-based diagnostics approach has already been realized by Myriad Genetics' BRCA-1 and BRCA-2 tests. The concept of personalized medicine (pharmacogenetics) is also expected to play a huge role in the future of molecular diagnostics, whereby one day a doctor, before prescribing a particular drug to a patient, will test the patient to see how he or she will respond to a particular drug. The inclusion of pharmacogenetics testing to the molecular diagnostics market will undoubtedly change the industry and help grow the market to a significant portion of the in vitro diagnostics industry. This growth will be driven primarily by the availability and usefulness of content, i.e. SNPs and the owner of this content will be able to demand significant rents in the future.

### ***2.3. Competitive landscape***

A variety of companies have the opportunity to benefit from the impending explosive growth of the molecular diagnostics arena. Successful companies must either have access to amplification technology or be able to design around amplification requirements, be able to manage the significant regulatory hurdles that are required for market approval, and have access to sales channels. Sources of competition for Applera in molecular diagnostics include:

Traditional diagnostics companies - The competitive landscape contains entrenched players, such as Roche, Abbott Laboratories, Becton Dickinson and Bayer that have experience in maneuvering the complex regulatory approval process for diagnostic tests and have access to market channels. Applera is partnering with some of these players, including a potentially significant joint partnership in diagnostics with Abbott to develop and market molecular diagnostic assays.<sup>8</sup>

Amplification - PCR-based - Since PCR has become the standard in molecular testing in the life sciences research market, companies that have this technology should undoubtedly be included in any competitive analysis. Roche Molecular Diagnostics (Roche) holds the patents for PCR, which is widely accepted as the preferred amplification technology. Although this intellectual property position provides Roche with an edge in the molecular diagnostics arena, the company has also licensed this technology to

companies such as Applera<sup>9</sup>, Bayer, Chiron and BML (Japan). This licensing represents a huge source of potential revenue for Roche and is most likely the rationale behind Roche's decision to let competitors use its intellectual property.

In addition to holding the patents for PCR, Roche markets a system called COBAS Amplicor Analyzer that fully automates the PCR process, combining the processes of five instruments into one benchtop unit<sup>10</sup>. Roche is making a play to establish its platform in diagnostics laboratories, having already placed this unit in over 4000 labs worldwide. In addition, the company has developed and is seeking FDA approval to market a complementary instrument that will perform automated sample preparation. Roche appears poised to threaten any competitor's position in molecular diagnostics instrumentation.

Amplification - Non PCR-based - Other competitors are using technology other than PCR in an effort to design around the PCR patent owned by Roche. Companies such as Gen-Probe (transcription mediated amplification), Third Wave (Invader) and Becton Dickinson (strand displacement amplification) are offering alternative amplification technologies as substitutes for PCR. Ultimately these competing technologies have to be faster, cheaper or better, a difficult task considering the strengths of PCR. At this point in time, these potential competing technologies do not seem to be a significant threat to PCR-based systems, especially in the diagnostic testing, where the consumer is price sensitive. However, as seen in (Exhibit 3), a significant number of the FDA-approved tests use a non-PCR based amplification method.

No Amplification (potential disruptive technology)- Another group of competitors are attempting to bypass the amplification process completely. One rationale behind this is to avoid IP issues with Roche's PCR patent. Another reason revolves around the idea that amplification introduces both sources of error and increased cost, elements unwanted especially in diagnostics. These small companies, including Nanosphere, Inc., Clinical Microsensors (acquired by Motorola in 2000), and Molecular Staging all claim to have developed a more sensitive detection technology than simple fluorescence, the preferred detection method for PCR, offering the proposition that amplification can be totally eliminated. The technical and commercial success of one of these competitors would be a major threat to any company attempting to commercialize a PCR-based molecular diagnostics platform. Currently, these technologies still require

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<sup>9</sup> Applera includes Applied Biosystems, Celera Genomics, and Celera Diagnostics

<sup>10</sup> [http://www.rochediagnostics.com/ba\\_rmd/rmd\\_products\\_automated\\_pcr\\_system23.html](http://www.rochediagnostics.com/ba_rmd/rmd_products_automated_pcr_system23.html)

<sup>14</sup> [www.AppliedBiosystems.com](http://www.AppliedBiosystems.com)

more development before being commercially viable and they are not likely to be the first diffusive technology that enters molecular diagnostics, but rather subsequent generations.

### **3. Applera Corporation**

#### *3.1. Organizational Overview*

Applera Corporation, an established leader in the life science research market, is comprised of three subsidiaries, Applied Biosystems (ABI), Celera Genomics and Celera Diagnostics, a joint venture between ABI and Celera Genomics formed April of 2002.

##### *3.1.1. Applied Biosystems (ABI)*

ABI, headquartered in Foster City, California provides high quality instrument systems to the basic research, commercial research and standardized testing markets. Basic research includes work in academic facilities, government and other non-profit institutions that focus on uncovering the basic laws of nature, and comprises about half of the revenue of ABI. An additional one-third of the revenue of ABI comes from pharmaceutical and biotechnology companies, applying the company's products to molecular medicine: discovering new drugs more effectively. The remaining revenues come from standardized tests for customers who place priority on precise results from a high volume of automated tests.<sup>14</sup>

The company's products include: DNA sequencers, chromatography, mass spectrometers, thermocyclers (PCR<sup>15</sup> machines), test reagents, dyes, and consumable kits that are required for use with the instruments. An advertisement showing their platform lineup for the life science industry is shown in Exhibit 3. ABI's platforms have become the standard in the life sciences research industry by offering the consumer a variety of choices in throughput, flexibility in assay design, high quality reagents, and technical service.

##### *3.1.2. Celera Genomics*

Celera Genomics headquartered in Rockville, MD focuses on the generation of genetic content through DNA sequencing technology. In fact, many say that the sequencing of the human genome was entirely due to the efforts of Celera Genomics. From that effort alone, Celera Genomics has identified approximately 30,000 genes, and amassed a database of more than 3 million single nucleotide polymorphisms (SNPs). Although the human genome sequence is in the public domain, the SNPs and gene expression satellite information remains proprietary to Celera Genomics. Now that the genome is

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<sup>15</sup> polymerase chain reaction

sequenced Celera Genomics is focusing on further identifying the SNPs and their relationship with diseases. These markers will be used as diagnostic targets for its JV, Celera Diagnostics.

### *3.1.3. Celera Diagnostics*

While structured as a JV between ABI and Celera Genomics, Applera's corporate description reflects Celera Diagnostics as a "third" division, positioning the company for development and commercialization of diagnostics products using ABI's instrumentation and reagents and Celera Genomics' content. This integration of competencies is the first of its kind for molecular diagnostics and serves as a unique and insightful approach in the diagnostics industry.

## **3.2. Intellectual Property**

A molecular diagnostics product is comprised of two primary types of intellectual property assets, amplification technology and content. Applera's retains varying levels of control over these two assets.

### 1. Amplification technology (PCR)

Applera has licensed Roche's PCR patent, critical for success in the molecular diagnostic market, at least in the short term. However, this license is not exclusive and other players, including Roche can build competing products utilizing this intellectual property

### 2. Content – genes and probes

Content ownership is Applera's intellectual property strength. Celera Genomics owns vast quantities of genomic information or content, which is a key component of a particular molecular diagnostic test, and even though the Patent law surrounding genetic information remains unclear, the potential value of owning the content is high and an important consideration for anyone currently in the molecular diagnostics market. The early patent "Gold Rush" surrounding the human genome sequencing effort prompted many to question the validity of gene patents. Some effort has been made by the USPTO to clarify the issue and as a result, have raised the bar for the patenting of genes, requiring the establishment of "well-established utility". Since molecular markers of disease appear to satisfy the USPTO's requirement for utility, Celera Genomics may be able to identify key changes in disease states, and thus, should be able to establish some valuable intellectual property.

By analyzing DNA from many individuals, both healthy and diseased, Celera Genomics is identifying single nucleotide polymorphisms (SNPs) that may give insight into disease susceptibility. By appropriating this information through patents, a key component of the molecular diagnostics market

value will be captured by the company. Perhaps the biggest uncertainty in Applera's future ability to capture value in the molecular diagnostics market revolves around its content strategy and its attempt to secure intellectual property around these discoveries.

Regardless of the IP status of any individual gene test, Applera's enormous existing gene database is a key component to the company's commercialization strategy.

## **4. Commercialization Environment**

In assessing the likely patterns of commercial interaction in this emerging industry, we considered both the nature of the appropriability environment and the distribution of ownership and control over specialized complementary assets.

### ***4.1. Appropriability***

Appropriability is weak if competitors can imitate products or when other players control specialized complementary assets.<sup>19</sup> Today, there are few players that make good quality, cost-effective molecular platforms. Applera's proven strength in platform/instrumentation for the life sciences industry will have a direct impact on molecular diagnostics. However due to the fact that many players already make PCR-based instrumentation (and have a license from Roche to do so), Applera's instruments will not in their current form, preclude entrance from other competitors.

With respect to content, Applera has generated an enormous amount of genetic material it sequenced and should be able to leverage this content in the molecular diagnostics arena. Although this content does not preclude effective development of products by competitors (many other companies also own IP rights to genes and SNPs), the sheer magnitude of Applera's content could give them a significant level of total appropriability as no player will own more content.

### ***4.2. Complementary Assets***

In order to commercialize its product successfully, Applera must either own or obtain a variety of complementary assets including access to marketing, manufacturing, distribution channels, FDA approval expertise, and supporting technologies such as reagents and instrumentation.

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<sup>19</sup> "The product market and the market for "ideas": commercialization strategies for technology entrepreneurs"; Gans, Joshua S; Stern, Scott; *Elsevier Research Policy* 1441 (2002) 1-19

#### 4.2.1. *Strategic Partnerships*

In order to successfully compete with incumbents like Roche, Applera must gain access to marketing, manufacturing, distribution, and most importantly regulatory affairs for FDA approval. To do so, Applera has turned to a partnership strategy with a well-established firm in the diagnostics field, Abbott Laboratories. Abbott ironically found itself needing a partner to bolster its chances in the new molecular diagnostics arena after leading in the diagnostics industry for many years. In June 2002, Celera Diagnostics announced their alliance with Abbott Laboratories to develop and market diagnostic tests<sup>20</sup>. Under the agreement, Celera Diagnostics will be responsible for identifying and developing new molecular markers for diseases, and Abbott will contribute product development, marketing, and sales. This alliance with Abbott will assist Applera in its efforts to establish its platform for use in by tests later developed by both firms. As Kathy Ordonez, President of Celera Genomics remarked, “I think we’re going to develop the next-generation platform together”.<sup>21</sup> In this deal, the two companies have agreed to share patents, including a key patent for the Hepatitis C virus that Abbott licensed from Chiron. The viral testing business is what the Abbott-Applera alliance has focused on initially, hoping to follow these with products for other areas of disease diagnosis and progression. And in 2002, the FDA granted Abbott and Applera the right to market the HIV Viroseq genotyping kit for use in the ABI PRISM 377 sequencer. In February, 2003, clearance was granted for the upgraded kit to be used in the capillary format ABI PRISM 3100 genetic analyzer, an instrument that has gain widespread acceptance in reference labs and larger hospitals.

As shown in Exhibit 4, the complementary assets that Applera has gained access to through this arrangement should improve the company’s chances of success in molecular diagnostics.

As a leader in sales of other diagnostic technologies, Abbott can contribute established relationships with most clinical laboratories as well as established collaborations with other companies for test reagents and instruments that can be developed for use with the Applera platform. In addition, with an existing sales force of over 2500, extensive resources in distribution and sales of diagnostic instruments and reagents can be leveraged by the joint venture. Abbott’s in-house experience in regulatory affairs and large-scale production of reagents at quality levels required for FDA approved diagnostics reagents and instrumentation is also a key component of this partnership. Abbott will be able to aid Applera in

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<sup>20</sup> <http://www.applera.com/corpcomm/applerapress.nsf/CDXdisplaypress>

<sup>21</sup> [http://www.forbes.com/2002/6/25/0625celera\\_print.html](http://www.forbes.com/2002/6/25/0625celera_print.html)

developing and receiving marketing approval from the FDA through its experience in developing reagents in other areas of diagnostics

To further enhance its chances at successfully commercializing molecular diagnostics, Applera has recently entered into agreements with large diagnostic laboratories such as LabCorp of America and Quest Diagnostics.<sup>22</sup> These companies will provide clinical expertise and samples to aid discovery of genes associated with diseases such as diabetes, cardiovascular disease, and connective tissue disorders. In return, Applera will be a preferred provider for molecular diagnostics instruments and reagents to the firms. This is significant as Quest Diagnostics and LabCorp are the two leading providers of diagnostic testing, information, and services, including gene-based medical testing. In addition, Applera has recently partnered with Bristol-Myers Squibb to study genes associated cardiovascular disease and diabetes in the hope of identifying new opportunities for diagnostic development coupled with therapeutics. These partnerships are critical to Applera's successful strategy in molecular diagnostics.

#### *4.2.2. Reagents*

ABI has a key core competency in its ability to manufacture high quality and cost effective reagents. This is extremely important, as reagents are a significant cost of producing a molecular diagnostics test. Furthermore, since the quality of the reagents is essential to securing a reliable assay (integral to FDA approval), maintaining good quality control in-house is essential to the success of the diagnostic test. ABI has been a standard high quality reagent producer for many years and has a good reputation to stand behind.

#### *4.2.3. Instrumentation*

Applera has built a reputation for quality and technological excellence in the life sciences arena, and the one place this can be easily seen is in their platform technologies. Its plethora of analytical instruments gives Applera a leg up as it attempts to make the move from the research to the diagnostics arena. Applera's strategy includes leveraging its genetic analyzers, including the ABI PRISM 7700 and ultimately offering a complete package or system that includes the instrument/platform, molecular test, reagents and software.

### **4.3. Position in the Commercial Environment**

Based upon the above analysis of both appropriability and commercialization, we have concluded that Applera's ownership of essential assets, in particular, instrumentation and especially genetic content can

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<sup>22</sup> <http://www.applera.com/corpcomm/applerapress.nsf>

preclude effective development by the incumbents. However, the complementary assets held by Abbott add to the value proposition of Applera's technology, and therefore the company will be trading in the "Market for Ideas" and acting as an "Ideas Factory". Please see Exhibit 5 for a table depicting this analysis.

#### ***4.4. Value in the Commercialization Environment***

A question remains as to who will capture the value from a successfully developed and commercialized Applera molecular diagnostics product. Certainly, for any product that significantly advances diagnostic medicine in areas of unmet medical need such as cancer, there is little doubt that the end-user, the patient will garner the vast majority of value. But who else stands to profit from Applera's innovations?

- Physicians and health care workers will benefit by more accurate and insightful testing procedures (like x-rays did for medicine).
- Applera stands to profit significantly if it can build its library of intellectual property for content. If the company is successful at maintaining instrument base in advanced clinical laboratories, it will also minimally (as compared to its content piece) benefit through sales of instruments and consumables.
- Complementary products, such as content companies developing tests on Applera's platform (i.e. Abbott) other firms that license content to or develop tests for use on Applera instruments and themselves obtain licenses from the company
- Roche Diagnostics, the current leader in the molecular diagnostics market, has all of the necessary complementary assets and will benefit from PCR licensing revenue on Applera products, as well as potentially being able to piggyback on any commercialization or customer development efforts that Applera enters in to.

## **5. Commercialization Strategy**

### ***5.1. Standards Strategy***

Our analysis indicates that Applera can leverage its early strength in platform technology and content (IP) to attempt to create an industry standard for molecular diagnostics. Due to its position in the commercialization structure, its partnership with Abbott will be essential to build this standard.

The development of an open Applera platform that will be compatible with both Applera and competing companies tests would mirror the strategy utilized by Microsoft in the computer industry. Similar to the computer industry, the standardization of the molecular diagnostics industry will require

hardware/platform players, content/software players, and operating system players. In the computer industry companies such as IBM, Intel and Microsoft created and drove industry standards:

- Hardware - IBM used its dominant position to define a standard and attempted to diffuse it using open standards for most of the system, while retaining what was expected to remain a proprietary essential component, ROMBIOS;
- Operating System – Microsoft built a proprietary operating system with open standards and created a stronghold by encouraging the creation of many complementary products and building an extremely high level of network externalities;
- Microprocessor – Intel created and marketed a processor which became part of the “Intel-inside” standard on most PC’s in the 1990’s;
- Content/ Software – through its open standards, Microsoft encourages competitors to build complementary products such as software, which increases network externalities and strengthens the position of the Microsoft operating system. In addition, Microsoft also competes in the lucrative software market by creating software and leveraging its unique position as the standards holder to disseminate it.

For the molecular diagnostics industry, one can envision a similar standard setting phenomenon. If Applera took the initiative to try to create a standard, it could look something like this:

- Hardware – Applera uses its dominant position in instrumentation/platform in the life sciences research industry to define a standard (i.e. ABI PRISM 7700) in the molecular diagnostics industry and attempts to diffuse it using open standards for most of the system, while retaining a proprietary essential component, i.e. some key proprietary “lock” that hopefully will be stronger than IBM’s ROMBIOS. This proprietary “lock” will help Applera secure rents and block out competitors attempting to “clone” the platform;
- Operating System – Applera already has a well accepted operating system used with its platforms (sample in answer out), thus with the willingness to create an open standard, Applera could create a stronghold by the recruitment of players to write tests, and with each test, building a greater consumer base and network externality;
- Microprocessor – It is in Applera’s best interest to make sure PCR becomes the “Intel-inside” for molecular diagnostics testing (see Exhibit 6 for PCR flowchart). This will help preclude disruptive technologies, such as non-PCR based platforms from competing with Applera;
- Content/Tests – Through its open standard platform, Applera will encourage competitors to build diagnostic tests and with each test offering, will increase Applera’s network externalities and thus, strengthen Applera’s position as a standard operating system. In addition, Applera will also

compete in the lucrative “molecular testing” market by creating its own tests and leveraging its unique IP position (for content) and will be the standards holder to disseminate it.

### ***5.2. Speed to Market and Market Acceptance***

Applera must develop a commercialization strategy that installs its platform and portfolio of tests in hospitals and clinics as soon as possible. Because the field is changing rapidly, Applera can follow the MS Windows strategy of capturing the market quickly and then revising later version of the technology based upon feedback from the clinical setting. Ultimately, Applera will generate the greatest amount of revenue from the consumables and thus, should consider the “razor blade” strategy, give away the instrument, recoup revenue from the tests and reagents.

Many clinical diagnostics labs that already perform more advanced molecular-based techniques utilize ABI instruments. The company hopes to exploit this fact to establish a base within these labs. As the molecular-based tests diffuse into more mainstream clinical labs, Applera will have the initial customer base serve as a reference for these later adopters. In addition, many of the techniques and assays utilized for molecular diagnostics were developed in life sciences research labs. Therefore the key personnel in large clinical diagnostics laboratories that utilize diagnostics techniques have often been trained in research labs. This experience and reputation is something that Applera can leverage as it begins to infiltrate the molecular diagnostics industry. Applera needs to utilize its life science industry customers to provide a good reference in order to rapidly build a loyal following in diagnostics labs (influencers to help cross the chasm).

### ***5.3. Powerful Technology Proposition***

Applera’s experience in the life sciences arena should allow the company to create a high quality molecular diagnostics platform. Applera must follow their existing model of creating a platform of machines since customers will have varying requirements. For example, research hospitals will require expanded capabilities over local clinics. The first generation platform may be more appropriate for research hospitals, where skilled technicians work. Going forward, Applera can learn how to strip the model down to expand into the lower end market while maintaining all technical and regulatory requirements. For example, the portion of the platform that is approved by the FDA must be portable across all models in the platform lineup.

### ***5.4. Complementary Assets***

In order to build an industry standard, a company must leverage a variety of complementary assets including strategic partnerships, customer relationships, distribution channels, and supporting

technologies. Applera is accessing complementary assets through its alliance with Abbott as well its enormous content portfolio.

Similar to Microsoft's strategy of encouraging the development of complementary products such as software, a standard setter in the molecular diagnostic arena must also ensure that there is wide availability of supporting technologies and this must encourage development of complementary products such as tests and analysis software. An interesting lesson from the computer industry is the availability of software to run on the PC, product that can be considered analogous to assay and content in molecular diagnostics. The availability and compatibility of software programs was what drove computer buyers to choose the open standard IBM instead of the closed standard Apple. Comparing this to the molecular diagnostics industry, a wide array of companies own intellectual property on genes and probes and therefore establishing an open standard may attract these companies to build compatible tests. By making an array of compatible tests available under the 'big tent' of a single platform will increase the overall utility of the platform and therefore will reinforce its market dominance.

In addition to encouraging other companies to create assays for its platform, Celera Diagnostics will also continue to develop its own proprietary tests. This is similar to Microsoft's strategy of encouraging companies to write Windows compatible software, while also competing in that software market with its own products such as Excel. By encouraging both the proliferation of its own and its competitors' tests, Applera will drive demand for the complete system, which will also drive significant ancillary revenue for the company such as reagents and consumables test kits. The creation of a standard will not only create value for the sponsoring company but will also build value for the market through economies of scale, network externalities, product complementarities, and learning by using.

## **6. Conclusions and Outlook for Applera**

The combined assets of ABI, Celera Genomics and Celera Diagnostics make Applera a formidable player in the emerging molecular diagnostics market. For Applera to have long-term success and fend off the intense competition in this marketplace, it needs to continue to improve upon many of the facets of the strategy it appears to have embarked on.

- It needs to entrench itself in the larger clinical diagnostics labs and build the reputation there that it successfully established in life sciences labs. Using these larger labs as references, it should expand its

presence by developing instruments that provide customized features for clinical labs (sample handling/throughput/documentation).

- In combination with the instruments, it need to provide a wide variety of tests for use on these instruments will power the establishment of Applera's platform as a standard in molecular diagnostics. To do this, the company must continue to secure content, both from within its own discovery efforts (Celera Genomics) and with external licensing and collaboration, to provide a large variety of tests to run on its instruments. Until its internal content becomes fully realized, Applera needs to recruit content players to make tests (or have Applera make) on its platform.
- Applera's partnership with a company like Abbott Labs appears to provide the complementary assets to accelerate commercialization in the diagnostics market and establish its platform in the face of intense competition from the likes of Roche Diagnostics. Applera should try to form as many partnerships as possible (assuming the relationship with Abbott does not preclude this)
- As Applera becomes the standard platform for molecular diagnostics tests, it will benefit directly both from sales of instruments, reagent sales as well as the tests it develops with strategic partnerships such as Abbott and the tests it develops in house. As a standard, Applera then has the opportunity to profit from other firms that develop tests based on these platforms through granting licensing fees for use of its reagent/instruments. While further growing the number of tests available for its platform and thus its network externalities, Applera would have some control through this licensing process to avoid having tests that directly compete with its own (Celera Diagnostics) offerings (similar to Microsoft's strategy; although one can say they took it far too far considering the Netscape fiasco).

**EXHIBIT 1****In Vitro Diagnostic Market Definition by Segment**  
(\$ Millions)

	<b><u>1998</u></b>	<b><u>2003E</u></b>
Clinical Chemistry	\$6,570	\$7,000
Immunochemistry	\$5,650	\$6,400
Glucose Monitoring	\$2,700	\$3,800
Hematology/Flow Cytometry	\$1,300	\$1,350
Microbiology	\$900	\$1,000
Blood Banking	\$775	\$950
Nucleic Acid Probes	\$500	\$900
Coagulation	\$450	\$500
Other	\$300	\$400
<b>Total</b>	<b>\$19,145</b>	<b>\$22,300</b>

Source: US Bancorp Piper Jaffray Research: In Vitro Diagnostics in the Millennium, March 1999

**EXHIBIT 2**

**FDA-APPROVED MOLECULAR DIAGNOSTICS TESTS**

The following table is a listing of the *in vitro* molecular diagnostics tests that are cleared for diagnostic use in the United States by the US [Food and Drug Administration](http://www.fda.gov). Such tests are classified as "biological devices" and they are listed by year of approval at <http://www.fda.gov/cber/products.htm>.

TEST or ANALYTE	METHOD	COMPANY
B/T cell gene rearrangement	Southern blot	No longer commercially available
<i>bcr</i> gene rearrangement	Southern blot	No longer commercially available
<i>Chlamydia trachomatis</i> and <i>Neisseria gonorrhoeae</i> detection <sup>1</sup>	PCR <sup>2</sup>	Roche
<i>C. trachomatis</i> detection	LCR	Abbott Laboratories
<i>C. trachomatis</i> detection	TMA	Gen-Probe
<i>Gardnerella</i> and <i>Trichomonas vaginalis</i> and <i>Candida spp.</i>	Hybridization	Becton Dickinson
<i>C. trachomatis</i> / <i>N. gonorrhoeae</i> detection <sup>3</sup>	Hybridization and Amplification	Gen-Probe
Culture confirmation for <i>Mycobacteria spp.</i> ; different fungi and bacteria <sup>4</sup>	Hybridization	Gen-Probe
Direct detection of Group A <i>Streptococci</i>	Hybridization	Gen-Probe
HIV quantitation	RT-PCR	Roche
HIV quantitation-ultrasensitive	RT-PCR	Roche
HLA Class II Typing	PCR	Gen-Trak
HLA Class II Typing	PCR	Biotest Diagnostics Corp.
Human Papillomavirus typing/screening	Hybridization	Digene
<i>M. tuberculosis</i> detection	PCR	Roche
<i>M. tuberculosis</i> detection	TMA	Gen-Probe
<i>Neisseria gonorrhoeae</i> detection	LCR	Abbott Laboratories
Chr. 8 quantification in leukemia patients	FISH	Abbott Laboratories <sup>5</sup>
CEP 12 SpectrumOrange DNA Probe Kit to assess chromosome 12 status in CLL	FISH	Abbott Laboratories <sup>5</sup>
AneuVysion™ assay to detect Down syndrome and other chromosomal abnormalities associated with birth defects and mental retardation	FISH	Abbott Laboratories <sup>5</sup>
INFORM HER-2/ <i>neu</i> Gene Detection	FISH	Oncor, Inc. <sup>6</sup>
PathVysion™ HER-2 DNA Probe Kit	FISH	Abbott Laboratories <sup>5</sup>
Hybrid Capture CMV DNA Test	Hybrid Capture	Digene
Hybrid Capture II HPV DNA Test	Hybrid Capture	Digene
Cytomegalovirus (CMV) pp67 mRNA	NASBA	Organon Teknika

BDProbeTec ET system for <i>C. trachomatis</i> and <i>N. gonorrhoeae</i>	SDA	Becton Dickinson Microbiology Systems
Hybrid Capture II <i>N. gonorrhoeae</i> DNA Test	Hybrid Capture	Digene
Hybrid Capture II <i>C. trachomatis</i> DNA Test	Hybrid Capture	Digene
HLA-DR oligo detection kit	Hybridization	bioMerieux
HCV	PCR <sup>2</sup>	Roche
UroVysion test for monitoring recurrence of bladder cancer	FISH	Abbott Laboratories <sup>5</sup>
Trugene HIV drug resistance test and OpenGene DNA sequencing system	DNA Sequencing	Visible Genetics
CEP X SpectrumOrange/CEP Y SpectrumGreen Chromosome Enumeration DNA Probe Kit for measurement of engraftment of sex-mismatched bone marrow transplantation	FISH	Abbott Laboratories <sup>5</sup>
NucliSens HIV-1 QT Quantitative Viral Load Assay	NASBA	bioMerieux
HIV/HCV in blood donations	TMA	Gen-Probe (distributed by Chiron)
VERSANT HIV-1 RNA 3.0 Assay bDNA	bDNA	Bayer
Group B Streptococcus	Real Time PCR	Infectio Diagnostics
ViroSeq HIV-1	DNA Sequencing	Celera Diagnostics (distributed by Abbott Laboratories)
Versant HCV RNA (Qualitative)	TMA	Gen-Probe (marketed by Bayer)

Abbreviations: PCR, Polymerase Chain Reaction; LCR, Ligase Chain Reaction; TMA, Transcription Mediated Amplification; RT-PCR, Reverse Transcriptase Polymerase Chain Reaction; FISH, fluorescence *in situ* hybridization; CLL, chronic lymphocytic leukemia; NASBA, Nucleic Acid Sequence Based Amplification; SDA, Strand Displacement Amplification; bDNA, Branched Chain DNA Signal Amplification.

<sup>1</sup> *C. trachomatis* and *N. gonorrhoeae* detection may now be done using the Roche COBAS Amplicor system directly from Cytyc Corporation's ThinPrep Pap test collection kit; this use is FDA approved.

<sup>2</sup> Microtiter plate-based and COBAS-AMPLICOR-based

<sup>3</sup> Casco Standards (Portland, ME) received FDA approval of its Document Molecular Pathology STD controls (positive and negative) for *C. trachomatis* and *N. gonorrhoeae* as formulated specifically for the Abbott LCx system. (7/98)

<sup>4</sup> *Campylobacter spp.*; *Enterococcus spp.*; Group B *Streptococcus*; *Haemophilus influenzae*; *N. gonorrhoeae*; *S. pneumoniae*; *Staphylococcus aureus*; *Listeria monocytogenes*; Group A *Streptococci*; *M. avium*; *M. intracellulare*; *M. avium* complex; *M. gordonae*; *M. tuberculosis* complex; *M. kansasii*; *Blastomyces dermatitidis*; *Coccidioides immitis*; *Cryptococcus neoformans*; *Histoplasma capsulatum*

<sup>5</sup> Formerly a Vysis Product

<sup>6</sup> acquired by Ventana Medical Systems in November 1998

**ABI's Life Science Platform**

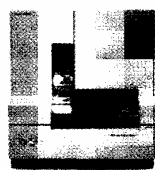
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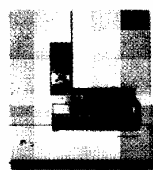
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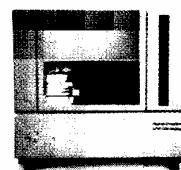
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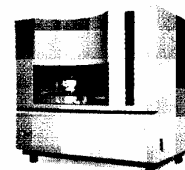
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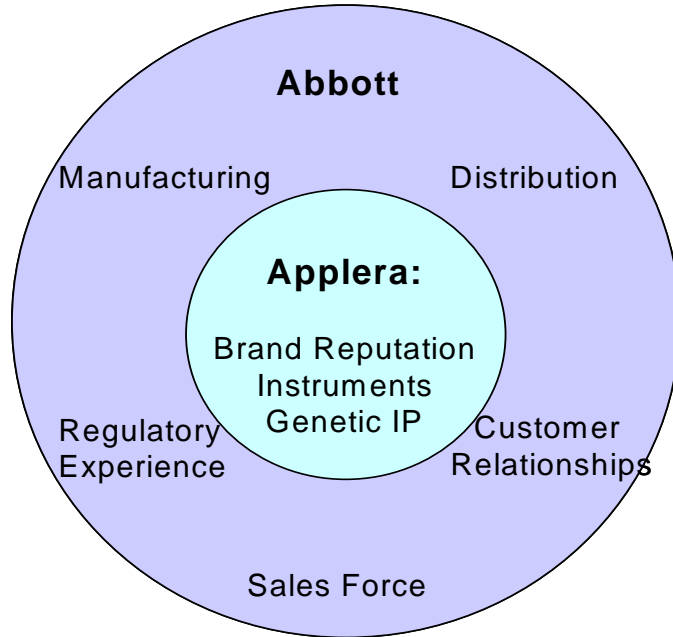
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**EXHIBIT 4**

**Assets Contributed to June 2002 Applera / Abbott Alliance**



**EXHIBIT 5**

**Applera's Commercialization Environment**

		Do incumbent's complementary assets contribute to value proposition from new technology? ( <i>Abbott, Roche</i> )	
		NO	YES
Can Invention by the start-up preclude effective development by the incumbent? ( <i>Applera</i> )	NO		
	YES		<b>Molecular Diagnostics Ideas Factory</b>

## EXHIBIT 6

### Flowchart of an automated PCR analyzer

