1 November 2010

INTERSUISSE

Genera Biosystems Limited (GBI)

Best in Class – The Future of Pathology Diagnostics

Important: *Intersuisse and associate companies Phillip Capital Pty Ltd and IB Managers Pty Ltd are currently retained by Genera for capital market services on commercial terms. For Disclosures, refer to the back page under "Important Information"*

The technology platform can be used to enhance a number of commonly used commercial pathology laboratory assays.

PapType™ for the detection of HPV, the causation of cervical cancer, has the potential to redefine HPV diagnostics.

In May 2010, Genera entered a collaboration with Healthscope to develop a single diagnostic test for respiratory pathogens.

'Genera' develops and commercialises multiplexed molecular diagnostic tests, based upon its proprietary AmpaSand™ bead-based technology. Its products compete in the US$3-5 billion global market for molecular diagnostic tests.

- **Its PapType™ HPV assay has Australian Therapeutic Goods Administration (TGA) approval and CE Mark (European) approval. It is used as the HPV assay of choice by Healthscope Limited**
- **Genera has entered a research and development agreement with a 'Top-10' Global Diagnostics Group**
- **This is expected to lead to licence fees early in 2011.**

Snapshot

Last Price	$0.48
Market Cap.	$30 million
52 Week High	$0.91
52 Week Low	$0.40
Sector	Diagnostics

NB: Currency is Australian $ unless marked US$

Price Chart

AmpaSand™ beads are an ideal platform for the kind of medium density multiplexed tests (5-150 analytes) of most use to pathology labs. Genera's bead-based tests are high throughput, simple to use, and leverage existing laboratory infrastructure and expertise.

Genera's first product on sale is PapType™, a highly competitive molecular diagnostic test for the simultaneous detection and genotyping of the 14 types of HPV that are responsible for causing cervical cancer.

See www.generabiosystems.com

Investment Highlights Genera Biosystems Limited, 'Genera', (ASX:GBI) is an Australian Diagnostic company, marketing the next generation human papillomavirus (HPV) diagnostic in Australia with plans to take its advanced diagnostic platform to the world. Genera manufactures its products at a custom-built facility in Melbourne.

Recognising the clinical and commercial advantages of PapType™ the company has entered into a research and development agreement with a Top-10 Global Diagnostics Group. There is a strong alignment between the profile of PapType and the partner's technology. In the event that the development programme proves successful, it's likely that the combination of both companies' products will introduce a new approach to cervical cancer screening.

Any deal associated with the outcome of the R&D agreement is anticipated around March 2011. The deal would be expected to lead to an upfront license fee in the order of $15 million to $25 million, milestone fees and a near double-digit royalty on sales.

So, within the next 9 months, Genera could shift from being a Research focused company to a Development and Commercialisation company. The deal would be a transformational event.

The PapType certifications, validations and platform development work achieved to date 'on the smell of an oily rag', are not reflective of the value of its IP in an acquisitive molecular diagnostics market.

We consider it not unreasonable that Genera could be worth $100m+ within a reasonable time frame, given the market in which it operates, the maturity of its relationship with a significant diagnostics partner, the versatility of the technology, and comparisons with similar companies.

Contents:

A: The Genera Story – A simplified summary

On these two pages we present a summary overview of Genera, its platform, products and current and potential place in molecular diagnostics. References, eg *(21),* indicate pages for further detail.

MDx & IVD a growing …

The Landscape is Molecular Diagnostics, "MDx" – a US$3-5 billion[1] market and one of the fastest growing sub-segments of the larger *In Vitro* Diagnostics (IVD) market, where major companies are putting new research competencies into work to identify and treat disease. Diagnostics comprise less than 5% of hospital costs and 1.6% of US Medicare costs, yet influence 60-70% of healthcare decision-making[2] *(4).*

… and acquisitive space

The market is characterised by rapid growth and demand for innovation from biotech advances. Big players want breakthrough techniques for leadership, revenue and profit growth *(15-16)*.

Enter the Young Genera:

In the late '90's, Dr Karl Poetter joined a genomic technology development programme of the Walter and Eliza Hall Institute for Medical Research (WEHI) and the Australian Genome Research Facility (AGRF). At the heart of Genera is the method of identifying very subtle differences in DNA sequences developed by Dr Poetter *(5-6).* Many different types of DNA in one sample can be identified in one pass through commonly available PCR and flow cytometer lab equipment, with proprietary operating treatment and systems and automatic software analysis *(8)*. The technology can be applied to any DNA, whether human, viral or other, In addition, small modifications in the technology make it suitable for identifying other important biological molecules, such as proteins.

AmpaSand™

How it works

Genera was formed, its platform technologies developed, proven and patented, and used to solve research problems in a variety of fields. A case of Products seeking Markets, the technology is ideally suited for the kinds of molecular diagnostic tests used by pathology laboratories. Gribbles, a pathology business that was acquired by Healthscope *(4,6,9,10+)*, approached Genera to develop a test which could detect and genotype human papillomavirus (HPV), and PapType was born**.** *(4)***.**

Healthscope PapType™

Diagnostics in Cervical Cancer Screening, and Genera's advantage *(17-21)*

Within the last decade, it has been found that HPV is the causation of 99.8% of cervical cancers. The cervical cancer screening market is dominated by cervical cytology – originally the Pap Smear but now largely Liquid-Based Cervical Cytology (LBCC) in developed markets. Taking consistent and effective samples for cytology is difficult and analysis requires expert clinicians. It has become accepted that HPV tests indicate pre-cancerous conditions with higher accuracy and repeatability.

The market for HPV testing for cervical cancers appears to be here to stay and whilst it is currently around US$350m, estimates of its eventual size are ~US$1-2bn. While debate remains about its changing role in cervical screening, the overall market is moving towards HPV and the move is likely to accelerate as accurate individual one-pass HPV-type evaluation (such as with Genera's PapType) becomes globally available, particularly with effective allied instrumentation *(18-19)*.

The target market For Genera's first Product – Pap-Type

In the last 15 years, cervical cancer screening has progressed through three phases. Phase I: Cytology using Pap test & LBCC; Phase II: adding HPV where abnormalities are seen ("Reflex" testing) or as an adjunct to cytology; Phase III: now underway with HPV genotyping increasingly used to add sensitivity; we are now entering Phase IV: screening in the new era of vaccines *(19)*.

Qiagen and Hologic are the only companies that currently market FDA approved HPV diagnostic tests in the US. Roche is expected to launch a product in the near future, and also Gen-Probe. Whilst PapType is not short of competition from larger and smaller companies, PapType has perhaps an optimum combination of the provision of actionable clinical data with speed of throughput and automatic objective data analysis. PapType can distinguish all cancer-causing HPV genotypes, in a single reaction, and provides software-generated results *(21, 7-9)*.

In the next 10 years, Phase IV will emerge, likely led by HPV testing. **Genera is well positioned to take advantage of both the third and fourth phases**; in Phase IV, Genera's PapType can have **first mover advantage**. Vaccines will change cancer incidence only gradually, say over 20 years as vaccinated women become predominant, so any decline in testing needs will be gradual, and offset by greater needs for accuracy and specificity, particularly with sharply declining numbers of graduates electing to become cytologists and as rising costs drive the need for more automated systems *(19)*.

By 2004 Genera had developed PapType and applied for patents. It launched a partnership with Gribbles, which put PapType into use in its labs in 2005 after substantial testing. Healthscope continues to use PapType as its HPV test of choice *(4, 7-9)*.

[1] 2008 Roche diagnostics presentation.
[2] Gen-Probe 2009 Corporate presentation

Genera History (25)

Clinical Studies *(9)*

Shareholders *(26)*

Manufacture to TGA & ISO standards

PapType hasTGA approval & CE Mark

'Top-10' Group

IP, Other Products & Prospects

Automation

The Beach™

RTI-plex™

Board & Advisers

Accounts, Estimates

News Flow

Partnership

Other Products

Prospects

Genera Drives Forward Strongly with PapType, Finds a Potential Partner

Having settled on PapType as its initial product, Genera pushed ahead to gain progressive validation. PapType was tested at the Royal Women's Hospital in Melbourne (RWH) *(9,12,21,23),* where it outperformed existing HPV tests. It was tested by Sonic Healthcare *(5,14,23),* which helped explore its potential through repeatability studies in exchange for a shareholding in Genera. Sonic is not yet a commercial customer for PapType but remains in dialogue with Genera.

Regular capital raising has funded Genera's development; its IPO raising $5m in June 2008 *(26)*.

A major step was a move to new labs at Scoresby, customised for manufacture of diagnostic tests and subsequently accredited by ISO and the Australian Therapeutic Goods Administration (TGA). All Genera's critical processes are managed using ISO13485 standards, the quality standard that governs diagnostic testing. The TGA audits the manufacturing to these standards as well. The FDA uses its own standard, but this is highly analogous to ISO 13485 *(4,23,25).*

Following ISO/TGA manufacturing systems accreditation, PapType was approved by the TGA and carries the CE Mark *(4,5,25)*, making it available for use in Europe. Genera's strategy has been that a partner would fund any US trial –a prerequisite for use in the USA.

In May this year a 'Top-10 Global Diagnostics Group' - within the top 10 in terms of global sales - entered into a Research and Development agreement with Genera *(5,14,24,26).*

Genera says the partner's instrumentation could, with minor modifications of Genera's technology, use PapType and such modifications are now in hand preparatory to the partners' validation on its equipment. Genera says the technological and strategic fit of PapType with the partner is very close; it is also interested in Genera's platform and possibly other products *(5).*

That Genera's assay is relatively simple to perform, using commonly utilised molecular biology techniques; that it should integrate with the partner's own technology; and that Genera's test is CE marked and TGA approved, should allow the partner to rapidly enter half of the global market on integration *(5).* The partner has indicated that the US, and obtaining the implied FDA approvals, is within its plans should the R&D be successful *(19)*.

Meanwhile, Genera has been developing its IP and its Product Portfolio

Genera has dedicated almost a decade to the development and applications of its platform and AmpaSand bead technology. The Intellectual Property continues to be built up *(6)*, while other paths of commercialisation have been initiated *(9-13)*.

Automation is a critical factor in the purchasing decisions of pathology laboratories *(7,18-19).*

Some major players are keen on the AmpaSand platform technology—which lends itself to integration into an automated laboratory—but not to use it without dedicated instrumentation, following the classic 'razor - razor-blade' model for diagnostics businesses *(10)*. Genera has been encouraged to develop its own desktop automated instrumentation to perform its tests.

A prototype integrated device will use largely *off-the-shelf* components; it should cost $0.75-1.25m for a 'beta' version, probably the same again for a production version; the aim is a beta developed desktop instrument 'The Beach™' in 2011 and a partnership / market launch in 2012 *(11,24).*

In May 2010 Genera agreed to collaborate with Healthscope to develop a test for simultaneous detection of multiple different respiratory tract pathogens in a specimen—'RTI-plex™' *(9-10)*; Healthscope will fund and provide resources and can buy the tests for its own use. Genera retains global commercialisation rights; it expects TGA approval & CE Mark in 2012 *(24)*, and is currently in dialogue with the FDA in order to understand the requirements for a US filing *(10).*

Genera's strategy is to continue to provide multiplex solutions to major diagnostic partners *(14).*

We join Genera at a significant inflexion point in its commercialisation

In the last section of the report we introduce the Board, Scientific Advisers and Genera's team *(22-24).* We also summarise Genera's accounts, with an estimate for FY11 and FY12 based on the top-10 partnership proceeding, but excluding the prospects from other areas and products *(26-27).*

The strategy for the next 24 months is likely to produce steady news flow *(24)* as Genera moves:

a. On successful adaptation and integration of PapTest with the equipment of the Top-10 global diagnostics group, to become a reagent and technology provider to that group. A license fee could be worth say $15-25m plus milestones and near double-digit sales royalties *(5,26).*

b. also to be a reagent, technology and equipment provider to one or more diagnostic marketing companies retailing its branded and unmodified version of the AmpaSand technology; while also developing and offering an automated instrument. As well as RTI-plex, Genera is working on STI-plex™ and other products with markets equal or larger than PapType *(9-12,16,24).*

Genera is now near a significant commercialisation point in making PapType a lead player in the diagnosis of Cervical Cancer: it appears to have the technology and fit for a valuable partnership. Genera's IP platform and its prospects for launching other products and supporting technology also stand to benefit from the ensuing validation of PapType and its model. **Genera may offer both rising long-term earnings prospects and corporate transaction potential** *(16)***.**

B: Key Features for Investors

Genera's Business – Molecular Diagnostic 'MDx' Tests

Genera's business is to develop, manufacture and sell molecular diagnostic tests for the global commercial pathology market. These tests are based upon the company's proprietary silica-bead based 'multiplexing' technology - bringing together several related tests into a single assay. Multiplexing reduces the complexity of testing for multiple markers, since they can be assayed in fewer reactions, requiring reduced manpower and infrastructure.

Molecular Diagnostic 'MDx' Tests

Genera has developed an attractive platform for molecular diagnostic tests—a rapidly developing market already worth US$3-5 billion in total. The first of Genera's tests, PapType, a next generation HPV diagnostic test, has been in use in Australia since 2005. Clinical testing and regulatory approval has validated not only the test but Genera's underlying platform.

Genera's first diagnostic, approved and in use - PapType™

PapType is a diagnostic test for the simultaneous detection and identification of Human Papillomavirus Virus (HPV). HPV infection appears to be the most common sexually transmitted virus and may be the most common sexually transmitted disease (STD)[3]. Within the last decade, it has been found that HPV is the causation of 99.8% of cervical cancers[4].

Example of Genera's product characteristics

PapType individually identifies the 14 HPV types that account for over 95% of all cases of cervical cancer (refer p.7). This means that PapType can:

- Eliminate the need for a second HPV genotyping diagnostic as outlined in US clinician guidelines for the management of cervical cancer screening,
- Personalise the remedial action required for each woman, and
- Detect co-infection with multiple HPV strains.

PapType has a number of features that make it highly competitive in the HPV testing market, compared to the principal competitors. Specifically:

- PapType can not only indentify the presence of HPV, it also is able to determine which of the 14 cancer causing types are present in the specimen. This is valuable, since not all HPV types are equally dangerous.
- PapType detects and differentiates all 14 high risk types in a single reaction – a feature not shared by the current FDA-approved alternatives.
- PapType contains a "human control" which reduces the chances of a false negative result.
- PapType requires less than a quarter of the clinical material of the market leading product. It also lends itself more readily to automation and to integration with other systems.

In addition, the test is well suited for a market where many women have limited protection from certain types of HPV infection, which can now be conferred by the recent HPV vaccines. The test is sufficiently sensitive to identify rare events, and also will help to identify newly prevalent HPV types in a post-vaccinated population.

PapType has Australian Therapeutic Goods (TGA) approval and CE Mark (European) approval. It is used as the HPV assay of choice by Healthscope Limited[5], Australia's third largest private pathology provider, until recently listed on ASX. Dr. Keith Byron, Scientific Director of Healthscope's Advanced Pathology business stated, 'PapType has been an extremely useful and successful product for us for several years, providing our customers with more valuable and actionable clinical data than that provided by other HPV tests.'

The Core Value Proposition

Whilst PapType is Genera's lead diagnostic, the bead-based platform (page 5) underpinning PapType can be used in a large number of other tests.

The Case for Genera

The company is currently developing diagnostics for other sexually-transmitted diseases (STDs) and a range of respiratory pathogens. The latter is being co-developed with Healthscope. Again Dr Byron stated that, 'we see RTI-plex [the respiratory pathogen test] as doing the same [for Healthscope as what PapType has already done for the company]'.

[3] Int J Gynecol Path. 1992;11:197-203.
[4] Arch Pathol Lab Med. 2003;127(8):959-968.
[5] Healthscope was acquired by the Carlyle Group and TPG Capital, through Asia Pacific Healthcare Pty Ltd in September 2010.

Potentially transforming R&D deal with a 'Top-10 global diagnostics group'

Of the many industry participants and potential major users and development partners with which Genera has made and kept up contact, in addition to collaborators Healthscope and Sonic Healthcare, there are four global companies with which it has maintained an ongoing dialogue for a couple of years.

Prospective Top-10 Partner

Recognising the clinical and commercial advantages of PapType, one such major international diagnostics group - within the top 10 in terms of global sales – the 'top-10 global diagnostics group', entered into a Research and Development agreement with Genera in May 2010, with the intent of a commercial partnership following further evaluation. This has several highly prospective implications:

1. There is a strong alignment between the profile of PapType specifically—and Genera's AmpaSand platform more generally—with the partner's technology and instrumentation. A joint development programme is now underway for Genera, funded by the partner, to make 'minor modifications' to optimise PapType to work on the partner's instrumentation platform, after which the partner will evaluate the modified version to ascertain reliability, consistency and efficacy.
2. In the event that the work on PapType proves successful, the potential partner has the option to negotiate a licence for PapType. It is likely that the combination of both companies' products will in time introduce a new approach to cervical cancer screening which will, in addition to providing important and actionable clinical data to physicians, deliver considerable value to pathology providers and payment agencies.
3. Not only has the partner a strategy in the field of women's health in which PapType closely fits, but the partner has also indicated that it would be interested in discussing access to other tests based upon the AmpaSand platform.
4. The fact that Genera's test is CE marked and approved by the TGA should allow the partner organisation to rapidly enter one half of the global market after the integration of Genera's PapType with its instrumentation platform.
5. A deal to commercialise PapType globally will be transformative for Genera, taking it from an R&D focused development-company to a cash-flow positive organisation, and launching it as a significant participant in the large and rapidly growing global molecular diagnostics market.
6. In our view, an agreement could realistically be expected to lead to an upfront license fee in the order of A$15 million to A$25 million, event based milestone fees and a future near double-digit royalty on sales. For illustration, a royalty at the industry standard rate of around 7% on the estimated 2009 revenues of Qiagen's less precise but importantly FDA-approved HPV diagnostic—understood to have been around US$300m— would likely be in the order of US$20m per annum on those sales.

Genera's Platform Technologies

AmpaSand™

The Platform

Genera and its research team have dedicated eight years to the development of AmpaSand beads—coded silica microspheres which can be used as a versatile, high-efficacy and inexpensive DNA analysis platform. This platform is amenable to any DNA or RNA-based test, which has allowed Genera to develop and market specific and innovative diagnostic tests for commercial pathology laboratories.

The system allows multiplex testing, where multiple different DNA targets can be identified in a single reaction. Potentially up to 150 different DNA analytes can be detected simultaneously. This may be applied for example, to the detection of pathogenic microorganisms, or to the identification of individuals who have particular disease susceptibilities.

This has compelling commercial and clinical benefits for common infections such as:

- HPV (where different types of HPV have different cancer causing properties),
- Respiratory disease (different pathogens require different clinical management) and
- Sexually Transmitted Diseases (STDs) where co-infections, requiring multiple management strategies, are common.

Increasing knowledge of the genetic structure of pathogens, the human genome, and how genes influence the response to disease, will open up many more opportunities for mid-range multiplexing of the type ideally suited to the AmpaSand platform.

AmpaSand silica bead-based systems offer advantages over latex bead technologies. Silica beads are stable to 1,000º Celsius, and this heat stability permits certain processes, some of them proprietary to Genera, that would not be possible with latex beads. Such processes include high-stringency DNA hybridisation and single-tube PCR/Hybridisation processing.

The first product developed and in use is the 'one-pass' multiplex test to determine 14 HPV strains in one sample, PapType, outlined on page 4 and more fully on page 7 below.

Products

The second product now being developed is RTI-plex, a novel test for a range of common respiratory pathogens (page 10). Being co-developed with Healthscope, this will detect in one pass a range of important respiratory pathogens such as influenza and whooping cough.

A further product in development is STI-plex, a novel test for common STDs (page 14). Other products are under review (page 15). The potential variety of molecular diagnostic tests that could be worth developing is very broad. But with constraints of money and people, Genera has identified a major priority as the development of **an automated and integrated desktop test instrument** in which to run the tests – 'The Beach' (page 12).

Intellectual Property

The company believes it has a strong intellectual property position that allows it to move forward effectively and license the technology. We gain comfort from the fact that Healthscope, certain investors, and the Top-10 global diagnostics group evaluating the technology have all undertaken due diligence on Genera's patents and were satisfied.

I P

Genera's IP is based around three classes of patents.

- The first class protects aspects of the technology used in all Genera products. The three patents here protect the methods involved in the sensitive DNA hybridizations used for allele specific discrimination (PCT/AU01/00635), creating the silica microspheres (PCT/AU03/00696) and the multiplexing of microspheres in diagnostics (PCT/AU2004/000894).
- In the second class, patents protect specific applications such as detection of aneuploidy (abnormal numbers of chromosomes) (PCT/AU2005/000991) and HPV detection (PCT/AU2005/001865, PCT US2008/004441).
- The third class includes those patents over new technologies not yet in use in commercial products. In this class are a patent on solid phase PCR (PCT/AU2008/000120), being applied currently in the development of RTI-plex, and two patents around the QSand 'Whispering Gallery Mode' detection technology (PCT/AU2005/000748 and PCT/AU2009/001515). Most of the patents cover multiple jurisdictions.

PapType / Other Application	Invention / Subject	Priority Date	Granted (Accepted)	Pending	Patent #
Design of Ultra-sensitive Competitive Hybridization system	SiFT: Sequence Identity by Flow Test	29-May-00	Australia, New Zealand	USA	PCT/AU01/00635
Construction of AmpaSand™ Beads	Covalent anchoring of oligonucleotides to silanized microspheres (Joining 'hybridising' probes to beads)	04-Jun-02	Australia, New Zealand, USA	None	PCT/AU03/00696
Design of Multiplexed AmpaSand™ Beads	Single tube diagnostics using microparticle multiplexing using 4-dimensional parameter arrays (size, color, intensity, number)	04-Jul-03	Australia, New Zealand, China, Europe, (USA, Hong Kong)	Canada, Japan	PCT/AU2004/000894
Design of Chromosome or Organism specific fingerprinting	Multi-Sand detection system	06-Jul-04	Australia	USA	PCT/AU2005/000991
Design of PapType™ BeadSet	HPV detection I (Design & construct HPV type specific probes)	10-Dec-04	New Zealand, (Australia)	USA, China, Japan, Europe, Brazil, Canada, Mexico, India	PCT/AU2005/001865
Design of PapType™ PCR system	HPV detection II (Design of primers for bias-free universal amplification of hypervariable HPV L1 gene)	05-Apr-07	None	Australia, USA, China, Japan, Europe, Brazil, Canada, Mexico, India, New Zealand, Russian Federation	PCT US2008/004441
Beads pre-incorporated into PCR, minimising handling, improving throughput - using in RTI-plex	Solid Phase PCR	02-Feb-07	None	Australia, USA, China, Japan, Europe, Brazil, Canada, Mexico, New Zealand	PCT/AU2008/000120
Future Generation potential ultra-high throughput optical test method	QSand I: Whispering Gallery Mode solid phase detection system	26-May-04	(Australia, New Zealand)	USA, China, Japan, Europe, Brazil, Canada, Mexico, India	PCT/AU2005/000748
Future Generation potential ultra-high throughput optical test method	QSand II: Whispering Gallery Mode liquid phase detection system.	20-Nov-08	None (due May 2011)	None (due May 2011)	PCT/AU2009/001515
Other non-patented IP involved in Genera's platform and PapType	Bead Construction - Microsphere raw material assessment; Silanisation; Fluorescent labelling	Analysis - QPlots© software	Design History File, Design Master Record, Standard Operating Procedures, Work Instructions, QC protocols		

PapType

PapType™

To revert in more detail to Genera's current main focus and first product, PapType has been approved by the Australian Therapeutic Goods Administration (TGA) and carries the CE Mark, making it available for use in Europe. Healthscope, Australia's third largest private pathology provider, routinely uses PapType and it is their HPV test of choice.

PapType is a diagnostic test for the simultaneous detection of high risk and certain low risk types of HPV associated with cervical cancer. The test can individually detect and distinguish HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. The ability to discern individual infecting genotypes is an important advantage over assays on the market, which can only detect the presence of a pool of HPV.

PapType comes into an existing and changing market

The rapid adoption of the two globally marketed HPV vaccines and the inclusion of HPV testing into cervical screening programmes attest to the recognition of the major health issue that encompasses this virus, and the ability of modern medicine to reduce the incidence of cervical cancer. The American Society for Coloposcopy and Cervical Pathology (ASCCP) has issued screening guidelines which incorporate the use of HPV testing into primary screening in conjunction with cytological analysis.

More recently, it has been recognised that a single HPV test is a more effective cervical cancer screening tool than either a Pap test or Liquid-Based Cervical Cytology (LBCC) for reducing mortality associated with cervical cancer[6].

The two leading HPV assays, produced by Qiagen and Hologic, approved by the FDA and in general use in the US, have significantly improved the process of screening women for cervical dysplasia (abnormalities) and cervical cancer, and informed new strategies for ongoing patient management.

Yet these, and other assays in development, have one core weakness:

- They are not able to individually identify and distinguish infecting HPV genotypes in a single reaction. At best they have partial genotyping capability; at worst, a follow-on test is required to confirm whether a woman is infected with one of the highest risk HPV types.

Given that different HPV types have different propensities to cause cervical cancer, these tests can only broadly quantify risk.

In contrast Genera's PapType can detect and distinguish individual types of HPV in a specimen. This characteristic allows the PapType to:

- Eliminate the need for a follow-on genotyping test,
- Better triage (prioritise on severity) women into follow-on treatments, and
- Track a woman's infection status over time and across different HPV types.

These features translate not only into operational benefits for the pathology laboratory conducting the test, but also clinical benefits for the woman and her attending physician.

PapType will also be particularly helpful as vaccine use grows, in that it will be able to be used not only as a routine test, but also as an epidemiological tool to track changes in HPV type prevalence. Other tests such as Qiagen's HC2 are not able to genotype, instead measuring whether or not one or more of a pool of HPV types is present in a specimen.

A Technically Simple Protocol

Operationally, PapType uses Polymerase Chain Reaction Biochemistry (PCR) and Flow Cytometry, two very commonly used pathology laboratory techniques. As such, little in the way of additional specialised equipment or training is required. The current version of PapType has comparable operator characteristics to other tests. However, Genera is actively working on refinements and automation which will significantly improve throughput. Genera's assay is relatively simple to perform, using a range of commonly utilised molecular biology techniques. The company is currently working on automation, and expects to have completed the validation of *off-the-shelf* automation solutions by early 2011, with a custom-designed solution in 2012. Automation is a critical factor in the purchasing decisions of pathology laboratories[7,8].

[6] N Engl J Med. 2009;360(14):1385-1394.
[7] Diagnostic Histopathology (2009); 15:7:323-329

Genera has already blueprinted its own integrated instrumentation, 'The Beach', with testing of the prototype device anticipated by the third quarter of 2011 and the commencement of manufacture for marketing expected around the fourth quarter of 2011.

PapType
- Continued

PapType is a multiplexed Polymerase Chain Reaction (PCR) test, using AmpaSand beads, followed by flow cytometry and Genera's in-house developed interpretive software, QPlots™.

How PapType works, using AmpaSand Beads, PCR, a Flow Cytometer & QPlots software

- PCR is a process that amplifies target sequences of DNA many thousands of times. The PapType test uses Genera's PCR biochemistry to amplify target sequences of HPV DNA.
- The PapType AmpaSand beadset consists of 16 uniquely identifiable clusters of HPV detection beads, coded by size and colour. Each uniquely coded bead cluster has probes for a different HPV type on its surface.
- Any HPV PCR products generated by the PCR are labelled by a red fluorescent reporter dye during the reaction, and then mixed with the PapType beadset ('bead hybridisation'). DNA from a specific HPV type will bind to a particular and uniquely identifiable bead cluster.
- Because each new fragment of HPV DNA is labelled with a red dye, beads which have hybridised with HPV DNA will fluoresce red.
- The fluorescence can be measured in a flow cytometer, a standard piece of laboratory equipment that uses lasers to identify the size and colour characteristics of the beads.
- PapType also contains PCR biochemistry which amplifies a particular human gene, known as MLC. DNA from this reaction hybridises to a seventeenth bead cluster. This so-called "human control" is an important quality control measure, which alerts the operator if the specimen is of poor quality, minimising the risk of a false negative result. The market-leading test Hybrid Capture 2®, manufactured by Qiagen has no such control. Poor samples contribute to a number of false negatives in this assay[9].
- The results are generated using Genera's proprietary QPlots™ software, which reports the bead type that hybridises with the pathogen's DNA. One important benefit of PapType, over some other types of multiplexed assays, is that the results are software driven. The software programme called QPlots automatically interprets the output from a flow cytometer, and provides the result to the technician – there is no opportunity for subjective assessment by the operator.

Illustration in HPV testing of Genera's Multiplexing advantage

Illustration

Genera's HPV assay has a major technical advantage over the market leading HPV assays, by being able to detect and individually identify 14 clinically important HPV types in a single reaction. By way of an illustration, consider a patient infected with HPV types 16, 31 and 52.

- PapType would confirm the presence of types 16, 31 and 52 in a single reaction;
- Hybrid Capture 2 (Qiagen) would confirm the presence of high-risk HPV only, but not identify the specific types;
- Cervista HR (High Risk) and Cervista 16/18 (the pair of Hologic assays) would confirm the presence of type 16 only in this case, after two separate reactions;
- The Cobas 4800 (Roche) assay would confirm the presence of type 16 only.

Current guidelines in the USA prescribe more aggressive management for women identified with HPV types 16 or 18. However, in this illustration with three significant HPV types present, the co-infected woman has a higher potential for complications than a woman only infected with HPV type 16. This could only be identified with PapType (see schematic, page 9).

Moreover, there is considerable value in knowing whether a particular infection has persisted. Should the same patient return the following year and test positive only for HPV type 31 (her immune system having eradicated the other two types) only PapType would be able to confirm the persistence of this particular type. Persistence of a specific infection is an important determinant of whether an HPV infection progresses to cervical cancer.

Thus, PapType's technical advantage is translated into a clinical advantage in that it allows the physician to implement the necessary clinical vigilance and (if appropriate) interventions in women who carry a certain HPV type, but have not yet developed cervical cancer.

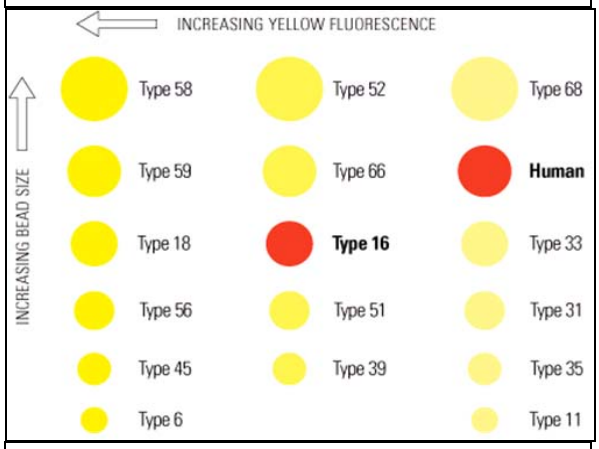
[8] Annals of Diagnostic Pathology 14 (2010) 347–354

[9] Am J Clin Pathol 2006;125:223-228

PapType
- Continued

Illustration

A schematic representation of a PapType beadset showing an HPV-16 Positive Result



Source: Genera Ltd

Clinical Results

Clinical Validations

PapType has been the subject of several studies, which examined specimens from over 6,000 patients, and the benefits of the technology are underscored by Healthscope using PapType for all its routine HPV testing.

A clinical study was carried out in conjunction with the company's partners at the Royal Women's Hospital (RWH - Melbourne), and included specimens from almost 900 patients who had presented to the hospital with abnormal Pap smears. That study compared the ability of PapType to detect histologically-proven pre-cancerous lesions, with that of the market leading Hybrid Capture 2® HPV assay (Qiagen). In addition, PapType was compared to a reference genotyping test, Roche's Linear Array HPV.

Of most importance, the RWH study demonstrated that PapType was significantly better at detecting pre-cancerous lesions of the cervix than the Hybrid Capture 2. Hybrid Capture HPV assay had a false negative rate of 20.9%. In contrast, PapType™ had a false negative rate of 8.9%. This number went down to below 6% when the most serious precancerous lesions were examined in isolation[10]. In the context of this study, a false negative result is where the HPV test has failed to accurately predict the presence of advanced cervical pre-cancer.

Examining the specific genotypes, PapType compared well to Linear Array, with a 95% full or partial match to the reference method. Whilst there is no "gold standard" for genotyping,it is important to confirm that the PapType test performs comparably to an accepted reference method.

Whilst it is important to accurately detect the presence of cervical pre-cancer, it is equally important to return a negative result when pre-cancer is absent. In a retrospective database analysis of Healthscope patients who had had a cytology test and a PapType test simultaneously, PapType demonstrated a negative predictive value (NPV) of over 99% - that is, PapType correctly predicted the absence of cytology-determined pre-cancerous lesions. A large study of approximately 2,000 US specimens showed that PapType and Hybrid Capture 2 returned very similar levels of HPV positivity in a population (31.6% PapType, compared to 27.0% for Hybrid Capture 2).

Products under Development

Products Under Development

Respiratory Pathogen Diagnostics – RTI-plex™

RTI-plex™

In May 2010, Genera entered into collaboration with Healthscope to develop and manufacture a test, RTI-plex™, capable of simultaneously detecting and differentiating multiple different respiratory tract pathogens in a clinical specimen.

[10] Genera Announcement – 4 September 2009

RTI-plex™
- Continued

A key driver for the development of this test was the emergence of new respiratory pathogens, particularly after the swine and avian influenza scares. These outbreaks led to significant increases in the numbers of respiratory diagnostic tests carried out by pathology laboratories. They also dramatically increased the need to know which particular organism is responsible for a respiratory infection. In a non-epidemic year, the market opportunity is estimated at US$100m[11] for RTI-plex. In epidemic years, such as 2008, the major US diagnostic laboratory chain Quest reported a 30-fold increase in influenza test requests[12].

- During the last influenza season, considerable resources within commercial pathology laboratories were directed to respiratory diseases.
- The high throughput multiplexed nature of Genera's system has the potential to alleviate the periodic high workload demands placed on pathology resources by respiratory pathogen outbreaks, freeing labour requirements within laboratories.

The current list of target organisms for RTI-plex is:

Influenza A, B	Metapneumovirus
Influenza A (H1N1 – swine)	Adenovirus
Influenza A (H5N1 – avian)	Rhinovirus
Respiratory Syncitial Virus (RSV) #	Bordetella pertussis @
Parainfluenza 1, 2, 3 and 4	Chlamydia pneumonia
Mycoplasma pneumonia	

\# – important in young children and adults with bronchiectasis
@ - an organism that causes whooping cough

A multiplex respiratory pathogen test could be associated with very positive health economic outcomes. In the United States, it is estimated that over half of all antibiotic prescriptions for respiratory tract infections are wasted, since the aetiological agent is a virus[13]. Moreover, molecular tests can save money in the hospital environment, by returning more rapid results compared to conventional viral culture[14]. The reimbursement level in the United States for a similar test manufactured by Luminex Incorporated (NASDAQ: LMNX) is $US200.

Under the terms of the agreement, Healthscope will support the development with resources and all development costs up to the point that it can get a test in-house for self-validation and use in its laboratories, in exchange for the right to purchase future test supplies from Genera to use in its own labs at favourable rates. Any additional development costs (e.g. possible US clinical study) fall to Genera, which will retain all commercialisation rights in all territories.

European and Australian approvals are anticipated in early 2012, and the company has also had exploratory discussions with the FDA with a view to preparing the product for the US.

An Automated and Integrated desktop system – 'The Beach™'

The Beach™

Whilst a corporate agreement remains a possible, or even likely, outcome for Genera, the company is also preparing itself to continue as a standalone entity, albeit one that will continue to work with larger partners. As such, in addition to its work with the prospective partner, the company is aggressively pursuing other product development plans, and central to these is the design of a desktop instrument specifically designed and optimised to run AmpaSand bead-based tests. This machine, provisionally named 'The Beach' will integrate 96-well PCR, bead hybridisation and flow cytometry into a single unit, and will be targeted at commercial pathology laboratories.

This development work has been informed by discussion with potential partners who, whilst seeing great potential in the AmpaSand platform, require a more holistic solution – a dedicated instrument, and a range of high value assays which run on it. This aligns with the classic 'razor - razor blade' model adopted by most *In Vitro* Diagnostic (IVD) companies, whereby the majority of revenue is derived from the sale of disposable reagents that run on a substantial installed base of dedicated instrumentation.

[11] Luminex research initiation, UBS – 15 October 2008
[12] Quest Diagnostics media release, 24 July 2009
[13] Gonzales, R et al. 2001. *Excessive antibiotic use for acute respiratory infections in the United States*. Clin. Infect Dis. 33(6): 757-62
[14] Woo, PC et al. 1997. *Cost-effectiveness of rapid diagnosis of viral respiratory tract infections in pediatric patients*. J Clin. Microbiol. 35(6): 1579-81

The Beach™
- Continued

Development of The Beach and an associated menu for its operations will better equip Genera to strike deals with major partners, and may ultimately increase the prospects of a corporate transaction. In particular, the instrumentation prototype on which Genera has now started work will use largely *off-the-shelf* components, which will significantly reduce its development time, cost and resources. Genera's management has had discussions with equipment manufacturers on the design, and plans to direct financial resources to commission development of a prototype system as soon as possible.

It is reasonable, subject to the availability of adequate funding, to expect Genera to have blueprinted, designed and developed its first desktop instrument in 2011, with a partnership around this technology and/or a market launch of this device in 2012.

The Beach will be designed to run PapType but should also run all future Genera tests. It will automate the stages of PCR, bead hybridization and flow cytometry into a single unit, and is expected to provide a 3-4 hour turn-around time for 96 specimens. Genera estimates that The Beach will cost $0.75 to $1.25m in order to get to beta stage, with a similar amount again required to develop a final instrument.

Sexually Transmitted Infections - STI-plex™

AmpaSand beads are amenable to any DNA-based test, and in particular, those assays which it makes sense to bring together into a single multiplexed assay.

The STI-plex™ diagnostic has potential to reduce pathology laboratory requirements for labour and consumables in this field, by having a multiple STD test conducted in one reaction tube.

The global market opportunity for chlamydia and gonorrhoea testing is in excess of US$400m and is likely to continue rising. The growth is being driven by two factors: firstly, more healthcare authorities are recommending chlamydial screening for young women, as chronic Chlamydia infection is known to cause pelvic inflammatory disease, which can in turn lead to ectopic pregnancies and infertility. Secondly, regulatory authorities around the world are increasingly moving to prevent laboratories from using so-called "home-brew" tests (tests that have been developed and manufactured in-house) which do not had the same level of validation and manufacturing quality control as products manufactured by the regulated diagnostics industry.

STI-plex™

Genera, in conjunction with a large hospital partner in Australia, has commenced planning and development of STI-plex, a single assay that will detect and differentiate multiple different sexually transmitted infections. The target organisms would be: *Chlamydia trachomatis* (including sub-typing of more virulent strains), *Neisseria gonorrhea*, *Trichomonas vaginalis*, *Mycoplasma genitalium*, *Herpes simplex* (types 1 and 2), *Triponema pallidum* (syphilis), *Haemphilus ducreyi* (chancroid).

Chlamydia is somewhat similar to HPV in that there are different strains (known as serovars), which have different levels of pathogenicity. In particular, there are some serovars which can cause a serious condition called lymphogranuloma venereum. Genera's AmpaSand beads will be able to differentiate the more serious from the less serious serovars, and physicians will be able to respond accordingly.

Similarly, the gonorrhoea portion of the test will contain multiple markers for the organism on different beads, unlike the single marker tests available today. This will likely make the Genera test much more specific than competing assays.

Self-sampling for STI tests

Genera is also in discussion with the Royal Women's Hospital in Melbourne and the Johns Hopkins University in the USA, to investigate the possibilities for self-sampling in the home for sexually-transmitted infections. The sampling would be done by the patient using a special kit, with the sample posted off to the lab to conduct the pathology test.

In certain countries, the rates of sexually transmitted infections are particularly high. In the USA for example, there are 117 cases of gonorrhea per 100,000 of population (c.f. 36 in Australia) – this is thought to be on account of relatively poor access to primary healthcare. In Japan, the gonorrhea rate amongst men is 150 per 100,000, thought to be due to high levels of prostitution usage.

Self-sampling for STI tests

In particular, Genera is interested in developing STI testing packages, consisting of the self-testing sampler, and the accompanying molecular diagnostic test, which might be distributed via substantial retail partners.

Genera plans to develop the STI-plex test and the collection device concurrently, and its estimates of cost to completion are $4-6m. Development of these assays will be subject to adequate funds being available.

Other Forward Projects:

Genera has a very versatile technology, its AmpaSand beads and other IP being amenable to any nucleic acid-based test. As previously noted, Genera has plans for a range of tests and products with interesting potential, as and when adequate funding becomes available:

- **Gastrointestinal infections:** Genera is in confidential discussions with an Australian University to commence development of a test focused on one of the more common gastrointestinal infections. More generally, a test which would differentiate for example, Shigella, Salmonella, *E. coli* and giardiasis may have value, not simply as a diagnostic agent, but also as an epidemiological tool for tracking particular infection outbreaks.

- In addition to detecting infectious agents, nucleic acid tests can also be used to analyse **an individual's genetic makeup**, for example with a view to ascertaining their risk of developing disease or assessing their suitability for a particular drug. K-RAS markers are used to determine an individual's likely response to certain anti-cancer drugs. Genera is in discussion with a pathology partner in relation to such a test. It is likely that developing such a test through to approval by the major regulatory authorities would cost approximately $5m.

Other Products in planning

- **Hospital acquired infections**: Severely ill patients in a hospital are at risk of contracting serious infections from organisms such as Klebsiella, Pseudomonas, Enterococcus and MRSA. Patients are usually given expensive broad-spectrum antibiotics; however, a rapid test which could differentiate these organisms would promote more rational antibiotic use in the hospital and likely save money.

- Finally, all of Genera's work so far has focused on **DNA** testing. However, a significant proportion of current *in vitro* diagnostic tests look at **protein** biomarkers – from blood, cerebrospinal fluid or other sources. There appears to be no reason why AmpaSand beads could not also be used for protein-based assays, and Genera is keen to demonstrate efficacy in these areas as soon as practically possible.

QSand™

Other Products – QSand™

The company's current product suite is based upon the AmpaSand platform. However, Genera's researchers are also keen to develop its proprietary IP, QSand™, a versatile, ultra-sensitive optical detection system, capable of identifying extremely small quantities of unlabelled analyte in a specimen, without the need for DNA amplification.

QSand has the potential to be a disruptive technology in both biological and non-biological detection systems.

QSand is based upon the modulation of Whispering Gallery Modes of light in translucent microspheres:

- When a translucent sphere is briefly illuminated by laser, a small amount of light enters the sphere and briefly undergoes total internal reflection. It is emitted with a characteristic spectrum, the shape of which is influenced by the sphere's refractive index and diameter.
- The bead can be engineered to present probes specific to a target analyte of interest. When the probes bind to an analyte, they change the properties of the bead, and this changes the shape of the emission spectrum. The change can be used as a means of detecting whether or not analyte has indeed bound to the surface of that bead.

QSand is a complex, physical, high-tech challenge. Despite its important potential, the likely development costs and distraction to research capacity have relegated it so far to the 'blue-sky' category. This opportunity would most likely be addressed on Genera receiving significant funding from partner milestone payments, probably by a spin-off to a single-purpose company.

Multiplexing, the Core to Genera's Commercial Success

We understand that the multiplex nature inherent in Genera's AmpaSand technology would be a major advantage in the other product prospects outlined above. Multiplexing has been a feature of Genera's commissioned research work since its early days, with examples undertaken across fields as diverse as forestry and veterinary specimen analysis in addition to several diverse human molecular test assays.

Multiplexing

Multiplexing can be achieved by bead-based systems such as Genera's, or from fixed microarrays, where probes are "spotted" onto the surface of some kind of chip, and image analysis techniques used to determine where hybridisation to an analyte has occurred. However, for multiplexing within the clinically useful range of 5-15 analytes, bead-based systems represent a more practical option. They can be used in high-throughput 96 well systems, and also have better biochemical reaction kinetics, which lend themselves to more reliable results. In addition, it is difficult to accurately Quality Control fixed microarrays – the only way to tell whether a chip works is by using it, which simultaneously destroys its utility. However, a sample of one particular type of Genera's beads can be tested prior to pooling with all the other types, giving greater confidence to the manufacturing process.

The most direct competitor to Genera's bead-based system is Austin, Texas, based Luminex Incorporated (NASDAQ: LMNX), with a current market capitalisation around US$750m. Luminex manufactures and sells a range of medium and high density multiplexing systems, aimed at both the research and clinical testing markets. Importantly, Luminex uses internally-dyed latex beads for its multiplexing, rather than the silica that Genera uses.

Silica has an important advantage over latex, in that it is much better able to withstand the high temperatures and corrosive chemicals sometimes required for biochemical reactions. Genera takes advantage of this property in its proprietary **Solid Phase PCR process**, in which PCR and hybridisation occur simultaneously in the same reaction vessel, cutting down processing time and handling steps. RTI-plex is now being designed using solid phase PCR.

Australian HPV Reimbursement Prospects and Public Sector Grants

Possibility of Australian HPV Reimbursement

Genera is understood to be participating in the early stages of discussions with the Australian Government in respect of reimbursement for PapType in Australia. Unlike the USA and many European countries, Australia still uses traditional Pap smears in its cervical screening programme, and reimbursement for HPV testing is, to date, restricted to testing specimens from women who have had surgical intervention to treat cervical pre-cancer. However, Australia has one of the highest uptakes of the cervical cancer vaccine, which is causing policymakers to consider how cervical screening programmes should be modified to accommodate the new paradigm. HPV testing will inevitably be part of that consideration.

Australia conducts approximately 2 million Pap smears per annum, of which more than half may be considered as potential targets for HPV testing. Genera has commercial arrangements already in place with Sonic Healthcare and Healthscope – respectively No. 1 and No. 3 in the Australian pathology market. It makes a lot of sense commercially that Genera would push hard for reimbursement.

Prospects for Public Sector Grants

Aside from any cervical screening reimbursement possibilities, there are a number of public sector grants for which Genera is or may become eligible and they are being pursued as circumstances permit. At least one of these involves Genera providing matching funding, which is dependent on cash flow priorities.

The Partnership Strategy

In vitro diagnostics is a competitive and highly consolidated space, with over 80% of the market shared amongst just ten companies[15]. Genera's management recognises the importance of strong partnerships in order to access the necessary marketing strength to compete effectively and aims to enter commercial partnerships across its product range.

Partnership Strategy

The first instance of this (page 5) is the current evaluation of Genera's technology, and in particular PapType, by an undisclosed diagnostic company, which is within the top ten global diagnostic companies by revenue. This suggests the potential partner carries a sales force in US, Europe and probably Asia, and over one billion dollars in sales revenue.

Genera has been in discussion with this partner for over two years, and its patience and tenacity was rewarded when the partner elected to sign an R&D agreement pertaining to HPV tests, in May 2010. In brief, there is a strong technological alignment between the AmpaSand platform and the partner's technology, as well as a strong strategic alignment with PapType specifically. However, prior to signing a more definitive agreement, the partner wanted reassurance that the PapType test could be modified slightly, and optimised to work on its own instrumentation. Consequently, an agreement was struck whereby the partner would fund a programme of development work aimed at developing and assessing a modified version of PapType. The modification revolves particularly around some changes to the multiplexing method (though these methods are still captured within Genera's IP suite), and the use of alternative molecular dyes for use in the reagents.

Evaluation of the modified system is expected to be completed in the first quarter of calendar 2011. Should the modified product be successful, a license will be negotiated by the second quarter of 2011.

Backup plans in the event of no early deal with a Partner

Alternatives

Genera's principal commercialisation strategy has been to work through substantial partner organisations. In this respect, the current development plan for PapType is of pivotal importance. However, in the event that this project does not proceed as planned, the company remains in dialogue with a number of other potential partners, all of whom retain a high level of interest in the PapType test specifically, and the AmpaSand platform more generally. Moreover, other companies have already expressed an interest in Genera's Beach instrumentation, since an instrument allied to a range of attractive tests fits in well to their existing business paradigm.

Genera's Future Direction

Thus, over the next 24 months, Genera is expected to follow two broad strategies:

- The first is to clinch a deal and become a reagent and technology provider to the Top-10 Global Diagnostics Group, using a subtly modified version of its technology
- The second is to become a reagent, technology and equipment provider to one or more diagnostic marketing companies, retailing its branded and unmodified version of the AmpaSand technology
- Meanwhile progressing The Beach, STI-plex and other prospective products, in that priority, and to the maximum extent funding will allow.

Strategy

It is our opinion that such a strategy would progress Genera's product range as rapidly as practical, create competitive tension amongst interested parties and increase the probability that Genera would in due course be acquired as part of a blocking strategy by a future partner.

[15] : April 2009 Micronews

Market Transactions

As HPV diagnostics have been becoming more entrenched in clinical practice, a number of sizable transactions have occurred in the HPV / Molecular Diagnostics and related fields.

Acquirer	Acquiree	Price, US$m	Date	Notes
Cervical Screening Acquisitions				
Becton Dickinson	Tripath	350	Dec-06	Liquid-based Cytology
Hologic	Cytyc	6,131	May-07	Liquid-based Cytology
Qiagen	Digene	1,450	Jun-07	Acquire Hybrid Capture 2 HPV test
Hologic	Third Wave	540	Jul-08	Acquire Cervista HR & Cervista 16/18 HPV tests
China Medical Tech's	Molecular Diag'c Tech's	345	Oct-08	HPV Test
Other Molecular Diagnostics & Screening-Related Acquisitions				
Becton Dickinson	Clontech	200	Aug-99	Drug Discovery & MDx Tools
Becton Dickinson	GeneOhm Sciences	230	Jan-06	MDx, especially HAIs
Quest	Enterix (AUS)	43	Sep-06	Bowel Cancer Screening (Licence led to acquisition)
Cytyc Corporation	Adeza Biomedical	352	Feb-07	FullTerm(TM) FetalFibronectin Test
Inverness Medical Innov.	Biosite Inc.	1,651	Mar-07	Proprietary protein markers, cardiovascular platform
Inverness Medical Innov.	Cholestech Corp	283	Jun-07	Healthcare diagnostic tools
Inverness Medical Innov.	Matritech	36	Aug-07	Cancer Screening, esp. bladder cancer
Celera	Berkeley HeartLab	195	Sep-07	MDx tests; cardiovascular genetic markers
Inverness Medical Innov.	BBI (UK)	123	Dec-07	Non-invasive tests
Inverness Medical Innov.	PanBio (AUS)	36	Jan-08	Dengue Fever
Immucor	BioArray	117	Mar-08	MDx systems for DNA analysis of blood
Solvay	Innogenetics	305	Apr-08	InnoLiPA HPV Test
Imucor	Bio-Array Solutions	117	Aug-08	HLA Typing
BioMérieux	AviaraDx	60	Sep-08	Validated cancer biomarkers; gene expression profiling
GenProbe	Tepnel (UK)	132	Jan-09	MDx, multiplexed onto Luminex

Genera's CEO compares Genera wistfully to Third Wave Technologies. Both companies started out looking to use their technologies in the service sector; both then focussed on molecular diagnostic test development, and in particular HPV testing. Prior to its IPO, Third Wave raised US$70.7m, followed by a further US$82.5m at the IPO. This is in stark contrast to Genera, which has raised $20m in public and private financings over its life. Yet Genera claims a technology and a test which, whilst not FDA approved (the cost of such a trial and application being in the region of US$25m) appears superior to that of ThirdWave: -

- PapType differentiates all genotypes; Cervista only differentiates types 16 and 18
- PapType does full genotyping in a single reaction; Cervista partial genotyping in two reactions
- PapType can handle three times as many patient specimens as Cervista in a single test plate
- PapType requires less than half the specimen volume of Cervista.

Genera envies the early capital backing enjoyed by Third Wave; it also notes that when acquired by Hologic, Third Wave was selling few HPV tests. Although now a few years later and based in Australia rather than the USA, this simplistic comparison does suggest an apparent mismatch between Genera's technology delivery and its current price.

An acquisitive MDx / IVD market

As reported by the journal 'In Vitro Diagnostic Technology', the number of strategic acquisitions is expected to grow in 2010[16]. It notes that:

- Large IVD companies will continue to try to grow their top lines through acquisitions
- Large diversified healthcare companies will continue to become more involved in IVDs
- Life science tools companies will try to leverage their biomedical research technologies into clinical diagnostics
- Diagnostic service groups will be looking at acquisitions so as to expand geographically, and
- Some IVD companies that have new tests will be looking at M&A as a means for commercialisation strategies.

[16] www.ivdtechnology.com/.../strong-ma-activity-expected-ivd-industry

An acquisitive MDx / IVD market
- Continued

The table above shows some of the transactions in the diagnostic sector, and we agree with the journal that there are two key drivers for this recent M&A activity.

The first is that diagnostic companies are moving rapidly into emerging areas; but tend to be acquired once the diagnostic has been validated through sales.

The second is a search for technologies that allow expansion of the product offering, in a rapid and cost effective manner.

We thus see a fair prospect that Genera would ultimately be acquired; equally because of the AmpaSand technology as specifically for PapType. It is our view that the company's current and planned partnership strategies are likely to facilitate such an event, while the faster it can progress its various development plans—for The Beach and RTI-plex as much as for PapType—the more it may accelerate an acquisition and, importantly, derive value from it.

These features seem to have been recognised by Genera's prospective partner. The history of corporate activity around HPV testing assets suggests it occurs particularly when the acquiring company has strategically aligned assets. It is thus possible that a licensing transaction with Genera's R&D partner could morph into something more substantial, and there may be a danger that the terms of any licence agreement may preclude competitive tension.

Corporate activity potential in Genera's fast growing markets

As noted before, the global HPV testing market is worth approximately US$350m, and is growing at approximately 20% per annum. We have also seen that Genera is developing its interests in respiratory pathogen testing, a market currently worth US$100-200m globally, and sexually transmitted infections testing, currently worth in excess of US$400m annually.

It is possible that, in considering the value of a licensing transaction, the partner organisation may well consider a more substantial transaction. Genera is developing products across molecular diagnostic testing sub-segments which have a combined market value approaching one billion dollars. The total potential market opportunity for multiplexed tests is likely to be a multiple of that. As such, the complexity of a licensing agreement, allied to the economics of the target segments, may well point to an outright acquisition rather than a licence.

Summary and Conclusion

Cost and value of technologies are invariably different. To look at the cost of Genera's technologies for a moment, we refer to the change in net assets on the balance sheet at 30 June 2010 since the proforma as at 31 December 2007 used in the IPO prospectus (page28). Over the 2 ½ years since the IPO, Capitalised Development Costs have increased by $2.9m and Intangible Assets by $0.6m while Operations have cost $5.7m—a total of $9.2m. This work has been funded by $6.7m of further capital raised since the IPO and the use of $2.5m of the $5.0m IPO Share Issue. Over almost a decade since incorporation, Genera has raised $20m of capital and still has cash left.

Our take-away conclusion from this and our review of Genera's current platform and product offering is that, as we often see with Australian biotech companies, considerable progress has been achieved on the scant investment capital injected. Again by comparison with our experience of Australian biotech companies, the share price is significantly leveraged upwards or downwards by whether or not the company is seen to have adequate funding to achieve its next milestones to commercialisation.

"There is a tide in the affairs of men. Which, taken at the flood, leads on to fortune ..." (Brutus). Genera is perhaps at that tide, with PapTest having passed TGA, CE Mark and validation hurdles, RTI-plex in development with Healthscope and a top-10 partnership in prospect.

The best results are achieved by striving

We believe that for Genera to obtain its optimum future value, additional funding, whether from licensing or other sources, should enable more development to be done faster and more effectively for the relatively low-risk expansion of the product and equipment portfolio from this inflexion point. We consider this approach, if practical, is likely to generate a significantly enhanced return on the funds involved within a fairly short timeframe.

Validated platforms, one proven product and several aligned products with (in biotechnology terms!) near-term and relatively low risk commercial outcomes, typically attract a very valuable multiple of the cash expended to complete that last lap with aplomb, negotiating strength and without financial stress.

C: Background on Cervical Cancer and HPV assays

Cervical Cancer usually develops slowly over many years and often has no symptoms. We will not discuss here the clinical manifestation or clinical management of cervical cancer. Some readers may like to explore the many recent reviews in the field—some referenced below[18,19,20,21].

Over 99% of cervical cancers are caused by persistent infection with one or more types of high-risk HPV. The table here shows *(at left)* type-specific frequency of HPV genotypes present in cervical cancer[17], compared with *(at right)* the HPV genotype distribution in a sample of 1,000 Australian patients tested with Genera's PapType (figures from a Genera presentation[17A]), which may be a proxy for a general 'population frequency' rather than the 'cancer frequency' shown on the left.

Type-specific frequency of HPV genotypes present in cervical cancer [17]		Aust. test frequency - see # below and text [17A]
HPV sub-type	%	%
16	53.5	4.6
18	17.2	2.7
45	6.7	0.8
31	2.9	1.3
33	2.6	0.3
52	2.3	1.9
58	2.2	1.2
35	1.4	0.5
59	1.3	0.8
56	1.2	1.1
51	1.0	1.7
39	0.7	0.9
66	??	1.7
68	0.6	1.5

Right hand column shows HPV genotype distribution found in 1,000 Australian women tested with PapType - ie the 'population frequency' - while the middle column shows the 'cancer frequency'

Progression from low-grade to high-grade dysplasia and invasive disease is rare in the absence of HPV[22].

There are more than 200 known types of HPV, of which 15 are known to be associated with cervical cancer to a greater or lesser degree. The chief cancer associated HPV types are types 16, 18, 31 and 45. In particular, types 16 and 18 cause about 70% of cervical cancer cases. HPV 16 is also the most commonly-identified type among women in the general population. Large case studies have shown that approximately 50% of women with high-grade cervical pre-cancer (CIN3) or cervical cancer are infected with HPV16.

HPV types 16 and 18 are also known to cause anal cancer, vulvar cancer and penile cancer, and type 16 is also associated with head and neck cancer.

HPV is one of the most common sexually transmitted diseases, infecting 80% of women at some time in their lives.

Generally, the immune system of younger women inhibits cancer formation, but increased cancer incidence is associated with increased age and persistence of infection. Whilst only a small proportion of infections will ever progress to cervical dysplasia and a much smaller proportion progress to cervical cancer, disease incidence can be substantially diminished by cervical screening.

The Cervical Cancer Screening Market

The cervical cancer screening market is dominated by cervical cytology (the direct examination of cervical cells) either by the traditional Pap smear test or by LBCC tests in higher income economies. LBCC provides a more uniform cell preparation than the traditional Pap smear and can be partially automated by use of computer aided imaging.

Currently, HPV DNA tests are typically used either as a follow up to an equivocal cytology test or as a primary screening tool in conjunction with cytology.

In many of the studies conducted, data is demonstrating the importance of HPV genotyping to increase the accuracy of assessing cervical cancer risk, especially by identifying the two highest risk HPV genotypes (16 and 18). Other studies have underscored the limitations of relying upon cytology testing alone in identifying women with cervical dysplasia.

First Generation Cervical Cancer Tests

Until recently, the Pap smear test was the primary screening methodology for cervical cancer. At its simplest, cells are scraped from the surface of the cervix, smeared onto a glass slide and chemically stained. Cells showing signs of cervical dysplasia and cancer are distinguishable under a microscope.

Despite having a relatively low sensitivity (as low as 50%), the traditional Pap smear test has proven effective in mass screening programmes. However, the limitations of the Pap smear test drove researchers and companies to develop assays that provide inherent advantages over traditional screening methods.

Second Generation Cervical Cancer Tests

Liquid-Based Cervical Cytology (LBCC) tests have largely replaced traditional Pap-based cytology in developed markets.

[17] Nature Reviews Cancer 6. 753-763 (October 2006)

[18] Ann N Y Acad Sci. 2010 Sep;1205(1):57-68.
[19] Nat Rev Cancer. 2010 Aug;10(8):550-60.
[20] APMIS. 2010 Jun;118(6-7):520-8.
[21] Cancer. 2010 Jun 1;116(11):2531-42
[22] Natl Cancer Inst. 2005;97:1072–1079

Cervical Screening
- Continued

Marketed tests include ThinPrep® (manufactured by Hologic) and SurePath® (manufactured by Becton Dickinson). These assays were approved by the FDA for marketing into the US in 1996 and 1999 respectively. Both have approximately equivalent clinical performance[23], although Thin Prep® is technically easier to perform. The technologies differ, but they are in essence identical in that they both deliver a clean, uniform layer of cervical cells onto the surface of a glass slide, where they can be stained and examined for abnormalities. The ThinPrep® System is the most widely used method for cervical cancer screening in the US, with about 70% market share of the Pap / LBCC assay market, SurePath® having some 30%. Hologic does not report the revenues generated from ThinPrep®. However, in 2007, the originator company Cytyc (for which Hologic paid US$6.2 billion) reported the ThinPrep® system's revenues at US$244.5 million.

LBCC tests have been highly lucrative for the manufacturers. They are easily automated, produce a more reliable cellular preparation than traditional Pap smears, and some trials also indicate a superior clinical performance. Crucially, they also primed the market for the introduction of widespread HPV testing, since with LBCC it became possible to perform both cytology and HPV molecular tests from the same clinical specimen (i.e. the LBCC vial)

Third Generation Cervical Cancer Tests

Cervical cytology techniques are relatively insensitive – that is, they generate a large number of false negative results. This is because specimens can be poorly taken, or the cytologists looking down a microscope for cellular changes indicative of cervical pre-cancer simply miss them. Approximately one fifth of cervical cancer cases in developed countries are found in women who have had an ostensibly clear cytological result. Moreover, despite the advent of computer-assisted technologies, it remains a relatively labour-intensive system.

The third generation cervical cancer screening assays are those tests which look for molecular evidence of the HPV virus – the underlying cause of the cellular changes which can lead to cancer. Testing for high-risk HPV DNA is highly sensitive, and results in a reduced incidence of false negatives. Moreover, newer HPV tests also facilitate more subtle triage of patients. Consequently, HPV diagnostic testing is becoming an increasingly important tool for patient management.

New guidelines from the American Society of Colposcopy and Cervical Pathology (ASCCP) make recommendations on how patient management should vary depending upon the infecting genotype.

The HPV test is typically used:

- to investigate women under the age of 30 years who have an ambiguous cytology result (so-called "reflex" testing);
- for women over the age of 30 years as an adjunct to cytology in screening (adjunctive); and
- in so-called "test-of-cure" – where HPV testing is used to assess the persistence of HPV infections in a woman who has had a surgical intervention to manage cervical disease.

The FDA has approved two HPV diagnostic tests for both adjunctive and reflex testing:

- Cervista™ HPV HR, manufactured by Hologic;
- Hybrid Capture ® 2 HPV DNA manufactured by Qiagen.
- A follow on partial genotyping test, Cervista™ HPV 16/18 is also approved.

Fourth Generation Cervical Cancer Tests

Most recently, molecular tests have been developed that are capable of identifying cervical cells transforming (becoming cancerous), although these have yet to be widely adopted and none has been approved for use by FDA regulators. These are assays to identify expression of the E6/E7 genes. In the future, it is envisaged that E6/E7 assays would be used to monitor tumour progression once a patient presents with CIN2, CIN3 or cervical cancer. The E6/E7 gene expression systems are regarded as relatively insensitive tests although they are quite specific. Therefore, they're likely to find their niche as a reflex test to a positive HPV result and subsequent monitoring, rather than in routine screening programmes.

[23] Cytopathology, published online: 8 Jun 2010 DOI: 10.1111/j.1365-2303.2010.00772.x

The impact of the HPV vaccine on the cervical cancer screening market

Cervical Screening
- Continued

Recently, both Merck and Glaxo SmithKline have introduced vaccines which protect women against infection from HPV types 16 and 18 (and the genital wart-causing types 6 and 11 in the Merck version). It is important to consider how the introduction of these products will affect cervical cancer screening in the short and long term.

The immediate consequence of the vaccines' introduction has been a massive increase of the awareness of HPV and the role that it plays in cervical cancer. Whilst this is hard to quantify, it is likely that this has boosted the uptake of HPV tests in cervical cancer screening.

Importantly, the introduction of the vaccine will not eliminate the need for cervical cancer screening, and it's likely that the amount of disease in the population will not diminish significantly for a generation. This is because the HPV vaccine is targeted at young women prior to the onset of sexual activity (typically 12-15 years), whereas cervical cancer is typically a disease of older women (35+ years). As such, there will not be a substantial diminution in the amount of cervical disease detected until the vaccinated cohort get to the age where they require routine screening.

Moreover, they will still require routine screening, since whilst the vaccine diminishes the chances of developing cervical cancer, it does not eliminate it. The vaccine protects against disease caused by HPV types 16 and 18; however, there are another twelve types known to cause cervical cancer. As such, screening will need to continue.

However, it's likely that the nature of screening will change in a post-vaccinated community. In particular, since cervical disease will be rarer, more sensitive tests will be required. If it has not happened earlier, this will be the time when the relatively insensitive cytology test gives way to the highly sensitive HPV test.

The value and drivers of the HPV testing market

Currently, the HPV testing market is worth US$300-350m per annum, and it has been growing at around 20% for the last few years. It has been, and is likely to remain for the foreseeable future, the fastest growing sub-segment of the molecular diagnostic testing market. The principal drivers in general are increased awareness of the role that HPV testing plays in cervical screening, direct-to-consumer advertising (in the USA), and the adoption of new guidelines incorporating HPV testing into cervical screening schedules. Over time, as other products enter the market and knowledge of the subtleties of different HPV type infections grows, other factors will assume an increased level of importance. Being able to respond to the knowledge of specific infecting genotypes will be perhaps the most important of the clinical benefits that will emerge. Already, the American College of Colposcopy and Cervical Pathology has published guidelines, advising doctors how to best manage patients with HPV type 16 or 18 infections. The National Cancer Institute is currently embarked upon a substantial study which will risk-stratify all HPV types, meaning that even more detailed patient triage may become possible. Of the non-clinical drivers, ease of use for the pathology laboratories will be critical. Automated, high-throughput systems will be the assays that predominate.

Penetration rates for HPV testing remain relatively low – for example, in the USA, which is currently the largest single market for HPV testing, the penetration rate is still only 30-40% of potential. Moreover, other countries such as the United Kingdom are only now moving to formally integrate HPV testing into their overall cervical cancer screening programme. Estimates of the eventual market size vary, but are generally thought to be US$1-2 billion pa.

Those companies that have a broad strategic interest in Women's Health, and who are able to sell a portfolio of related products around cervical screening, are likely to be the ones that succeed. Hologic is the classic example of this, with their Cervista suite of tests complementing their ThinPrep LBCC products. Importantly, Genera's partner also has a broad strategic interest in this space, and might therefore be expected to devote significant resources to capturing market share.

It is understood that Genera's prospective partner has already indicated an interest in engaging with the FDA with PapType, which would be logical given the (presumed) resources of the partner, and the sheer size of the US market. It is possible that the versatility of PapType – in particular its ability to identify all infecting genotypes in a single pass – allied to the increased availability of type-specific pathogenicity data, believed to be being generated by the National Cancer Institute, would put Genera's partner in a very powerful position as new treatment algorithms emerge.

The HPV Diagnostic Competition

Cervical Screening
- Continued

The Competition

The key competitor is Qiagen's HPV diagnostic Hybrid Capture 2®, with competition also coming from Roche Diagnostics, Gen-Probe Inc., Hologic Inc. and other companies with earlier stage developments.

Hybrid Capture 2® (Qiagen - NASDAQ:QGEN)

Qiagen acquired its Hybrid Capture 2 HPV asset through its June 2007 acquisition of Digene Incorporated for US$1.6 billion, on a 47.9 times EBITDA multiple.

Currently, Hybrid Capture 2 test is the global market leader, and in April 2009, Qiagen reported that more than 40 million of its HPV tests had been performed since launch in 1999. However, whilst there is a considerable amount of clinical data to support its use, Hybrid Capture 2 is deficient in a number of important ways. In particular:

- Hybrid Capture 2 only detects thirteen of the fourteen known high risk HPV types, and is not capable of distinguishing particular infecting genotypes
- The test lacks an internal human control, which renders it more susceptible to generating false negative results
- It requires a large volume of LBCC material in order to generate a reliable test. Since LBCC processing depletes the fluid in which the cervical cells are preserved, in a number of cases, reported to be 5-7%, there is insufficient material remaining after LBCC processing to produce a reliable HPV result
- It is subject to inappropriate cross reactivity, which can lead to a false positive result. Up to 11% of positive Hybrid Capture 2 results may arise from single infections by types not supposedly detected by the kit——HPV53 (10%) and HPV66 (1%)—leading to incorrect management of a patient[24].

Cervista™ HR (Hologic - NASDAQ: HOLX)

In July 2008, Hologic beat several other companies in the acquisition of Third Wave Incorporated for US$580 million. Third Wave had developed two HPV tests: Cervista HR, a non-genotyping HPV test, and Cervista 16/18, a partial genotyping test, designed to assess whether or not Cervista HR positive specimens were positive for HPV types 16 and/or 18.

FDA approval was granted for these tests in March 2009 and CE marking was achieved in January 2009 for Cervista HPV HR and in May 2009 for Cervista HPV 16/18.

Whilst in many ways the Cervista suite of products offers improvements over HC2, it too has a number of limitations:

- It is a relatively low throughput test, with only 28 patient specimens being able to be assessed on a single, 96-well reaction plate
- The partial genotyping is achieved via a separate, follow-on test, which makes it expensive and time consuming.

Hologic does not report the sale of Cervista, but for the year ending September 2009, the diagnostic business generated US$547 million in sales in a group total of around US$1,650m.

Cobas 4800 HPV (Roche)

The Roche cobas® 4800 HPV Test simultaneously detects 12 high-risk HPV types (HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) as a pooled result, as well as HPV genotypes 16 and 18 individually.

It was the subject of a large US-based registration study of more than 47,000 women, called ATHENA. In the trial, 1 in 10 women aged 30 years and older who tested positive for HPV genotypes 16 and/or 18 by the cobas® 4800 HPV Test had cervical dysplasia, although the cytology test was reported as normal.

Roche launched the cobas® 4800 HPV Test with CE Mark in 2009. The test is currently under review and pending Pre-Market Approval by the FDA.

[24] Eur J Cancer Prev. 2009 Sep 7. [Epub ahead of print] (Abstract)

APTIMA HPV (Gen-Probe)

Cervical Screening

The Competition

- Continued

Gen-Probe has developed HPV assays which run on their TIGRIS and PANTHER platforms. The US clinical trial has been completed and the company expects to file in Q4 2010 with US regulators. The APTIMA HPV Assay detects disease progression markers from the viral E6/E7 oncogenes. Studies show that this test is highly sensitive, yet significantly more specific for cervical disease compared to Hybrid Capture 2.

RealTime High Risk HPV (Abbott)

The Abbott product profile is very similar to that of the cobas 4800 Roche assay. It runs on the Abbott m2000 platform.

Other HPV Tests – an overview

Apart from the tests discussed above, a number of others have been developed by companies around the world. Some will not compete directly with PapType. For example, NucliSENS EasyQ HPV manufactured by BioMerieux, and HPV Oncotect (Invirion Diagnostics) are tests that look for the presence of transforming cervical cells – i.e. infected cells which are becoming cancerous. These tests are very specific, but not very sensitive – as such, they are suited as follow-on tests where a specimen has been found to be HPV positive by a more conventional HPV DNA assay.

Other tests have relatively poor processing characteristics. Linear Array HPV (Roche) and InnoLiPA can genotype; however, they are so-called "line blot" assays, which are expensive and have low throughput. Moreover, they, like certain others (Seeplex HPV Genotyping by Seegene and Papillocheck by Greiner BioOne) provide information not only on clinically relevant high-risk types, but also on certain low risk types, for which there is to date no associated pathology.

A paper published earlier this year provided some data on HPV assays in use or development. It highlighted the need for quality assessment for HPV testing in laboratories. The author was Sepehr Tabrizi, a member of Genera's Advisory Board *(page 23)* and Associate Professor of the Department of Microbiology and Infectious Diseases at The Royal Women's Hospital, Melbourne [25]

The paper listed a number of the commercial, as well as in-house, assays available for HPV testing. It suggested that laboratories performing such assays should assess accuracy and reproducibility of their results by ongoing internal control as well as by participating in external quality-assurance schemes—a growing requirement for laboratories engaged in HPV testing. Laboratories should select the appropriate panels for detection of targeted types covered by assay used. Failure to do so could possibly alter patient management and increase the cost of treatment.

Each assay has different sensitivity and specificity and would need to be utilised appropriately for the particular clinical algorithm. Several assays also have ability to identify a particular genotype present, some of types 16 and 18, a number covering the high risk types, some yet more types.

In summary, PapType:

- Contains probes for and can differentiate all of the 14 high-risk, cancer causing HPV types. Some tests do not include all of these types
- Contains probes for just 2 low risk types – those which cause genital warts. Some tests include probes for HPV types that have to date shown no clinical relevance
- Can detect and differentiate HPV in a single pass. Other products require a follow-on genotyping test
- Works in a commonly used high-throughput 96-well format, with one patient specimen per well. Some other tests require multiple wells per patient (meaning lower throughput), or are available as single-patient tests in a unique format
- Requires relatively little starting material from the specimen. Other tests require over four times the material required by PapType
- Has a "human control" to reduce false negatives. Some (particularly older, first generation) tests have no such control
- Has objective and repeatable data analysis by proprietary software. Some tests rely upon subjective human assessment.

PapType looks a contender for HPV diagnostic leadership

After reviewing the various alternative HPV tests available, our view is that the PapType test offers perhaps the best combination of data provision, clinical relevance and processing characteristics. We understand it is also both relatively cheap to run and lends itself to automation and integration.

[25] Quality assessment for human papillomavirus testing; Sexual Health, 2010,7,335-337

D: Board, Management, Advisers, News Flow, Shareholders, Financials & Market Transactions

Board and Key Management

Board and Key Management

Fernando Careri - Chairman (Non executive)

Chairman and Co-founder of Ecotech Group Pty. Ltd. and CEO, Infracap Pty Ltd.

Previous management roles include CEO Metropolitan Transport Trust (TAS), CEO Ausdoc Integrated Services (VIC), CEO On Demand Printing (VIC), GGM Projects Public Transport Corp (VIC), GM Stonington City Council (VIC), GM Brambles Cleanaway (VIC), Chair Brotherhood of St Laurence Management Review Committee and Member European Australian Centre for Cooperation.

Karl Poetter - Executive Director

Chief Scientific Officer of Genera Biosystems;

Formerly, Senior Research Scientist with the joint Australian Genome Research Facility/Walter and Eliza Hall Institute for Medical Research programme for new technology development in genomic science. Former Scientific Advisory Board member for MycroLab Pty Ltd and the CRC for Diagnostics. Author or joint author of eleven patents and fourteen peer reviewed publications.

David Symons - Director (Non executive)

David Symons currently writes the "Insider" column that appears in weekday editions of the Sydney Morning Herald and The Age newspapers. He has over 10 years experience in private equity, investment banking and corporate management.

Formerly, he has held executive roles at ABN AMRO Capital, Macquarie Bank, Merrill Lynch and Promina Group. Prior to the IPO of Genera, David sat on the Company's Board from October 2007 through to March 2008.

William (Bill) Tapp - Director (Non executive)

William Tapp brings over 40 years of entrepreneurial and commercial experience.

This has included a key role, as one of four partners, in the establishment of Dovuro Seeds Pty Limited in 1990. Mr Tapp has had significant board experience, and is currently the chairman of Ag-Sun India, a 200-employee seed business headquartered in Mumbai with processing plants in southern India.

Mel Bridges - Director (Non Executive)

Mel Bridges has extensive experience in the Australian and global biotech industry especially in the diagnostics industry. He is currently Chairman of ASX-listed companies Alchemia Ltd (ASX: ACL) and ImpediMed Ltd (ASX: IPD); Non-Executive director of ASX-listed Benitec Ltd (ASX: BLT). Formerly he was Founder and MD of Pacific Diagnostics (sold to Baxter Corp in 1986); Chairman of Peptech and other companies; and also Founder and, until 2003, CEO of Panbio Ltd. In addition, Mel has been the winner of prestigious national and state business awards including the 2005 AusBiotech Chairman's Industry Medal and the 2004 Queensland Entrepreneur of the Year.

Mel Bridges intends to retire at Genera's AGM on 25 November 2010.

Two new directors, introduced to Genera by Mel Bridges, will join the Board at that AGM:

Jim Kalokerinos – to become a Director (Non Executive)

Jim Kalokerinos has held senior management and board roles in international diagnostics businesses and smaller local operations over 30 years. From 1984 to 1993, he was Executive Director of Sales and Marketing at Pacific Diagnostics, an Australian pathology products supplier. He was then Pacific Region Director of California-based *in vitro* diagnostics manufacturer Metra Biosystems Corp. to 1999. Then until 2005 he was Director of the Asia-Pacific Region for Quidel Corporation, a San Diego-based manufacturer and marketer of *in vitro* diagnostics.

Jim has held board roles in ASX-listed and other biotechs in Australia since 1987, including from 1987 to 2006 as non-executive director of Panbio. He is currently a director of five unlisted businesses, including Athlomics, an *in vitro* diagnostics company using genomic IP for health and wellness testing.

Board and Key Management
- Continued

Lou Panaccio – to become a Director (Non Executive)

Lou Panaccio is currently a board member of Sonic Healthcare, which is a shareholder in Genera. His thirty year professional career has included a decade practising as a Chartered Accountant followed by twenty years of involvement in a number of healthcare businesses.

Lou's involvement in the pathology sector commenced in 1990, as director and CEO of the Melbourne Pathology Group. This was acquired by Sonic Healthcare in 2000 and Lou joined the Sonic Healthcare board in 2005. He is also currently non-executive chairman of the Inner East Community Health Service in Melbourne and Health Networks Australia Group. Lou's was CEO of Monash IVF between 2007 and 2009

Allen Bollands – Chief Executive Officer

Allen Bollands has been with, and the CEO of, Genera since 2005. Prior to joining Genera, he spent seventeen years with the multinational pharmaceutical companies Novartis and SmithKline Beecham in the UK, Europe and the USA as well as Australia, where his roles focused on marketing, sales, product development and business development.

He was previously the CEO of Repromed and has also worked as a consultant with several other Australian biotechnology companies.

Genera's team has increased from just three in 2005 to a full-time and part-time staff today of twelve, plus a number of external consultants. The company has retained functional expertise across areas critical to its business objectives. Specifically:

Finance and Compliance: Tony Panther is the company's CFO and Company Secretary. He has qualifications in commerce and law and is a member of The Institute of Chartered Accountants in Australia and of Chartered Secretaries Australia. With over 20 years in public accounting and various industry sectors, he has previous listed biotech experience with ASX-listed CogState.

Quality Assurance: A *sine qua non* for diagnostics manufacturers is that they comply with ISO13485 – the quality standard that governs the design and manufacture of medical devices. Genera's quality systems are overseen by Ronda Charkass, a highly experienced regulatory, quality and compliance professional with ten years very relevant experience with the life sciences industry. She joined Genera in November 2008 from Hospira, where she had covered a range of roles in quality management, product stability and regulatory audits.

Manufacturing: Genera has designed and built a custom manufacturing facility at its Scoresby, Victoria site. This was overseen by Janette Manalo, who continues to take overall responsibility for manufacturing. She has considerable experience in the areas of Production, R&D, and Quality Assurance and Control, and specialises in process optimisation, 7 Waste (Muda) Elimination, CAPAs, Continuous Improvement Programmes, ISO9001 and ISO 14000 auditing, complaints handling and supplier accreditation.

Genera naturally employs a number of well qualified (Bachelor's degree or PhD) scientists doing **Research and Development** work on the company's product range, and working in related areas such as quality control.

Advisory Board

Advisory Board

Professor Suzanne Garland (Chair)

Professorial Fellow in the Department of Obstetrics and Gynaecology of the Faculty of Medicine at the University of Melbourne, and Head of Clinical Microbiology and Infectious Diseases at the Royal Women's and Royal Children's Hospitals, Melbourne. Principal research interests include the use of molecular biology in the diagnosis and prevention of sexually transmitted infections. She has consulted to the WHO and in 2005 chaired a WHO technical workshop on detection of HPV in global disease prevention and control. Author or co-author of over 250 publications.

Professor Ian Frazer

An inventor of the technology which enabled the first HPV vaccine to prevent cervical cancer, now licensed to CSL, Merck, and GSK. Director of University of Queensland Diamantina Institute. Current research interests include immunoregulation and immunotherapeutic vaccines for papillomavirus associated cancers. Fellow of the Australian Academy of Science and 2006 Australian of the Year.

Associate Professor Sepehr Tabrizi

Senior Research Scientist, Department of Molecular Microbiology, Royal Women's Hospital and Associate Professor at the Faculty of Medicine, Dentistry and Health, Department of Obstetrics and Gynaecology, University of Melbourne. His expertise in STIs, particularly HPV, is reflected in over 100 publications. A chief investigator on projects including WHO STI Pacific prevalence surveys, he has been a WHO consultant on techniques for detection of STIs.

Advisory Board
- Continued

Professor Michael Quinn

Michael is Professor of Obstetrics and Gynaecology at the University of Melbourne, and Director of Oncology/Dysplasia and Clinical Director of the Gynaecological Cancer Research Centre at the Royal Women's Hospital, Melbourne. A former chair of the scientific committee for the International Gynaecological Cancer Society, and current Secretary/Treasurer, Michael has published over 170 articles, including two monographs (one with Suzanne Garland) on HPV screening and management. His current research interests include both scientific aspects and clinical management of gynaecological cancers.

Other Scientific Advisors

Professor Paul Mulvaney

Professor, School of Chemistry, University of Melbourne, in 2005 an ARC Federation Fellow for outstanding contributions in Nanotechnology and Physical Chemistry. Instrumental in the establishment of nanotechnology in Australia and a co-inventor on some of Genera's QSand IP.

And Other Advisors …

Professor Simon Foote

Former Head, Genetics and Bioinformatics Division, WEHI and Deputy Director, Australian Genome Reasearch Foundation, Now Director of the Menzies Institute in Hobart. Research interests include the study of genes involved in susceptibility to disease.

Dr. Keith Watson

A leading chemist with the structural biology group at WEHI, expertise includes drug discovery and patent management. In former senior scientific research and management roles at CSIRO, ICI Australia and Biota Holdings he helped develop the anti-flu drug Relenza.

… & Organisations

In addition to its Board and Advisers and staff members, the company has retained several highly credentialed organisations to assist its development and commercialisation, including two of Australia's largest pathology providers, Sonic Healthcare and Healthscope. Genera has conducted two clinical studies at the Royal Women's Hospital, the WHO reference centre for HPV in the Asia Pacific. There, the department of infectious diseases under Genera's scientific advisory board chair, Professor Suzanne Garland, has considerable expertise in HPV and other STIs.

Genera's software including QPlots has been written to the standards required by the FDA, by Invetech, part of Leica Microsystems, itself a division of the multinational Danaher Corporation. Invetech has designed and built instrumentation and software for a large number of medical equipment manufacturers.

Anticipated News Flow

During the next 24 months, Genera expects to see a steady flow of significant news as it progresses its product developments and partnership deals, notably that with the top-10 global diagnostics group. The following table lists major possible developments over three years:

Potential News Ahead

4Q2010	Validation of robot liquid handling automation for PapType
1Q2011	Submission of HPV Test reimbursement application for Australia
1-2Q2011	Global PapType licencing deal with Top-10 partner
2Q2011	First supply of RTI-plex to Healthscope
3Q2011	Partner commences PapType US regulatory studies
4Q2011	Partner's EU launch of PapType / Milestone payment
4Q2011-1Q12	EU/TGA approval for RTI-plex
2Q2012	CE/IVD approval for The Beach integrated instrument
	Possible commercial arrangement for RTI-plex / The Beach
	First Partner PapType royalties start to flow
3Q2012	EU/TGA approval for STI-plex
	EU/TGA approval for self-sampling device
4Q2013	Partner PapType US studies completed

Possible sales in Europe, first of PapType and subsequently of other products, are not shown, nor any potential grant income. We note that the above timelines given to us are only Genera's best current realistic estimates, and that while its products generally follow the path already proven by PapType and hence the time for their development should be relatively predictable, such plans typically tend to be delayed.

Genera Milestones Already Achieved

2001

May: Walter and Eliza Hall Institute of Medical Research, Melbourne (WEHI) files patent on new genetic detection technology, SiFT™, capable of ultra-high-throughput mutation detection. *Dec:* Genera Biosystems begins trading, to develop & commercialise technology originating at WEHI & the Australian Genome Research Facility (AGRF)

2002

Jan: Genera licenses in WEHI SiFT™ technology; First round fundraising $525,000; *Apl:* AusIndustry BIF grant $250,000; *May:* WEHI seconds Karl Poetter (original inventor of SiFT™) & Brendan Toohey to Genera, at WEHI Biotechnology Centre, Bundoora; *June:* WEHI files patent on Universal Anchoring System; *Aug:* Genera files patent on coded nucleic acid carriers

2003

Jul: Files Aneuploidy Detection patent, also Multiplexing patent; $265,000 raised, after Proof of Practice milestone of SIFT™; *Sep:* SiFT™ patent granted in Australia; SiFT™ patent accepted in New Zealand; *Sep:* SiFT™ patent lodged in United States; BIF Grant completed, first milestone payment; *Nov:* Universal Anchoring System Patent enters PCT phase; *Dec:* Phase 1 of SNP proof of practice completed - 960 individuals, > 99% accuracy

2004

Jan: MOU with Gribbles to develop multiplex STD test (PapType); MOU with public sector organisation in environmental land use; end 2004 Gribbles acquired by Healthscope

2005

Focus on HPV, also STD tests; continue SNP (Single Nucleotide Polymorphism Detection) screening & analysis for University, hospital & CSIRO labs; developing QSand technology

2006

Royal Women's Hospital in Melbourne (RWH) found PapType detected 86.7% of high-risk HPVs in blind specimen tests; Genera working on its 'Sandstorm' DNA extraction technology with Pall Corp (NYSE: PLL)

2007

Sonic Healthcare agreement to assist with validation work on PapType & study for FDA purposes, in exchange for shares in Genera and rights (on internal validation) to purchase PapType supplies

2008

Jun: IPO & listed on the Australian Stock Exchange at $0.50, raising $5m for 19.5% of resulting capital; *Nov:* Healthscope headlines in its 'The Pulse' journal significantly fewer false negatives in a 100 specimen comparison of PapType with Qiagen's Hybrid Capture 2 test

2009

Jan: Equipped custom laboratory & manufacturing facility at Small Technologies Cluster, Scoresby, Melbourne; *Jun:* TGA audits facility & quality management systems; *Sep:* Royal Women's Hospital, Melbourne, study of almost 900 patient samples shows superiority of PapType over market leader in cervical cancer HPV detection; *Oct:* Compliant to ISO13485:2003; TGA licence to manufacture in-vitro diagnostic devices

2010

Jan: PapType receives TGA approval for entry into Australian Register of Therapeutic Goods; PapType repeatability & reproducibility study successfully completed by Sonic Healthcare; Genera appoints Lazard to advise on partnership/transaction alternatives; *Apl:* PapType is CE marked - CE mark allows for sales in Europe and other non-US markets; *May:* Agreement to partner with Healthscope in development of a respiratory pathogen test (RTI-plex™); Major R&D alliance agreed with a Top-10 global diagnostics industry partner, with intent of commercial licensing

Shareholders

20 Largest Ordinary Shareholders as at 13 Sept 2010 - source: Annual Report	% Held of Issued Capital
ANZ NOMINEES LIMITED	5.33
THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH LTD	4.47
UBS WEALTH MANAGEMENT AUSTRALIA NOMINEES PTY LTD	3.79
SANDHURST TRUSTEES LTD <JMMPS A/C>	3.56
SANDHURST TRUSTEES LIMITED <JMFG CONSOL A/C>	3.33
SONIC HEALTHCARE LIMITED	3.19
PUJURI PTY LIMITED <PUJURI SUPER FUND A/C>	3.12
GATEWAY CAPITAL LIMITED	2.83
DURBIN SUPERANNUATION PTY LTD <DURBIN FAMILY S FUND A/C>	2.59
QUEENSLAND INVESTMENT CORPORATION	2.55
ORBIT CAPITAL PTY LTD	2.18
MR CYRUS ADAGGRA	2.15
JPS DISTRIBUTION PTY LTD <RAFF FAMILY A/C>	2.06
MR LUCIUS ORSINI	1.85
FOLIGNO PTY LTD <REINHARDT SUPER FUND A/C>	1.77
SILICA INVESTMENTS PTY LIMITED	1.61
SEVEN 95 PTY LTD <EQUITIES FUND NO 2 A/C>	1.58
MR PATRICK O'BRIEN	1.32
MR DAVID FREDERICK OAKLEY	1.28
MR RONALD PENKARA + MISS MEREDITH NORTON <MERRON FAMILY S/F A/C>	1.27

Number of Share Holders	609	Total for Top 20 holders	51.83
Number of Option Holders	13	Total Issued Shares	62,670,279
		Options (all but 200,000 under Employee Share Option Plan)	4,044,325

Substantial Shareholders: JM Financial Group Limited 6.92%

Significant Investors

The original seed capital that allowed Genera to spin out from WEHI was provided by Orbit Capital – a Brisbane-based boutique investment bank. They, along with Perth-based Gateway Capital and Melbourne-based Silica Investments, are early investors who remain significantly invested in the company to today. All have participated in more than one round of financing.

Genera raised around $9.9m prior to its June 2008 IPO, at prices ranging from $0.10 to $0.80. Five million dollars at $0.50 was raised at the IPO. This has been followed by two further raisings - $2.8m at $0.40 in May 2009 and $2.3m at $0.80 in November 2009. The latter raising was a placement in large part to the JM Financial Group – another long term supporter of the stock.

The Walter and Eliza Hall Institute of Medical Research and Sonic Healthcare Limited are both significant Genera shareholders – the former receiving stock in exchange for the original IP, the latter for clinical development support services. Neither has sold down.

Financial Estimates for FY11 and FY12

In 1Q11, the first quarter of the current year, Genera's Appendix 4C report showed an operating cash outflow of $370,000, net of $11,000 receipts, and an outflow of $141,000 on IP and equipment making a total net cash outflow of $511,000. Cash at 30 September 2010 was $2,091,000, ostensibly sufficient for another four quarters at that rate.

Basis of Estimates
On page 27

The financial estimates below for FY11 and FY12 make the simplistic assumptions that:

- The agreement for technology evaluation currently being undertaken by a Top-10 diagnostics group leads to a licensing agreement. This agreement may lead to sums in the order of
  - a $20 million up-front license fee in 2011, and
  - a $10 million milestone payment for the market launch of Paptype product in FY12.
- No significant income is received from other sales or partnership revenues, although
  - By 2012, with a start in 2011, Genera is likely to see income from other partnerships and sales relating to PapType and RTI-plex, with added support from Genera's branded integrated and automated flow cytometer, The Beach.

Profit & Loss Account $m	2009 Actual	2010 Actual	2011 Est.	2012 Est.
Revenue	**0.15**	**0.65**	**20.85**	**10.96**
Staff Costs	0.83	1.48	2.20	2.89
Laboratory & Office Costs, Rent, D&A	0.42	0.88	0.99	1.07
Corporate, Professional, Travel, Other	1.17	1.09	1.17	1.23
Total Expenses	**2.43**	**3.44**	**4.35**	**5.19**
Profit/(loss) pre tax	(2.28)	(2.80)	16.50	5.77
Income tax (expense)/benefit	0.66	0.31	0.35	0.35
Net profit/(loss) for the year	**(1.61)**	**(2.49)**	**16.85**	**6.11**
Basic earnings per share	**(3.10)**	**(4.12)**	**26.14**	**9.40**
on wtd avg no of shares, million	52.01	60.43	64.48	65.05

Cash Flow $m	2009 Actual	2010 Actual	2011 Est.	2012 Est.
Loss for the year	**(1.61)**	**(2.49)**	**16.85**	**6.11**
Reclass int' rec'd as Invest. Cashflow	(0.11)	(0.04)	(0.08)	(0.06)
Non cash items				
Depreciation & amortisation	0.25	0.43	0.46	0.46
Share option expense	0.06	0.17	0.17	0.17
Exchange differences				
Employee provisions	0.05	0.06	0.07	0.08
Changes in assets and liabilities				
Trade and other receivables	(0.05)	(0.08)	(0.14)	(0.28)
Inventories		(0.06)	(0.10)	(0.14)
Prepayments	0.06	0.08	0.07	0.07
Creditors and accruals	(0.17)	0.20	0.19	0.42
Revenue received in advance		0.09	0.04	0.04
Tax receivable	(0.58)	(0.31)	(0.44)	(0.38)
Operating Cashflow	**(2.10)**	**(1.96)**	**17.09**	**6.49**
Payments for intangibles	(0.42)	(0.38)	(0.40)	(0.40)
Payments for development costs	(1.04)	(0.87)	(0.95)	(0.95)
Payments for PP&E	(0.23)	(0.11)	(0.25)	(0.31)
Interest received	0.11	0.04	0.11	0.22
Investing Cashflow	**(1.58)**	**(1.31)**	**(1.49)**	**(1.44)**
Proceeds from issue of shares	2.79	2.75		
Capital raising costs	(0.12)	(0.14)	(0.30)	
Finance insurance payments	(0.05)	(0.07)	(0.06)	(0.06)
Financing Cashflow	**2.62**	**2.55**	**(0.36)**	**(0.06)**
Net Overall Cash Flow	**(1.06)**	**(0.72)**	**15.24**	**4.99**
Cash, Beginning of Period	**4.38**	**3.32**	**2.60**	**22.84**
Cash, End of Period	**3.32**	**2.60**	**22.84**	**27.84**

Balance Sheet – In IPO Prospectus, at 30 June 2010, and the key changes

Balance Sheet, A$m:	31.12.07 Proforma		30-Jun-10		2 ½ year Change	
Cash	5.07		2.60		-2.47	
Total Current Assets		6.32		3.57		-2.75
Development Costs	-		2.92		2.92	
Intangible Assets	1.05		1.64		0.59	
Total Non Current Assets		1.21		5.29		4.08
Total Assets		7.53		8.86		1.33
Current & Non Curr. Liab's		-1.00		-1.31		-0.31
Net Assets		6.53		7.55		1.02
Issued Share Capital	13.11		19.35		6.24	
Accumulated Losses	-6.93		-12.64		-5.71	
Options Reserve	0.35		0.84		0.49	
Shareholders' Funds		6.53		7.55		1.02

Important Information

Confidential

This document is for the confidential use of the recipients only and is not to be reproduced without the authority of Intersuisse Limited.

Disclaimer

The persons involved in or responsible for the preparation and publication of this report believe that the information herein has been obtained from reliable sources and that any estimates, opinions, conclusions or recommendations are reasonably held at the time of compilation. No warranty is made as to the accuracy of the information in this document and, to the maximum extent permitted by law, Intersuisse Limited and its related entities, their respective directors and officers ("Intersuisse") disclaim all liability for any loss or damage which may be suffered by any recipient through relying on anything contained or omitted from this document.

General Advice

The content is of a general nature and is based on a consideration of the securities alone, and as such is conditional and must not be relied upon without advice from a securities adviser as to the appropriateness to you given your individual investment objectives, financial situation and particular needs. Whilst this document is based on information and assessments that are current at the date of publication, Intersuisse has no obligation to provide revised assessments in the event of changed circumstances.

Disclosure

Intersuisse and associate parties Phillip Capital Pty Ltd and IB Managers Pty Ltd (together "Intersuisse") have been engaged by Genera Biosystems Limited ("Genera") to carry out capital markets work and will receive fees on commercial terms. In the future Intersuisse may provide capital raising services to Genera on commercial terms. Directors and officers of Intersuisse or other associate companies may own securities in Genera. Intersuisse seeks to do work with those companies it researches. Intersuisse receives commissions from dealing in securities. As a result, investors should be aware that Intersuisse may have a conflict of interest that could affect the objectivity of this report.

Analyst Certification

The analyst responsible for this research report certifies that all of the views expressed reflect his personal views about the securities or the issuer; and that no part of his remuneration was, is, or will be, related to the recommendations or views expressed by him in the report. The author of this document owns shares in Genera Biosystems Limited and is related to an officer of Genera Biosystems Limited.

Peter Russell

INTERSUISSE LIMITED ABN 14 002 918 247, AFSL 246827 Market Participant of the ASX Group

Melbourne Office:		Sydney Office:	
Level 37, 530 Collins Street,		Level 7, 5 Elizabeth Street,	
Melbourne, Vic, Australia 3000		Sydney, NSW, Australia 2000	
Telephone:	(+613) 9629 8288	Telephone:	(+612) 9233 2100
Facsimile:	(+613) 9629 8882	Facsimile:	(+612) 9233 2117
Email:	suisse@intersuisse.com.au	Email:	sydney@intersuisse.com.au

Internet: http://www.intersuisse.com.au