Volume V, Number 2 Monday, February 9, 1998

Special Update! Automated Cytology Technology

From the Desk of R. Lewis Dark...

THE DARK REPORT

RELIABLE BUSINESS INTELLIGENCE, EXCLUSIVELY FOR MEDICAL LAB CEOs/COOs/CFOs/PATHOLOGISTs

Restricted information, see page 2

Commentary & Opinion by...

R. Lewis Dark

Founder & Publisher

Rate of Change Follows a Geometric Curve

JANUARY WAS A WILD MONTH FOR COMPANIES OFFERING automated cytology products. January opened with new CPT codes for automated cytology procedures taking effect. January closed with news that the FDA's advisory panel, convened on January 28, recommended approval of the PMA supplement of **NeoPath, Inc.'s** automated cytology instrument for primary screening of Pap smears.

Do not underestimate the impact of both events. Manufacturers of automated pathology systems invested long hours and much money in making the case for new CPT codes to cover their automated Pap smear procedures. Now that these procedures have an "official blessing" in the CPT code book, these same companies will press managed care plans to establish appropriate reimbursement for the new codes.

If "adding cost" to the system is a criticism of this new technology, then widespread agreement by payers to reimburse for the new procedures would surely knock the legs out from under that argument. Our editor predicts that such widespread reimbursement is coming sooner than later. After hearing his reasons for that prediction, I would agree. *(See pages 9-14.)* We may even see the overall reimbursement for Pap smears change from inadequate to possibly even generous! If that happens, remember that you read it here first.

But improved reimbursement for Pap smears cannot be evaluated without considering the impact of the FDA's expected approval of NeoPath's system for primary screening of Pap smears. With **Neuromedical's** system also in use for adjunct screening, and with clinical trials beginning for the systems developed by **AutoCyte** and **MorphoMetrix Technology**, the volume of clinical data documenting the efficacy of these technologies will become voluminous. Keep in mind that similar developments are under way overseas. In many foreign countries, these same cytology systems are being used for primary screening.

I believe this steadily increasing volume of clinical data will validate whatever economic and clinical benefits accrue from the current generation of technology. But here's the wild card: today's generation of technology will be rapidly eclipsed by continual refinements and radical breakthroughs in new technology for automating Pap smear diagnostics. Remember Peter Drucker's observation about change. He pointed out that there is always a point where the primary research breakthrough triggers a geometric explosion of new discoveries and applications. I think we are about to see precisely this occur during the next 18 months, first to cytology, then to anatomic pathology. If it turns out to be true, then we'd all better hang on. It's going to be a wild ride! TDR

Automated Pap Screening Gains Recommendation

FDA panel evaluated NeoPath's AutoPap® System for potential use in primary screening

CEO SUMMARY: Automated cytology technology received a big boost when the FDA's advisory panel voted to recommend that the FDA approve, with conditions, NeoPath's AutoPap® System as a primary Pap Smear Screener. The com-pany still awaits final FDA approval on this matter.

ON JANUARY 28, the **Food And Drug Administration's** (FDA) Hematology and Pathology Devices Advisory Panel unanimously recommended that the FDA approve, with conditions, **NeoPath, Inc.'s** premarket approval (PMA) supplement to authorize use of the AutoPap® System as a primary Pap smear screener.

The panel's recommendation represents a milestone event in cytology and anatomic pathology. If the FDA rules favorably upon NeoPath's PMA supplement, it marks the first time that a machine is positioned to make diagnoses from glass slides containing cells, without human intervention or review.

NeoPath's AutoPap 300 System demonstrates the rapid convergence of three basic technologies: video imaging, morphology algorithms and CPU chip crunch-power. The sophistication and sensitivity of automated cytology systems is increasing at a steady pace. As the quality and performance of such instruments continues to improve, many clinical procedures in cytology and anatomic pathology will evolve.

This directly impacts pathologists, cytologists and laboratory executives. Both clinical practices and the economics of Pap smear testing will soon undergo radical change.

Cytologists and pathologists may be surprised to discover that these changes are for the better. THE DARK REPORT predicts that clinical practices involving Pap smears will quantifiably improve during the next 24 months. This will be accompanied by enriched reimbursement for services involving Pap smear collection, preparation, diagnosis and review. In the short term, NeoPath's ability to sell the AutoPap System as a

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THE DARK REPORT Intelligence Briefings for Laboratory CEOs, COOs, CFOs, and Pathologists are sent 17 times per year by The Dark Group, Inc., 1731 Woodland Terrace Center, Lake Oswego, Oregon 97034, Voice 1.800.560.6363, Fax 503.699.0969.

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primary screener will stimulate these far-reaching changes to clinical practices and reimbursement.

The supplement NeoPath submitted to the FDA represents the company's starting point for primary screening of Pap smears. As requested by NeoPath, the supplement would allow a maximum of 25% of the slides to receive AutoPap review only. Those slides would go directly to the archives as normal. The remaining 75% of the slides would undergo manual screening, aided by AutoPap's ranking of each slide according to its risk of abnormality. Quality control rescreening would be done to 15% of the slides in both groups.

Strategic Decision

"We made a strategic decision not to request the highest sort rate that we feel the AutoPap can handle," said NeoPath's President and CEO, Alan Nelson, Ph.D. "In retrospect, that was the right decision. At the requested sort rate, 25%, we have demonstrable superiority and accuracy. This was substantiated in the clinical data reviewed by the FDA advisory panel.

"When the FDA issues a final letter approving the PMA supplement, AutoPap becomes the first FDA-approved machine in the world, strictly speaking, that is automatically identifying normal Pap smear slides," observed Dr. Nelson. For those 25% of the slides ranked as normal, a report goes to the doctor and to the archives and a human never sees the slide. "Even though it does not produce a report which says 'this slide has a high grade with the presence of HPV, for example, it does produce a report which says 'this slide has a ranking indicative of the likelihood of abnormality.

"AutoPap's accuracy improves as we continue to train the algorithms. Those algorithms shift upwards with every generation of refinements. Each time algorithm improvements are incorporated into the AutoPap System, we expect that clinical data will validate these improvements and allow us to gain approval for higher sort rates in the future."

Incremental Strategy

Nelson is describing an incremental strategy for validating the performance of the AutoPap System. Given NeoPath's installed base of AutoPap Systems already operating in a QC (quality control) function at large laboratories throughout the United States, the essential next step was to document the system's accuracy in primary screening at the requested sort rates, then obtain FDA approval.

"When the FDA issues a final letter approving the PMA supplement, AutoPap becomes the first FDA-approved machine in the world, strictly speaking, that is automatically identifying normal Pap smear slides."

Armed with that approval, NeoPath intends to help its client laboratories incorporate primary screening to their existing AutoPap instruments. NeoPath's strategy is viable because new CPT codes for automated cytology procedures became effective in 1998. These CPT codes make it easier for laboratories to negotiate reimbursement from insurance plans for automated cytology procedures.

"AutoPap technology has additional uses which spill over into other areas of cytology and anatomic pathology," he continued. "NeoPath provided data to the FDA that exclusively involved Pap smears. In-house, we have lots of data on many different specimen types.

"We see a future for AutoPap to become an information node for cytology and anatomic pathology." Nelson believes this is attainable because the AutoPap is 99.6% repeatable at a high rate of accuracy. "Given AutoPap's high quality and consistency, it would be possible to create an electronic archive, instead of archiving the glass slide. In Japan, we already have physicians requesting this feature."

Information-Intensive

"Managed care is information-intensive," continued Nelson. "Pathologists will need to access and use clinical data in ways never before imagined. We believe that innovative pathologists will soon want to exploit the capability of our instrument to create an electronic archive of cytology and anatomic pathology slides."

THE DARK REPORT already sees such developments. Michael Bechich, M.D., Ph.D. at the **University of Pittsburgh** School of Medicine, is one such pathologist actively pushing the boundaries. Using existing computer and imaging technology, he and his colleagues are actively striving to create "virtual" pathology practices that can function today.

Dual Capability

But simply archiving cytology and anatomic pathology slides to eliminate glass storage is not the real value to pathologists. "It is the dual capability of analyzing a specimen and archiving the measurements electronically which pathologists will find most useful," noted Dr. Nelson. "This gives any pathologist the resources to provide patient management plans with data never before accessible. At the same time, the pathologist can provide information in consultations with clinicians that improve clinical outcomes."

THE DARK REPORT concurs. Any pathology practice which can develop these capabilities in advance of their competitors will have a "value-added" service for which both clinicians and managed care payers will generously reimburse. The ability to create unique "value-added" pathology services is what will separate pathology's financial winners from its losers in coming years **TDR**

(For further information, contact Alan Nelson, Ph.D., at 425-556-2951.)

TIME LINE OF EVENTS FOR NEOPATH, INC.

Since FDA approval in 1995, events moved swiftly at NeoPath.

January, 1989: *NeoPath, Inc. is founded in Redmond, Washington.*

January, 1995: *NeoPath, Inc. becomes a publicly-traded company.*

September, 1995: *NeoPath's Pre-Market Application (PMA) for the AutoPap® 300 QC System gains FDA approval for quality control and adjunct testing.*

October, 1995: ***SmithKline Beecham Clinical Laboratories*** *signs agreement for 12-15 AutoPap 300 instruments.*

October, 1995: ***Quest Diagnostics Incorporated*** *(then known as* ***Corning Clinical Laboratories****) signs agreement for multiple AutoPap 300 QC units.*

March, 1996: *Laboratory Corporation of America signs contract for evaluation of AutoPap 300 QC units.*

March, 1997: *AutoPap 300 approved for primary screening in Japan.*

June, 1997: *SmithKline purchases ten additional AutoPap 300s.*

October, 1997: *CPT code for the AutoPap 300 is awarded.*

January, 1998: *FDA advisory panel recommends that NeoPath's PMA supplement for primary screening be granted with conditions.*

Neuromedical's PAPNET® Undergoing Enhancement

After a difficult year, Neuromedical seeks to reposition its automated cytology system

CEO SUMMARY: Financial pressures and a falling stock price impelled Neuromedical Systems, Inc. to revamp its sales and marketing plan for the PAPNET® System. During 1998, expect a new sales approach that supports a product with enhanced capabilities. Neuromedical is developing overseas markets while pursuing primary screening approval in the United States.

EXPECT TO SEE A NEW LOOK and a new marketing plan from **Neuromedical Systems, Inc.** of Suffern, New York. The company's PAPNET® System is undergoing a comprehensive makeover.

During 1998, the company intends to radically revamp how its PapNet System is packaged for laboratories. "It would be fair to say that we learned a lot from the experiences of 1997," stated Jack Henneman, Executive Vice President, U.S. Operations at NSI.

"Our corporate priorities during 1998 will be to build overseas sales of the PapNet System while developing the necessary clinical data to gain FDA approval for PapNet as a primary screener in the United States," he said. "Even as these priorities are addressed, we are making fundamental changes to the way PapNet itself is operated by laboratories and marketed to laboratories and physicians."

Neuromedical's financial performance throughout 1997 was disappointing. From a high of $24 in January 1996, share prices dropped steadily. NSIX shares currently trade at less than $3. The pressure to perform led to a change in leadership during the last part of 1997 as well as a reassessment of the company's product position in the marketplace.

Neuromedical's PapNet System was approved by the Food and Drug Administration (FDA) in 1995 only as an adjunct Pap smear test. Because of that, NSI decided that marketing directly to the consumer would be the best way to unlock new money for Pap smear screening and to educate women about the benefits of a PapNet Pap smear.

Need To Make A Profit

Laboratories that offered PapNet testing needed to make a profit. So NSI recommended a $35 patient bill fee while charging the referring laboratory $18 for the procedure.

For many reasons NSI chose to centralize scanning of Pap smear slides at laboratories operated by NSI in Suffern, Amsterdam and Hong Kong. As a result, the referring laboratory had to send the slide to the

scanning center, then wait for the slide and the scan file to be returned. Details of NSI's business plan and the technology involved in the PapNet System were presented in an earlier issue of THE DARK REPORT. *(See TDR, July 1, 1996.)*

"Our new business plan for PapNet recognizes the importance of involving both pathologists and cytotechnologists in the process of physician and patient education about PapNet and its benefits," stated Henneman. "We better appreciate the collaborative process between a physician, his patient and his chosen laboratory. We want to support that relationship.

"For PapNet itself, we are building in the capability for it to run unattended. This permits any laboratory to acquire and operate the instrument by itself. Ultimately, we will eliminate the need to ship the slide to a central scanning center."

Henneman recognized the importance of gaining authorization to use PapNet as a primary screener. "Given rapid developments in the marketplace, it is essential that we achieve this. Realistically, FDA approval for primary screening is probably 18 months away.

"During the time necessary to obtain primary screening approval, we see two useful applications of PapNet," he continued. "First, we have an existing rescreening business here in the United States. We will continue to support and expand that business. For laboratories which elect to rescreen 100% of their Pap smears using PapNet, we are now offering substantial discounts.

"Second, there are niche applications for PapNet as an adjunct test which make sense. These niches include high-risk populations of women, or women who choose to minimize even the small risk of a false negative by having a PapNet test done in tandem with the normal Pap smear."

Europe plays an important part in Neuromedical's short-term business plan. "The different regulatory environment there means PapNet customers in Europe can use the system for any clini-

USA TODAY

Reports Study Findings

Computer check no help on Pap smears

The Associated Press

CHICAGO --A computer system for double-checking Pap smears was no better than hu-mans with microscopes at finding possible early signs of cervical cancer in a new study, and the automation costs far more, researchers say.

The technology might be worth the cost in laboratories that process a higher proportion of abnormal Pap smears or that employ less accurate technicians than the lab in the study, researchers say.

The study was conducted at the Armed Forces Institute of Pathology in Washington, D.C., which does medical research and education for the Army, Navy and Air Force.

Researchers at the institute say a computer system called PAP.NET found only six slides containing unusual cells among 5,478 Pap smears that had been judged normal in 1994 and 1995 by technicians using microscopes. The Pap tests were done on military women and dependents.

A panel of experts who then studied the six slides found none of the cells to be even precancer-ous. The cost per slide was about $3 when examined by a technician and $9.38 using PAPNET.

"It is difficult to conclude on the basis of our results that there is any clinical value to PAPNET-assisted rescreening," say the researchers, led by Dr. Timothy J. O'Leary, director of cellular pathology at the institute.

The study was reported in Wednesday's issue of The Journal of the American Medical Association.

About 14,500 U.S. women are diagnosed with cervical cancer each year, and about 4,800 die of it, according to the American Can-cer Society.

An expert not associated with the study, Dr. Alan M. Garberof the Veterans Affairs Palo Alto Health Care System in Palo Alto, Calif., and of Stanford University, says the automated system -- one of several on the market -- might be more cost-effective in other labs than in the military, where women are usually screened yearly.

It is essential that automated cytology companies demonstrate both the economic and clinical efficacy of their technology. Here's a sample of the widespread media attention given to a clinical study by pathologists at the Armed Forces Institute of Pathology, as reported in the *Journal of the American Medical Association* on January 21, 1998. This *USA Today* story was one of many stories published on the same date reporting that study's unfavorable findings concerning the cost-effectiveness of PapNet technology.

cal purpose. Laboratories there are accumulating a vast quantity of data and experience with PapNet involving a variety of populations, including data from primary screening.

"Currently five significant clinical studies involving PapNet are under way in Europe," he said, "including a 20,000 smear study by the United Kingdom's Health Service. We expect these studies to confirm the clinical efficacy of PapNet and support further growth in European markets."

One key philosophy defines Neuromedical Systems and sets it apart from its main competitor. "Our philosophy is that a human should make the ultimate diagnosis," noted Henneman. "We recognize that the cytopathologist and cytotechnologist possess unique knowledge and experience that have clinical value. This is particularly true where an urban academic laboratory may triage more slides from a high risk population of women as compared to a suburban laboratory serving woman from an upscale community."

Operationally Robust

"We are making rapid progress in reconfiguring PapNet technology so that it is operationally robust and can run efficiently in the customer's laboratory," he said. "We released new scanner technology outside the United States. We expect to release an entirely new scanner configuration during the second half of 1998.

"The PapNet System has always been cytologically robust, in the sense that any given PapNet scanner can examine specimens with different staining and cover slips without recalibration or human intervention" explained Henneman. "This was an essential requirement for the scanning center business model, since we needed to run smears from any customer on any machine. This capability to handle a variety of stains, cover slips and other variables makes PapNet attractive to laboratories. This is particularly true with the increasing use of different cytology preparations, including liquid-based preparations."

Changes Under Way

Jack Henneman's enthusiasm and energy reflect the changes under way at Neuromedical Systems. NSI's new leadership is willing to acknowledge –and has learned from–the two crucial mistakes in the old business plan: marketing to women and emphasizing the "dangers" of the Pap smear did not endear the company to physicians; operating centralized scanning centers instead of placing instruments directly into individual laboratories failed to meet the needs of their laboratory clients.

Despite the handicap of FDA approval only as an adjunctive test, Neuromedical has made considerable progress. As of 1998, there is a CPT code for rescreening. A number of managed care plans have agreed to reimburse for the PapNet procedure. The company is known and recognized within the laboratory and physician communities.

Given the opportunity to redirect the company's marketing plan and product placement strategy, it is incumbent on NSI to develop unquestionable clinical data on the efficacy of PapNet's ability to significantly improve the accuracy of Pap smear diagnosis. If Neuromedical Systems can accomplish all of this during the next 24 months, then its PapNet System may yet carve out a profitable chunk of the Pap smear testing marketplace. **TDR**

(For further information, contact Jack Henneman, at 914-368-3600.)

Automated Cytology Products

Automated Instruments Primary & Rescreening

AutoPap 300®
NEOPATH, INC,

Automated cytology instrument approved by FDA for Pap smear QC rescreening. Awaiting approval from FDA for primary screening function.

PapNet®
NEUROMEDICAL SYSTEMS, INC.

Automated cytology instrument approved by FDA for adjunct testing. Preparing clinical trails to gain FDA approval for use as a primary screener.

SCREEN®
AUTOCYTE, INC.

Automated cytology instrument now undergoing clinical trials. Designed to screen monolayer Pap smears. Has yet to gain FDA approval.

CYMET A40®
MORPHOMETRIX TECHNOLOGIES

Automated cytology instrument entering clinical trials. Designed to screen monolayer Pap smears. Has yet to gain FDA approval.

Liquid-Based Preparation

ThinPrep®
CYTYC CORPORATION

Monolayer Pap smear preparation using filtration technology. Approved by the FDA for use in Pap smear testing.

PREP®
AUTOCYTE, INC.

Part of modular system for preparing and screening Pap smears. It is a monolayer Pap smear preparation using centerfuga-tion technology. Beginning clinical trials to gather data necessary to obtain approval by the FDA.

MonoPrep®
MONOGEN

Product is a manual method for preparing specimens. Creates a monolayer slide with filtration technology. Has FDA approval for non-gynecologic use only.

Integrated Microscopy Workstations

AcCell™, TracCell™
ACCUMED, INC.

AcCell is an interactive, computer-controlled, slide-handling, and precison microscopy workstation with integrated data management system. TracCell uses computer imaging to map slides and help the cytologist review relevant areas of the slides.

Pathfinder®
NEOPATH, INC,

Product is a microscopy workstation with enhanced features to support the cytologist with goal of improving accuracy and productivity. NeoPath purchased this product line from Compucyte, Inc . in 1997.

CEO SUMMARY: This is the year when automated cytology establishes itself. New companies will gain FDA approval and enter the marketplace during the next 18-24 months. Core technology will continue to evolve at a rapid rate. Pathologists and cytotechnologists will find themselves challenged to stay current with the pace of new product development. Because of this rapid-fire change, pathologists and laboratory executives must exercise caution when deciding how to invest in competing technology.

IN-DEPTH ANALYSIS & COMMENTARY

Automated Cytology Technology To Come Into Its Own In 1998

CYTOLOGY IS WIDELY RECOGNIZED by commercial laboratories as a money-losing segment of the business. In particular, reimbursement for Pap smears fails to recover the full cost of providing the service.

Cytology is also an area of laboratory operations which generates a disproportionate share of malpractice expenses and litigation. Many laboratory executives would be shocked if they understood how much money is spent annually on cytology malpractice premiums and legal expenses involved in defending malpractice suits involving cytology testing.

Because there are more than 50 million Pap smear tests performed annually in the United States, reimbursement and malpractice problems are significant to clinical laboratories. But given the current state of technology and clinical practices, there has been no effective and safe way for a clinical laboratory to solve these problems.

THE DARK REPORT believes that the arrival of automated cytology technology is about to revolutionize this segment of the laboratory business. During the course of this revolution, solutions to intractable problems in Pap smear reimbursement and litigation expenses will arise. Further, this same cytology technology will eventually transform anatomic pathology. But that is another story to be reported in the future.

Several key reasons lead THE DARK REPORT to believe that automated cytology technology is about to turn the cytology world upside down. In order to understand why this is true, it is necessary to look at the early entrants into the field. The analysis which follows is uniquely our opinion and insight. It is based on site visits to some of these vendors, as well as discussions with laboratorians using the technology, financial analysts, and other experts who track this industry.

In reviewing the players in the automated cytology marketplace, there is a fairly clean division between those companies offering improved preparation technology and those companies developing automated or enhanced diagnostic instruments.

In the preparation category, three companies are known to be addressing this market: **Cytyc Corporation** of Boxborough, Massachusetts; **AutoCyte, Inc.** of Burlington, North Carolina; and **MonoGen** of Herndon, Virginia.

Those companies offering instruments to improve Pap smear diagnoses are **NeoPath, Inc.** of Redmond, Washington; **Neuromedical Systems, Inc.** of Suffern, New York; **AccuMed International, Inc.** of Chicago, Illinois; AutoCyte, Inc.; and **MorphoMetrix Technologies, Inc.** of Toronto, Canada.

The first category to consider is Pap smear preparation. Basically, competitors in this market segment are advocating monolayer technology. A physician preparing the Pap smear in the traditional way smears the collection brush on the slide, fixes it and sends it to the laboratory where the slide is stained, a cover slip is added and the finished slide is ready for review.

Monolayer preparation is a simple concept. The physician takes the collection brush and puts it into a vial of transport liquid. The cells are diffused in the transport medium and the vial is shipped to the laboratory. This is one point of improvement claimed for monolayer preparation. On a traditional Pap smear, only about 20% of the collected cells typically make it onto the slide. Swishing the collection brush into the transport liquid consistently captures upwards of 90% of the collected cells. Thus, the monolayer preparation process starts with an enriched sample compared to a traditional Pap smear.

At the laboratory, technology is used to separate the target cervical cells from blood, mucous and other extraneous biological material. The resulting harvest of cervical cells is then deposited on the slide in a uniform "monolayer," stained, given a cover slip, and

prepared for review. Proponents of monolayer preparation point out that the monolayer process consistently delivers 70,000 to 80,000 readable cells per slide.

This contrasts with a traditional Pap smear, where as few as 4,000 to as many as 300,000 readable cells may appear on a slide. Given that sometimes as few as three or four cells on a Pap smear may indicate a potential disease state, the consistent presentation of 70,000+ readable cells on a monolayer is claimed to provide a improved ability to detect the finite number of abnormal cells crucial to early detection.

Different Approaches

Cytyc, AutoCyte and MonoGen all offer technology to produce a monolayer Pap smear slide. But they do it using different approaches.

Cytyc's ThinPrep® Process gained FDA approval for its use in Pap smear preparation. It uses a filtration approach to separate the target cervical cells from blood and mucous. Laboratories using the ThinPrep System must buy or lease the instruments which separate the cells. These instruments retail in the range of $30,000. Consumables per processed slide cost $9.75 at Cytyc's posted retail price.

AutoCyte is designing a combined instrument workstation. It will include a monolayer processing instrument, called PREP®, and an automated cytology reader, called "SCREEN." AutoCyte has yet to gain FDA approval. It is preparing the clinical data to support its Pre-Market Application (PMA).

AutoCyte intends to sell individual components of its system. Autocyte's technology uses centerfugation to separate the target cervical cells from blood and mucous. AutoCyte indicates that its consumables per slide will be priced significantly below those of Cytyc's. Since AutoCyte does not need to supply filters, that is probably a major source of its cost advantage.

Assuming that AutoCyte's monolayer prep expenses are less than Cytyc's, its eventual entry into the monolayer marketplace will probably trigger a price war.

Manual Preparation System

MonoGen is a small company which offers a manual system for producing a monolayer slide. Given the huge numbers of Pap smears that flow through the high-volume laboratories which specialize in this business, MonoGen will probably end up as a niche player in the monolayer market.

Moving to the diagnostic side of the Pap smear business, NeoPath would have to be considered the market leader in this category. Its AutoPap® 300 System was acquired and put into use by the three national laboratories and several national HMOs.

As reported in this issue *(see pages 2-4)*, NeoPath is close to gaining final FDA approval which authorizes the AutoPap System as a primary screener. NeoPath's business strategy is to design a machine which ultimately can read traditional Pap smear slides and provide a diagnosis of normal slides without intervention or review by humans.

Copies Coulter's Strategy

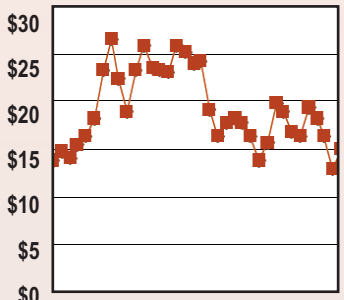
In that respect, its strategy is similar to that of **Coulter Corporation**. Coulter's blood counters eventually replaced hematechs, those laboratory specialists who put slides of blood smears under a microscope and counted cells. Just as Coulter and its eventual competitors transformed the way blood testing was performed in the laboratory, so also does NeoPath hope to eventually have the same impact on the way Pap smears are diagnosed.

NeoPath uses a software algorithm to evaluate video images and make an assessment of the risk of abnormality. This algorithm is undergoing constant improvement, based on actual clinical experience and new technology.

Automated Cytology Firms' Share Prices Reflect Market Successes and Setbacks

FROM AN INVESTOR'S VIEWPOINT, none of the publicly traded companies in the automated cytology field have performed well. Stock prices of these four companies demonstrate how difficult it is to introduce new technology into the healthcare industry.

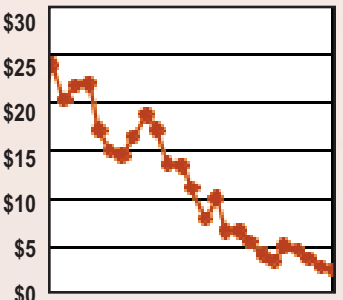
NeoPath, Inc.



Monthly Stock Price
2/28/95 Thru 1/31/98

NeoPath seems to be holding its own. FDA approval for primary screeening should help revenues to increase throughout the remainder of 1998.

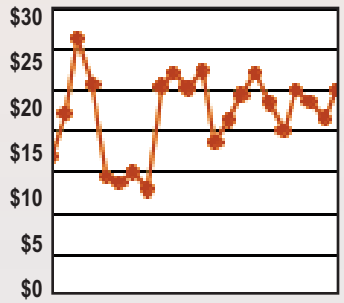
Neuromedical Systems, Inc.



Monthly Stock Price
12/31/95 Thru 1/31/98

Neuromedical's decline in its share price illustrates the poor market response to its sales strategy and product positioning during 1996-97.

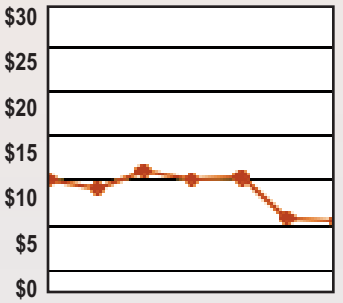
Cytyc Corporation



Monthly Stock Price
3/31/96 Thru 1/31/98

Cytyc expects improved revenue and earnings in 1998. Those expectations have not yet caused an increase it its share price. New CPT codes should help sales of its products.

AutoCyte, Inc.



Monthly Stock Price
9/15/97 Thru 2/4/98

AutoCyte just placed its initial public offering (IPO) in September, 1997. It is still in the development phase and must get its products through the FDA approval process.

Next closest competitor in the race to automate Pap smear diagnostics is Neuromedical Systems. Its PapNet System currently is approved by the FDA for use as an adjunct test. Neuromedical is revamping its business plan, as described in this issue. *(See pages 5-7.)*

Neuromedical's PapNet is built upon neural network technology. Each Pap smear is imaged and studied. The neural network crunches the data and produces images of 128 cells it believes are most likely to show signs of abnormality. These cell images are reviewed by a cytotech or pathologist who makes the final diagnosis.

Neuromedical believes it is 18 months away from obtaining FDA approval to use PapNet as a primary screener. The company is reengineering the instrument so that it can be sold directly to laboratories and run unattended. Neuromedical states that PapNet can read both traditional and monolayer Pap smear slides.

Marketplace Entry

AutoCyte expects to enter the marketplace when its "SCREEN" instrument gains FDA approval. AutoCyte's literature states that the instrument is designed "on the concept of close interaction between the machine and the cytologist. Its major advantage is to allow the rapid and reliable identification of normal samples (which represent 95% of all cases)." This system also is designed to only screen monolayers.

The other known entrant in the race to create a diagnostic instrument for Pap smears is MorphoMetrix. Its product is called CYMET A40®. It will incorporate image analysis hardware and software. The company is preparing to launch its clinical trials this quarter. It hopes to obtain regulatory approval by mid-1999. This system also is designed to only screen monolayers.

One sub-category of instruments exists. AccuMed International markets a line of automated instruments which help a cytologist evaluate a Pap smear with greater speed and accuracy. AcCell™ is an interactive, computer-controlled slide-handling and precision microscopy workstation. It is linked with an integrated data management system. TracCell™ uses computer imaging to map slides and help the cytologist review relevant areas on the slide, as opposed to areas with no cells.

Neopath purchased a similar integrated cytology workstation product in June 1997 from **Compucyte**. The system is called Pathfinder® and gives NeoPath a microscopy workstation to offer clients interested in that kind of solution.

Several Competitors

This run-down of the primary competitors currently in the automated cytology field demonstrates that a variety of products are entering the marketplace. Each company is investing substantial dollars in research, development, sales, and marketing. There will be many consequences from this competitive activity.

First, the core technology itself will undergo rapid improvement. Pathologists and laboratory managers who evaluate one vendor's product today should expect to see dramatic differences in the product's capability, price and productivity during the next 12 to 24 months.

This means that basic technology will be a moving target. Consider automated cytology technology to be on a continuous improvement curve. When looking to purchase or acquire this technology, do a careful assessment of how such technology may be outmoded by developments in the near future.

Second, the underlying economics of this technology will evolve in tandem with enhancements to the technology. What was cost-effective in early 1997 may be be inadequate at the end of 1998. Buyers are advised to do a careful analysis of the economics for this equipment.

Third, how will the clinical marketplace accept this technology? For labo-

ratories, this question should not be overlooked. Physicians, patients and payers all have needs and expectations for cost, effectiveness and clinical relevance. These vested interests may resist the new Pap smear technology introduced by the innovative laboratory which wants to pioneer its use. However, a coming deluge of clinical studies involving all the major cytology products will provide a wealth of data on the issues of clinical and cost effectiveness.

Fourth, reimbursement remains a key component in the decision to acquire and use automated cytology systems. The arrival of new CPT codes for 1998 will encourage payers to properly reimburse for the procedures. However, at this stage in its market introduction, automated cytology systems tend to add more costs to the laboratory than the revenue it generates.

Fifth, automated cytology systems have a valued capability which has yet to gain widespread recognition. By incorporating video imaging and data storage, these systems become critical links in forming an integrated data base of clinical information.

Valuable Capability

Perceptive pathologists will recognize the value in this capability. If properly developed, these pathologists will gain the ability to provide necessary information to managed care plans. More importantly, such data bases provide these pathologists with access to clinical information that adds value to their consultations with individual physicians.

It is critical for pathologists and laboratory executives to recognize that the arrival of competing automated cytology systems will complicate the marketplace. But at the same time, these systems have the potential to solve problems involving inadequate cytology reimbursement and onerous cytology malpractice expenses. This has the potential to improve the financial performance of laboratories.

THE DARK REPORT is confident in its prediction that automated cytology technology will find rapid application within emerging, clinically integrated healthcare systems. That alone promises to transform the economics of Pap smears. We further predict that one of the big surprises of 1998-99 will be increased reimbursement for conventional Pap smears. More on that story in future issues! **TDR**

(For further information, contact Robert Michel at 503-699-0616)

Consequences of New Technology

As automated cytology technology hits the marketplace, expect these major consequences:

- ***Rapid improvement to core technology...*** making earlier generations obsolete.
- ***Underlying economics moves in tandem with technology...*** changing the cost-effectiveness of each new generation of technology.
- ***Unpredictable acceptance by the market of new technology...*** increasing the difficulty of choosing appropirate cytology systems as they reach the marketplace.
- ***Reimbursement arrangements affect economics of specific technology...*** as some payers embrace specific cytology technology, their reimbursement may be more generous than for competing systems.
- ***New cytology systems promise better integration of clinical data...*** enabling early innovators to create "value-added" information packages for managed care plans and clinicians.

SmithKline May Merge With Glaxo Wellcome

World's largest pharmaceutical company would result from the proposed merger

CEO SUMMARY: Both companies confirm that merger talks are under way. The merger is another example of consolidation within the healthcare industry, and is expected to trigger mergers between other drug companies. Fate of SmithKline's clinical laboratory division in the merger with Glaxo Wellcome is unclear.

NEWS OF A POSSIBLE MERGER between **SmithKline Beecham PLC** (SB) and **Glaxo Wellcome PLC** electrified Wall Street and financial markets world-wide.

Not only would the merger of SmithKline and Glaxo Wellcome create the largest drug company in the world, but it would be the biggest corporate combination in history.

Both companies confirmed that merger talks were under way. The name of the new firm would be **Glaxo SmithKline PLC**. As proposed, Glaxo shareholders would hold 59.5% and SmithKline shareholders would hold 40.5% of the issued ordinary share capital of the combined group. Sales at SmithKline are $13.2 billion. At Glaxo Wellcome, sales are $13.6 billion.

The proposed merger of SmithKline and Glaxo results from market forces which encourage consolidation. Analysts predict that a wave of drug company mergers and consolidations will occur in response to the creation of Glaxo SmithKline PLC. These consolidation forces are the same ones transforming healthcare and clinical laboratories.

Merger talks between Glaxo and SmithKline came about because SmithKline earlier acknowledged that it was exploring merger options with **American Home Products**, another drug giant. Glaxo immediately approached SmithKline and American Home dropped out of the discussions.

> ***"We are in the middle of a revolution where biology meets chips."***
>
> ***Jan Leschly***
> *CEO, SmithKline Beecham PLC*

The SB-Glaxo merger could significantly change the clinical laboratory industry. **SmithKline Beecham Clinical Laboratories** (SBCL) would become a relatively small business unit within the new corporation.

Reimbursement declines, increased government regulation and falling test utilization plague SBCL and its laboratory competitors. Because the clinical laboratory industry is recognized as having poor potential for sustained growth in revenue and operating profits, SBCL would not be per-

ceived as a major profit center within Glaxo SmithKline.

That is particularly true given the corporate priority on researching and developing new drugs. SBCL's laboratory activities might be considered a distraction of corporate management and resources.

Evidence indicates that management discussions about the role of the laboratory division within the post-merger company took place. While talks with American Home Products were under way, news services reported from London that SmithKline was considering divesting both its pharmacy benefits division and SBCL.

Impact On Lab Industry

The clinical laboratory industry would see an impact from the merger of Glaxo and SmithKline. Should the merger occur, and should SBCL be spun-off, then the competitive marketplace for laboratory services would undergo fundamental changes.

For that reason, perceptive laboratory executives should watch this story as it unfolds. Of the three national laboratories, SBCL seems to have best weathered the financial storms. But any major restructuring to its corporate parent will directly bring about changes to the laboratory division.

Such changes will not be visible in the day-to-day operations at SBCL. As a billion-dollar operation, SBCL has the resources to sustain existing services. Instead, such changes will involve fundamental strategic decisions about what kind of business SBCL wants to become.

Those strategic decisions would affect marketing and sales activities within the laboratory company. It will also influence pricing decisions for laboratory testing. Because of SBCL's size and clout, any new directions would affect the competitive marketplace for laboratory services. TDR

(For further information, contact THE DARK REPORT at 503-699-0616.)

Radical Technology Drives SB Merger

Two technological developments push SmithKline Beecham PLC to consider merging with a competitor. Both technologies will similarly transform clinical laboratories.

First is the introduction of techniques to rapidly locate and identify genes. Genes and the proteins they produce are used by drug companies to decipher a disease's biochemical pathway, thus identifying "drug targets," sites where a pharmaceutical could have therapeutic value. These same genes and proteins will also create diagnostic opportunities.

Second, new robot chemistry is transforming the way chemicals are produced and tested. Automated instruments, combined with silicon chips, can now make thousands of new chemicals per day. Previously, chemists could only make such compounds one at a time. Technology used in these automated chemistry systems is working its way into diagnostic testing instruments for clinical laboratory use.

Richard Sykes, CEO of Glaxo Wellcome, noted the profound change this technology is bringing to the pharmaceutical industry. To "reskill" the company away from trial-and-error screening of chemicals for medicinal activity, he said "the future is in molecular genetics, cell biology and the modern sciences."

CEOs at both Glaxo and SmithKline decided that consolidation would give both companies the best chance of surviving this technological revolution. It is estimated that up to $3 billion of administrative, marketing and manufacturing costs can be eliminated through consolidation. This money will be applied to further research and development, improving the competitive position of the merged company.

Program Update

3rd Annual War College Highlights Managed Care

CEO SUMMARY: Laboratory executives seeking ways to survive and thrive with managed care contracts will find innovative strategies at this year's EXECUTIVE WAR COLLEGE on Laboratory Management in New Orleans on May 12-13. Also featured are powerful case studies that define effective management in the post-laboratory consolidation phase.

Managed care and its impact upon clinical laboratories gets special attention at this year's *EXECUTIVE WAR COLLEGE* in New Orleans on May 12-13, 1998.

Inadequate reimbursement for laboratory and pathology services from managed care plans is a major cause of financial instability at individual laboratories. "Can laboratories make money on a managed care contract?" asked Robert Michel, Editor In Chief of THE DARK REPORT and producer of the program. "Not if they continue to offer prices which are less than their costs.

"To help address this problem, the *EXECUTIVE WAR COLLEGE* offers special information on several key aspects of contracting for managed care services," he continued. "Laboratories will learn why they leave dollars on the table during contract negotiations. That is a first step to reclaim some of that money."

Not only is an extended session scheduled for the topic of managed care, but an optional third-day program is devoted exclusively to laboratories and managed care contracting. Kerry Kaplan, Principal at **Healthcare Connections**, will provide attendees with *Secrets That Managed Care Plans Don't Want Laboratories To Know.* Arthur Steinberg, M.D., formerly a Medical Director at several prominent eastern HMOs and now at **DIANON Systems, Inc.**, will reveal ways of *Creating the Value-Added Laboratory Services Wanted By Managed Care Plans.* From **Anthem/Blue Cross**, Maureen McKee will describe the *Provider Network Lessons Learned By Anthem.*

As a result of these presentations, *WAR COLLEGE* participants will acquire practical knowledge which adds dollars to their profit line. These are the real-world, hands-on techniques for making money. As in past years, the *EXECUTIVE WAR COLLEGE* brings laboratory administrators and directors proven, effective techniques for creating the high-performance laboratory organization. It's a "must attend" event. **TDR**

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Brian Carr and Haywood Cochrane's **Pathology Consultants of America** (PCA) is wasting no time. On January 19 the Nashville-based company announced the formal launch of operations. *(See TDR, January 19, 1998.)* This was followed by another announcement 15 days later that PCA had obtained a $15 million credit line from **NationsBank**. The pathology-based physicians practice management company (PPM) expects to use the credit line to "structure new affiliations with pathology practice groups."

Mercer/Foster Higgins released the results of its annual survey of healthcare costs. Overall medical costs for active and retired workers increased just 0.2% for 1997. The survey found that 82% of American workers with health insurance were now in managed care plans, up from 52% four years ago. More ominously, the Mercer/Foster Higgins survey polled 4,000 employers and determined that the average increase for healthcare costs in 1998 is expected to be more than 7%.

APR MAY BE IN MERGER DISCUSSIONS

Last issue of THE DARK REPORT noted the departure from **American Pathology Resources** (APR) of its CEO and President, George Goodwin**.** Sources tell THE DARK REPORT that APR, a Nashville-based pathology PPM, is negotiating a possible sale or merger with another pathology-based physician practice management firm. APR officials declined to return calls concerning the matter.

ADD TO:...AMERICAN PATH RESOURCES

Assuming that APR was negotiating a sale, another pathology PPM would be a logical buyer. Could Pathology Consultants of America, armed with their new $15 million credit line, be a party to negotiations? The only other pathology PPM known to have available funds is **AmeriPath, Inc.**

Last Monday, **Accumed, International, Inc.** of Chicago, Illinois disclosed the resignation of its Chariman, President and CEO, Peter P. Gombrich. Replacing Gombrich is Paul F. Lavallee, currently a director. Gombrich will remain as Vice Chairman of the Board of Directors. Accumed produces an integrated automated cytopathology system, along with other products. *(See pages 9-14.)*

Additional rumors involving laboratory mergers and acquisitions involve **Dynacare**. In different parts of the United States the Canadian-based laboratory has conducted direct negotiations with several independent commercial laboratories which might be for sale. Dynacare also kicked the tires at some laboratory sites which **Quest Diagnostics Incorporated** would like to shed as part of its restructuring. Despite all the shopping, there is no hint that Dynacare is ready to formalize an agreement to buy another laboratory.

MORE ON:...DYNACARE

Intelligence sources say that Dynacare's Milwaukee joint venture, known as **Dynacare/United Regional Medical Services**, gained provider status with **Wisconsin Independent Physicians Group**. WIPG is a significant player in southeastern Wisconsin.

That's all the insider intelligence for this report. Look for the next briefing on Monday, March 2, 1998

THE DARK REPORT

UPCOMING...

- *DIANON Systems, Inc. Enters Florida Market By Acquiring Tampa Pathology Laboratory.*
- *Red Or Black Ink? Public Laboratories Disclose 1997 Earnings.*
- *LabCorp Rolls Out New Laboratory Product To Attack Niche Market.*
- *Hospital Laboratory Outreach Programs Continue To Scoop Up More Testing.*