Practical Considerations for High Volume Blood Test Screening

Routine health screening today typically includes drawing a blood sample and running a twenty-test panel for serum lipids, metabolites, liver enzymes which sometimes includes electrolytes. These tests are typically run on people who are presenting for an annual physical exam and likely do not show symptoms of any disease.

Competition and cost containment pressures have imposed rather severe constraints on these routine blood tests for the laboratories that perform them, and on the raw material (reagent) suppliers. From the laboratories perspective, there are two factors impacting profitability: (a) the need to automate the routine tests to reduce the complexity of the steps involved and the processing time required to complete the test, and (b) the need to keep the reagent costs down.

From the reagent supplier's perspective, the laboratory profitability constraints impose pressure to keep their pricing low, forcing them to keep their cost of goods sold (COGS) under control to maintain profitability.

Clinical Laboratory Perspective

Clinical labs tend to be low margin businesses. The large number of facilities (labs in every city) means that there is intense competition and with tens of thousands of employees required to operate the equipment, the majority of their cost are labor costs. For the clinical lab to be profitable the gross margin (price minus raw material costs) on the screening test must be at least 70% or more and the labor costs must be kept at a minimum.

Level of Automation

To achieve low labor costs, routine test panels are now run on automated analyzers, which must be able to rapidly process samples at high throughput rates. These instruments are available in a variety of capacities, starting at about 100 samples per hour (producing about 600 test results per hour) up to larger machines that can process 600 samples per hour and produce over 2,000 test results per hour.

High volume equipment used to run routine tests is often operated by less experienced lab technicians who have limited expertise, so an important requirement is that the instruments have "full walk-away" automation. That is, once the samples and reagents are loaded into the machine, they require minimal operator intervention to complete the test panel. This high-volume screening equipment must also be simple to operate and the tests cannot take a protracted amount of time to complete. For example, routine metabolites and serum lipid tests involves adding all the reagents and serum, incubating them for several minutes and then reading the results. This level of simplicity fits easily into the high-speed equipment that run these tests. (More complex tests such as PCR-based assays are processed in the "special chemistry" section by highly skilled technicians).

Cost Structure of Routine Screening Tests

The full twenty test panel (serum lipids, metabolites, etc.) described above is typically reimbursed at about $25.00. The typical reagent cost (from the manufacturer) must be below $5.00 for the lab to be profitable (80% gross margin).

Reagent Manufacturer Perspective

As noted, the selling price for the reagents for this 20 test panel is around $5.00, and test suppliers aim to deliver a high gross margin (>80%) to cover non-production expenses. Thus the manufacturer's COGS must be less than $1.00. Reagents (and instruments) are usually produced in a central location with reduced overhead and lower labor costs (as a percentage of sales), but the manufacturers must still fund extensive R&D and sales operations.

Examples

High Volume Routine Health Screening **-** As noted, a full 20 test health screening panel has a $25.00 reimbursement rate. The reagent cost (from the manufacturer) is around $5.00. The manufacturer COGS is less than $1.00 for all 20 tests in the panel. Thus the cost of goods sold per test must be less than $0.05, example, the cost per test for glucose is less than $0.01. At these cost levels the test are profitable for both the lab and the reagent suppler.

Prostate Cancer Screening with the Current PSA Test - The PSA assay reimbursement rate is about $34.00. The reagent suppliers, (Abbott, Roche) sell the test for about $3.50 to the clinical lab. The COGS for this test for the suppliers is about $0.30 (90% gross margin), and is profitable for all. The ideal time for deploying a high predictive power blood based cancer screening test would be to order the tests and draw the blood at the same time as the blood draw at the annual physical exam. Thus cancer screening tests, at an annual health assessment, must be deployable in the same processing centers and throughput ranges as needed for high volume routine testing noted above.

Cancer Screening Opportunity at the Annual Physical Exam.

There are two potential ways being developed that can achieve this goal.

OTraces Method

The OTraces method uses simple immunoassays, similar incubation time to those discussed above for the twenty-panel test. For example, the Roche *Elecsys* system, that will process OTraces' Cancer immunoassay panel with only one reagent addition before the read step, again fitting nicely into the high volume front end of the clinical lab. These *Elecsys* systems are already deployed in the high volume clinical laboratory. Assay time is less than 10 minutes for most modern immunoassay systems used today, so this method fits into the cost/production time framework of the typical lab. It is estimated that there are over 100,000 instruments deployed around the world (from instrument suppliers such as Abbott, Roche, Siemens, et.al.) in the high volume front end of clinical labs that are capable of running, without modification, the five-assay panel needed for the OTraces method.

The sample preparation to run the tests is identical to that already deployed in labs around the world to perform routine clinical chemistry. The concentration levels of the biomarkers used in OTraces tests are available in the blood at routine concentration levels that do not require extensive and or complex amplification steps.

Liquid Biopsy

This is a complex assay that can detect either circulating tumor cells or mutated DNA associated with cancer. The method involves detecting very low level analytes in the blood. The process is complex, and involves: first, an enrichment step where the target DNA is extracted from the serum and super concentrated; then the DNA must be amplified (a polymerase chain reaction); and lastly, the target sequence must be detected to verify its presence.

These steps may require far longer than one hour, and involve enough steps that the long time and multiple steps render "full-walk-away" automation impractical. These tests are now offered by various so called "CLIA" labs, priced at $500.00 (and up). (These CLIA tests are not FDA approved and may well be suppressed by the FDA at some point in the future).

Reimbursement Rate Considerations

Reimbursement price restrictions are the driving factor to acceptance of these cancer screening modalities. We believe that for routine cancer screening, the upper price pressure point would be about $100.00. For example, mammograms are reimbursed at about $100.00. The HPV test for cervical cancer is also reimbursed at about $100.00; with a PAP smear added it is about $140 total. (N.B., the HPV test is not a true annual screening test. For many women the HPV test may be needed only once in lifetime, e.g., if they are monogamous).

With the current focus on cost control, higher reimbursement rates do not appear viable in today's health screening market. If they were, for example, ultrasound, which costs ~$250.00, would be approved for women with dense breasts as mammography does not work for them.

In order to be profitable the lab must be able to work within the current cost constraints, e.g., at a reimbursement rate of $100.00. We do not believe that liquid biopsy can achieve this, given the complexity of the steps involved. As the OTraces test utilizes simple immunoassays, expected to cost less than $2.50 to manufacture, it is better suited to the high-volume lab setting and is expected to be profitable at a $100.00 reimbursement rate (As an example, we have indications that the OTraces test for breast cancer being discussed for the Russian market will be reimbursed at $100).

Though price pressure is high note should be taken that these tests when run as routine annual health screen tests represent huge markets. The test is ordered for people who are healthy and they get the test once a year for life. The total available market (TAM) for routine health screen tests for prostate cancer is about $2 billion year for the reagent supplier. The market for breast cancer is about the same as the test is targeted to people over 40 and they are tested annually. At OTraces cost of goods sold and attractive reimbursement rates these test will produce a very high ROI, and company valuation.