



Personal Cell Analysis (PCA) System

Operational Analysis

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1 INTRODUCTION

Guava Technologies recently hired Tefen USA, an operations management consulting firm, to conduct an operational assessment of Guava's PCA system, a benchtop microcapillary cytometry system for single-cell analysis using fluorescence detection methods.

The assessment analyzed the performance of the PCA in comparison with traditional methods of conducting cell counting to identify benefits that may be expected by a company or lab switching to the use of a PCA and mainly to determine the return on investment (ROI) of the system. For that purpose Tefen has developed an Excel based ROI model and populated it with data collected as part of this study. The model identifies the operational cost of the PCA and the ROI based on company specific inputs such as the number of samples tested, the cost of labor, and other testing parameters.

The study focused on identifying the operational and financial benefits of using the system, specifically around labor requirements, material costs, cycle time, throughput, ease of use, and space requirements.

Additionally, the PCA system offers further, non-quantifiable operational benefits over current techniques due to some of the system features. These are discussed below in the case studies.

Even though the PCA has multiple applications, the ViaCount assay was identified as the most representative and most common biological application run on the system by its users, and therefore selected as the main focal point for this assessment.

This paper presents the findings of the study and a summary of the ROI analysis.

For any questions about the details or the findings of this study, please contact **Marc Puich** or **Amit Paz** at Tefen's West Coast regional office (1-800-9-TEFEN-9).

2 EXECUTIVE SUMMARY

Use of a Guava PCA demonstrated substantial benefits over the alternative reviewed method (manual Trypan Blue). From a financial standpoint, the PCA showed a good ROI with a breakeven point occurring at a five months for a 100 samples/day volume and at a little over two years with a volume of 30 samples/day. This single sample version of the PCA would therefore pay for itself in as little as 12 months if three or four people were running 12 –15 samples per day. It should also be noted that these savings are based on the ViaCount application only and do not take into account the use of the unit for any other applications, such as MutliCaspase, Nexin, Cell Cycle, TUNEL and Express. Any additional use will increase the ROI.

The return on investment over a 7-year period (net savings at a 50 samples/day level) is expected to be 470%.

If we extrapolate these findings to the newer PCA-96 the microplate capability would be expected to show a ROI in less than six months for a single full 96 well plate being ran once a day. Once again, the six month ROI is based only on one application (ViaCount). When additional applications of the unit are used, the ROI becomes faster and the savings greater.

In addition to the financial benefits, several other significant advantages of the system over other testing techniques were observed. The guava PCA tended to be more user friendly, provide consistent and standardized results, improve the lab operations and work flow (in the areas of availability and flexibility), reduced exposure to manufacturing and quality risks and overall improved the productivity of the laboratories. Details of these findings and benefits are provided in the following sections.

3 OBJECTIVE

The main objectives of the study were the following:

- Compare a typical lab's operation with and without a Guava PCA
- Identify any benefits a PCA may have to a lab's operation
- Develop a model that would determine the ROI of a PCA purchase, based on relevant variables

4 METHOD

Introduction:

Tefen's consultants familiarized themselves with the Guava PCA and its operation in Guava's laboratory in Hayward, CA and its technical features were summarized by Guava's staff.

Model Development:

An Excel model was developed to retain data relevant to the cost of operation of a PCA as well as alternative methods. The model was developed to receive an input detailing the expected usage of the PCA (samples per day) and provide the expected savings as a result of using the PCA vs. the alternative.

Data Collection:

Data required for the study was collected through visits to Guava as well as site visits to actual users of Guava's PCA. The data included cost elements making up the PCA's cost of operation, such as material and maintenance costs. A full description of the model inputs is provided in Appendix A. Operational standards were determined by conducting time studies of customers operating the Guava PCA and performing Trypan Blue assays for real research and development samples.

Data Analysis:

The data collected was analyzed and populated into the Excel model to determine the cost of operation and the ROI. Additionally, the observations conducted during the site visits with the Guava users were reviewed to identify the PCA's impact and benefits to the lab's operation. The benefits listed in the following sections are a summary of these observations and the feedback provided by the PCA users which identified or confirmed the benefits listed.

5 PCA BENEFITS AND AREAS OF IMPACT

5.1 Labor Requirements

One of the main and most apparent benefits of using a Guava PCA, is the reduction of labor requirements. The assay automation offered by the PCA greatly reduces the amount of labor time required, compared to those of Trypan Blue. These requirements at different sample volumes are illustrated in figure 5.1.1 below, which compares the direct labor requirements (labor hours per day) when using a PCA to the requirements when using Trypan Blue. The average labor hour cost to employer (used later for ROI calculations) is estimated at about \$30/hr, which is commonly the cost for a lab technician/scientist in areas such as California, New Jersey or Massachusetts.

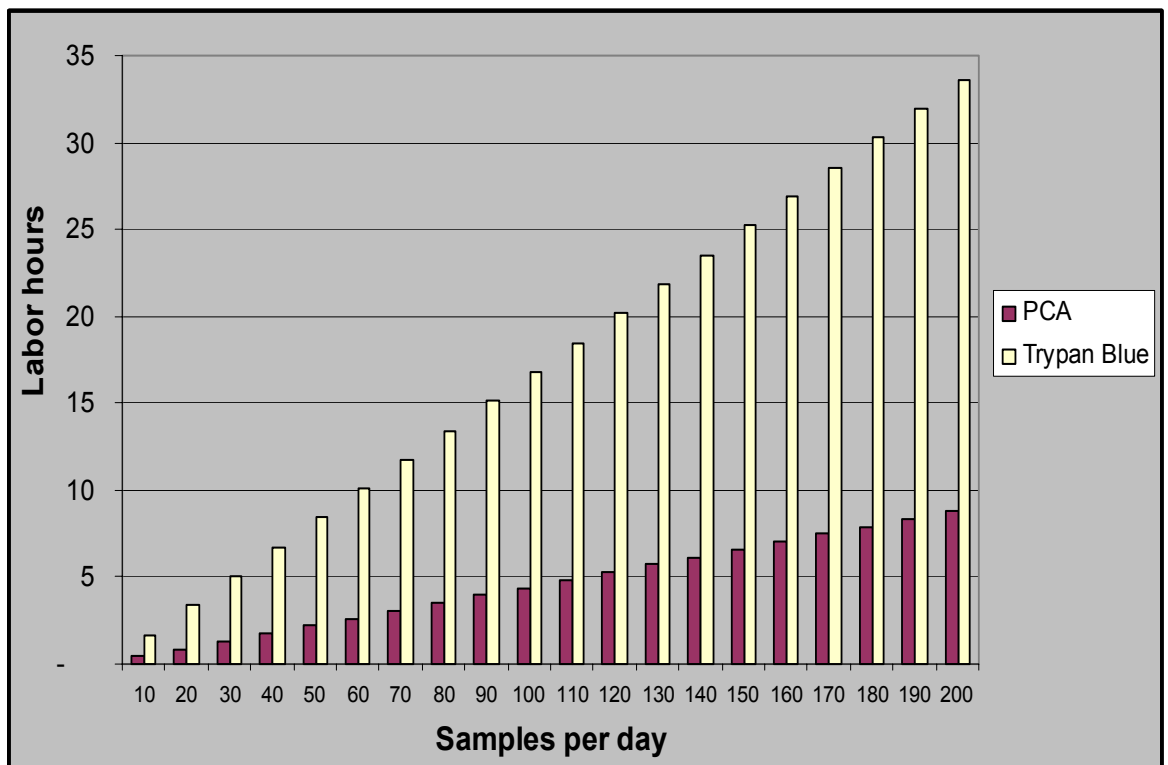


Fig. 5.1.1: Labor hours comparison

Naturally, the reduced labor hours correlate directly to reduced FTE requirements, which are illustrated in figure 5.1.2 below. These are calculated based on a single shift operation (8 hrs per day, 5 days a week) and reflect direct labor requirements for ViaCount testing only and not the entire workload of the analyst/scientist or the benefits when other applications are ran on the systems as well.

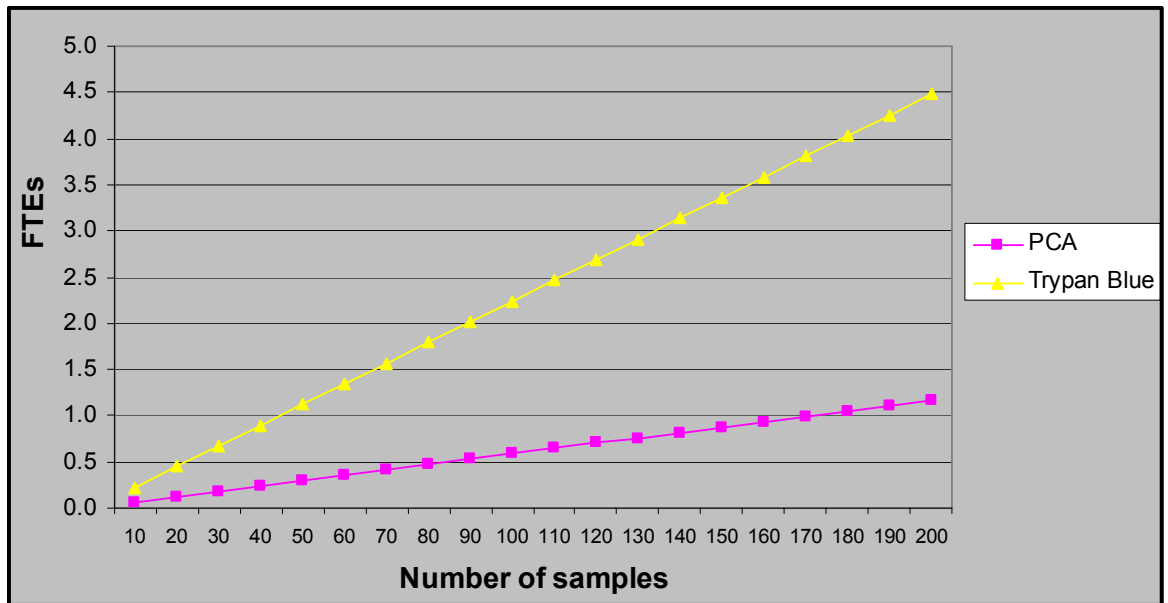


Fig. 5.1.2: FTE requirements comparison

Besides the direct savings resulting from such a reduction, this offers additional benefits to the lab’s operation which are discussed in section 5.7. These include enhancing the lab’s capabilities and flexibility and enabling it to take on additional tasks/projects with the existing resources which are often limited and overloaded.

5.2 Cycle Time

Another benefit of using of the Guava PCA is the reduction of the overall testing cycle time. The extent of this reduction is described by Little’s Law, which states that there is a direct link between the overall cycle time and the processing time. As a result, the PCA is expected to reduce the overall cycle time and the sample queue at the lab by approximately 60%. A reduction of cycle time carries many benefits to the operation, including the reduction of risk exposure, which is further described in section 5.5.

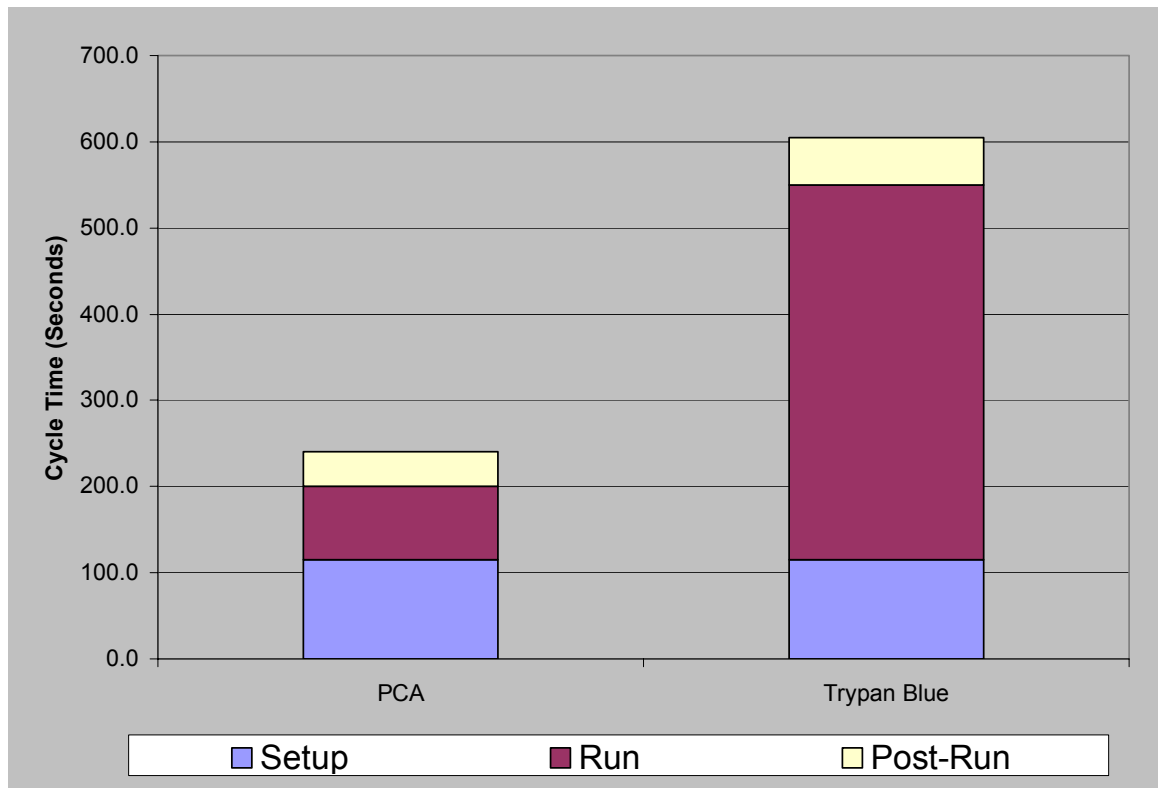


Fig. 5.2.1: Cycle Time Comparison

5.3 Biowaste Disposal

The requirements for biowaste disposal when using a PCA are negligible. The PCA allows the user to accumulate waste in a disposal bottle and dispose of it every 20 samples. In most cases the waste is treated with bleach and disposed of with no special or hazardous material requirements. While this is also true for Trypan Blue, it is not always the case with other methods and instrument, some of which were reported to generate substantial amounts of waste which require special storage containers and considerable labor time to dispose of.

5.4 Standardization

As with most automated processes, a major advantage over manual methods (i.e., Trypan Blue) is the consistency, reproducibility and standardization of results. The automated reading performed by the PCA is believed to increase both the accuracy and the reliability of the test results. The PCA allows the user to define standards for dead and apoptotic (unhealthy) cells and then repeatedly applies those standards throughout repeated subsequent analyses. It also allows the users to visualize this in a simple data format or a graphical scatter plot automatically, without any set up. This eliminates the subjectivity which, when using Trypan Blue, may cause variation of results between one analyst to another and even within a given analysts readings. This also gives the user a greater insight and predictivity in to the health and vitality of the cells on an ongoing basis.

5.5 Manufacturing Risk

The reduction of cycle time, mentioned in section 5.2 above, makes test results available much earlier and with more ease than would otherwise be possible. This in turn, increases the chances of salvaging a product lot when issues are observed that may compromise the product and mitigates the risk posed by such issues as the earlier detection reduces the chances of potential complications such as poor bioreactor or fermentor performance or bad plates for an HTS screen (All of which cost money and time). It is difficult to quantify such benefits, but given the value and cost of biopharmaceutical products and other samples, both from a financial and patient risk standpoint, the potential impact of the reduced risk factor is likely to be substantial.

5.6 Ease of Use

Aside from the substantially reduced labor time requirements (158 seconds per sample with a PCA vs. 605 with Trypan Blue), users of the PCA say it is much more user friendly and easy to use than manual counting methods that employ Trypan Blue. The instrument is very simple to operate and requires minimal training. While conducting assays using Trypan Blue is strenuous on the eyes and, to a lesser degree, the hands and fingers, the PCA is extremely simple to operate and requires minimal operator intervention.

5.7 Lab Operation

The reduced labor requirements and shorter cycle time that the PCA allows compared to Trypan Blue contribute significantly to the lab's operation by enhancing the lab's capacity, flexibility and capabilities. The decreased labor requirements free up considerable amounts of the analysts time and make them available for other projects and studies. This increased availability allows the lab to better handle its workload as well as take on additional studies. In the typical lab and research environment, where labor resources are often sparse and pressed to conduct more and more studies, this benefit is particularly valuable. Additionally, the PCA is capable of supporting several other assays including protein expression analysis, detection of biomarkers, cellular health analysis, cell cycle studies, and a suite of apoptosis assays. The ability of one instrument, especially one with the PCA's small size and footprint, to conduct multiple assays allows the lab a wide range of capabilities and flexibility with minimal resource requirements. Since floor and bench space are also often limited in labs, use of the PCA, which has a footprint 5-10 times smaller than that of a ViCell or a FlowCytometer, is highly beneficial.

5.8 Sample Size

The sample size required by the PCA is very small compared to other methods it can be estimated that the sample required for a PCA is at least a 100th of that required in other methods. This allows to lab to sample earlier in

the process, use less product/material for testing and to run more tests on the available samples. The financial benefit of this feature varies depending on the valuation of the sampled material.

6 ROI ANALYSIS

The benefits listed in previous sections amount to substantial financial savings over Trypan Blue and a significant improvement in productivity, which increase as a function of the number of samples being tested. When balanced against the investment, which consists mostly of the initial purchase cost of the PCA, the savings begin to show substantial return on investment (for a 7 year period) at a 10-20 samples/day level and this return increases to approximately 470% at a 50 samples/day level. If we consider the newly launched PCA-96 at even a single run of a full 96 well plate per day we will expect an ROI of almost 900% over a 7 year period.

Figure 6.1 below illustrates the return on investment at various sample volumes for a 4 and 7 year period. A zero ROI indicates a break even while a positive ROI indicates savings greater than the amount invested.

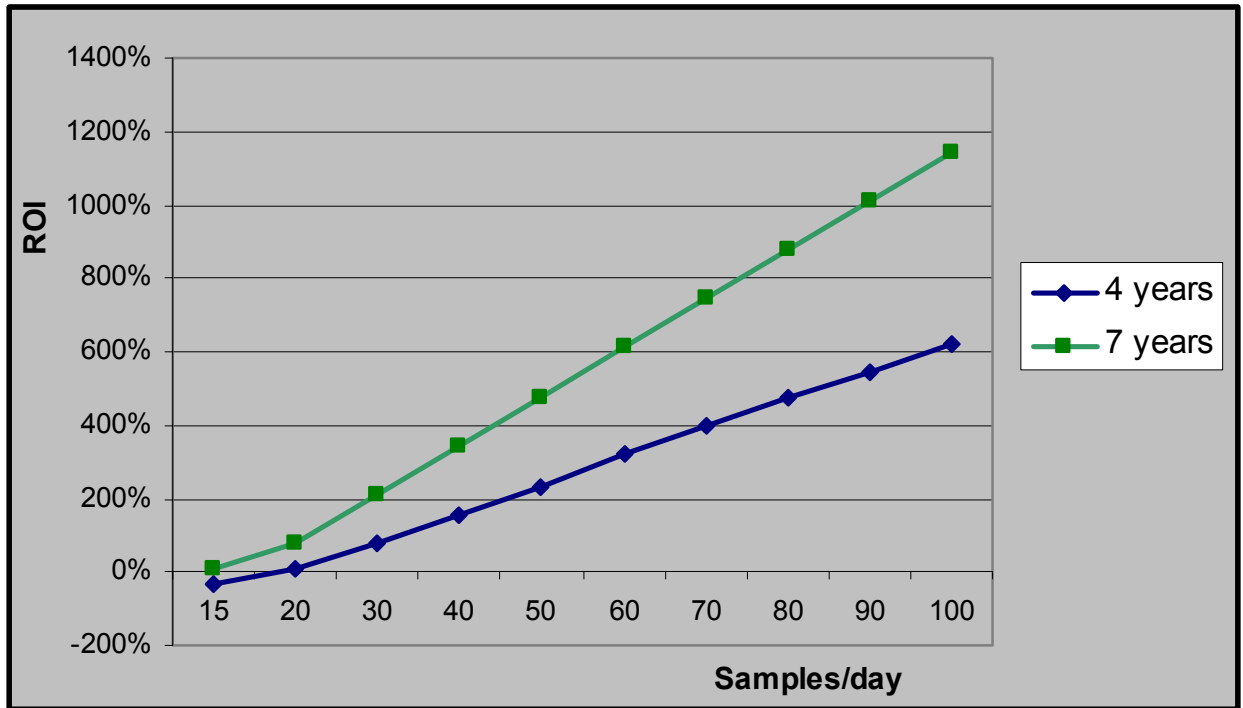


Fig. 6.1: Return on investment over a 4 and 7 year period

The saving used for the ROI calculation is the difference between the costs of the lab operation if using a PCA to those costs if using Trypan Blue. These costs include labor costs, material costs, maintenance, and others described in Appendix A.

Figure 6.2 below shows the time until a PCA investment is covered (break even) at various sample volumes. As the chart indicates, at a 50 sample per day level, the initial investment will be covered in about 1 year and at a 20 samples per day level break even will occur after about 3.8 years.

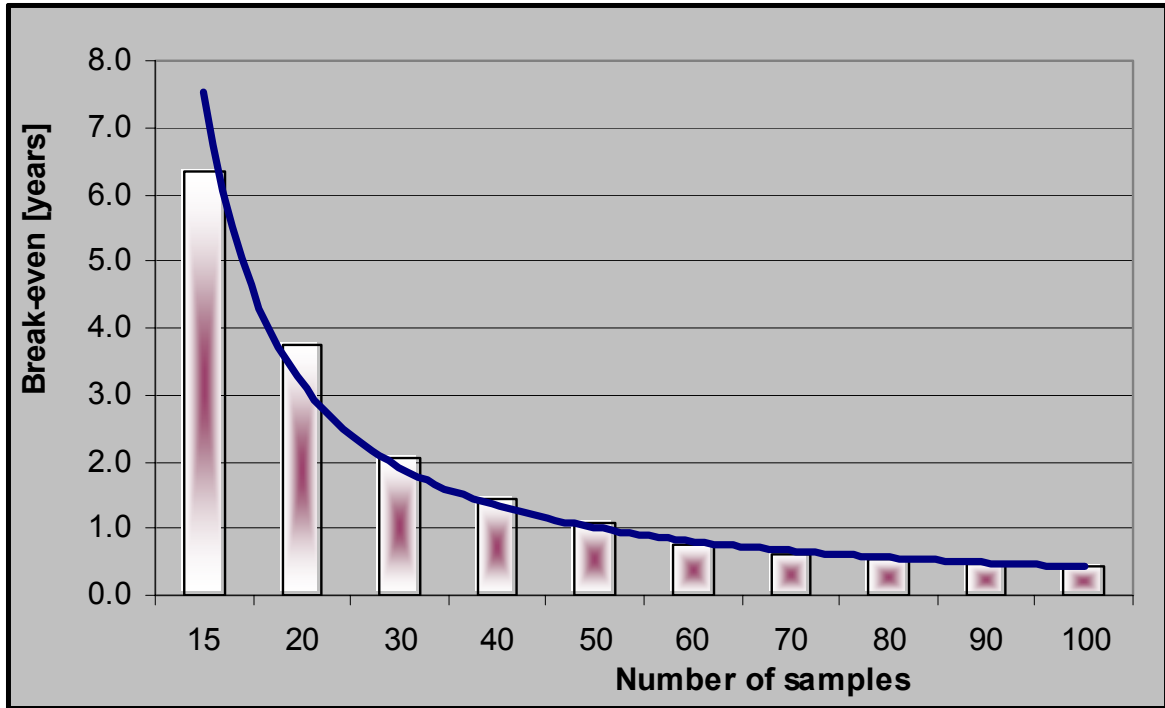


Fig. 6.2: Break-even period for a PCA investment at various testing volumes

The figures quoted in this section have been generated by the ROI model developed for this study. This model calculates the expected ROI given relevant inputs and assumptions and costs mentioned above.

7 CASE STUDY

Most of the benefits described in sections 5 and 6 above, were reported by and/or observed at customer sites, users of the Guava PCA. Below is a summary of the two site visits that were conducted to collect the included information.

7.1 Chiron Corporation

The site visit to their Biopharmaceutical Process Development Laboratory was conducted in July 2003. The PCA had been used by Chiron for approximately 6 months prior to Tefen's site visit. After purchasing the PCA, Chiron ran it side by side with Trypan Blue testing to validate the PCA's reliability and accuracy. The success of this validation resulted in the PCA becoming the primary technique for cell count and viability testing. Chiron also uses its PCA to conduct Protein Expression assays. Chiron has also bought units to be used in different areas as well and currently has over 5 units at this one site.

Users state a very high satisfaction level from the PCA and its performance and emphasize the following as the main benefits, in their eyes, of the PCA:

- High accuracy and reliability of results
- Less labor time required to conduct assays
- Smaller sample volume required for testing
- Quicker testing (shorter cycle time)

- User friendliness: eliminated stress on eyes and hands previously caused when using Trypan Blue

The details of these benefits have already been discussed in the previous sections of this paper.

A ViCell was also available in a nearby lab but the PCA users reported they preferred the PCA on account of its being easier to use and more reliable. From brief observation of the ViCell in use it seems that its run time (machine time) per sample is about 3 times longer than that of the Guava PCA (approximately 2 minutes of analysis per sample compared to about 40 seconds for the PCA). It should also be remembered that the PCA can be used for a further five applications one of which is a fully functional express assay that allows the user to carry out numerous assays.

7.2 Fox-Chase Cancer Center

The site visit to the Department of Pharmacology laboratory was conducted in June 2003. The PCA had been used by Fox-Chase for several months prior to Tefen's site visit. The PCA is used to conduct ViaCount and apoptosis assays, namely Annexin V labeling. The lab's management reported they have been searching for an instrument with the PCA's capabilities for a significant period of time prior to purchasing it and have spent considerable amounts of money and effort in the process.

Users state a very high satisfaction level from the PCA and its performance and emphasize the following as the main benefits, in their eyes, of the PCA:

- Less labor time required to conduct assays minimizes the load on the testing staff, allowing them to take on more projects and perform more experiments with the same resources
- High accuracy of apoptosis testing final results as well as a lower standard deviation within results make the data more reliable and easier to get accepted by journals and other scientists
- Smaller sample volume required for testing makes the testing more cost effective and less difficult for the patient

Additional details of these benefits have already been discussed in the previous sections of this paper.

8 CONCLUSIONS

Given the substantial financial and operational benefits described above, it is clear that the PCA offers a convincing ROI with features that greatly benefit the lab's operation and productivity. These include:

- Significant reduction of labor costs.
- 7-year ROI of 470% at a 50 samples/day level.
- An estimated ROI of almost 900% over a 7 year period for a PCA-96 running one full 96 well plate per day.

At low testing volumes, the financial benefits are not as clear, at which point the other benefits need to be considered as potentially being the deciding factor.

These benefits include:

- Reduced cycle time
- Standardization and reproducibility of test results
- Ease of use
- Smaller sample size requirements
- Improved lab capabilities and flexibility

Regardless, the merits of the PCA described by the positive customer testimonials support the fact that it will be a valuable tool for most labs conducting cell-based assays or cell biological research.