

A COMMERCIALIZED,
INSTITUTIONALLY
INTEGRATED, PERSONAL
GENOMICS BUSINESS MODEL

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Abstract

This report describes a commercialized, institutionally integrated, business model that would introduce a personal genomics product into the Thai marketplace. The broad spectrum product would require sequencing of customer DNA for the identification of between 500 and 1000 genetic markers selected to provide information on ancestry, possession of dangerous alleles, adverse response to drugs, disease susceptibility, and the presence of infectious disease. The product would be marketed to the general public throughout Thailand as well as through clinical settings to patients with immediate clinical needs.

The model proposes the creation of a commercial entity to be the provider of the product but requires that the product be partially subsidized by public sector institutions. In exchange for the subsidy, which would facilitate sales volume, the commercial entity would provide public sector researchers and health care planners and policy makers with anonymous metadata from all customer genomic data obtained. It is anticipated that the metadata, representing an unprecedented sample size, would provide substantial opportunities for Thai genetics research, as well as for the Thai health care system in its ability to assess expected future needs and thus plan for the use of resources.

The raw genomic data obtained from customer samples would be interpreted and presented to customers on a website, where each customer would access their own personal and anonymous webpage. In the cases where the product was purchased for clinical purposes, customers would share their data with their doctors. The website would provide more than just genomic data and interpretations. It would be designed as a genetic web portal with a mandate to educate the general public and the medical practitioner community in many ways.

The integrated nature of the business model, involving the participation of researchers, health care planners, medical practitioners, customers, and the commercial entity has many advantages in terms of synergies and positive feedbacks. Successful implementation of the model would result in the development of expertise and cross functional linkages that would benefit the Thai life sciences sector in many ways.

1. Purpose

The purpose of this report is to conceptually define and describe a commercial personal genomics business model that could be applied in Thailand. It is asserted that the model is close enough to commercial and economic viability to justify full economic analysis as a first step towards potential implementation. Should the model fail to meet immediate viability requirements, it is anticipated that it could be used, in part or in whole, as a basis for reconsideration at a later date when underlying conditions, economic or otherwise, improve.

Although this Consultant has been mandated

specifically to develop a commercial business model, many of the elements of the model could be implemented as part of an entirely public sector undertaking to bring personal genomics to Thailand. Nevertheless, as will be discussed in detail below, it is considered that the creation of a private sector entity will improve the likelihood of success of the model as a whole.

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2. Scope

The scope of this report is restricted to conceptual presentation. Some economic evaluation has been undertaken, giving positive indications for immediate implementation, but further economic modeling work will need to be performed to determine whether the business model passes requirements for commercial viability.

Any personal genomic business model, especially one involving a Commercial Entity, inherently has important sociopolitical implications, both in its implementation and in its operations as an existing entity. These implications have been taken into consideration from the perspective of how they are being expressed by the global community of experts in the field of personal genomics and its applications to health care. Since the majority of expert opinion comes from the United States, it should be expected that this perspective would have an American bias.

While the intersection of concerns and issues expressed in the international community and those specific to Thai conditions surely overlap considerably, there may be important distinctions that would be relevant for a model meant to be deployed in Thailand. In the development of the business model described herein, only a general awareness of broadly defined local conditions has been taken into consideration. No attempt has been made to tailor elements of the model to make it more immediately palatable to specific institutional interests as they exist practically in Thailand, only as they exist theoretically. Indeed, it is understood that the perceived value of this Con-

sultant's perspective is, in part, a result of the lack of a detailed understanding of Thai institutional conditions. It is an outsider's perspective largely free of interpersonal bias. Therefore, whether this model can be implemented politically is beyond the scope of this report.

The business model described herein does, however, heavily rely on the Consultant's own expectations of the value and concerns, practically and morally, related to the collection of personal data (in this case genomic data but also more broadly) in a global society that is increasingly able to collect it and extract meaning from it. Details of these expectations will be a constant theme of this report so it should be stated initially that it is this Consultant's belief that this trend is unstoppable, that there will be enormous net benefits to large swaths of human endeavor, and that privacy and abuse concerns can be managed.

3. Assumptions

The assumptions made in the development of this model are as follows:

3.1. Economic

Product pricing strategy is matter of considering the tradeoff between margin and sales volume. Sales volume at any given price can be increased with marketing expenditures but this puts downward pressure on margins. It is assumed that a product price exists in the space of public perception of expected value that will allow this business model to generate an adequate return on capital invested within an acceptable period of time.

3.2. Political

This business model has important implications for a number of institutional stakeholders, as well as for the public as a whole. It is assumed that any and all potential political obstacles to the implementation of this business model can, with considered argument and compromise, be eventually overcome by the model's widespread and collective merits.

3.3. Technological

As a personal genomics business model, the use of a genetics laboratory in order to perform sample preparation, PCR, and sequencing will be required. The capabilities of the Ion Torrent Sequencer, supplied by Life Technologies™, at the genetics

lab at Ramathibodi Hospital have been used as the template for the construction of the genomics product in this model. It is assumed that this technology, or better, as well as its material and personnel support infrastructure can be used for DNA sequencing in the delivery of the product to the customer.

It is furthermore assumed that all necessary hardware and software for data handing, storage, and manipulation can be procured by the Commercial Entity at a competitive price and promptly delivered as required.

3.4. Personnel

The Commercial Entity in this model will require personnel with very precise expertise for management and day to day operations. Although the requirements will be demanding, it is assumed that the Commercial Entity will be able to successfully employ personnel to fulfill these requirements, or perhaps in some cases outsource the capabilities to do so.

4. Business Environment Challenges

Almost every informed commentator agrees that personal genomics has the promise to revolutionize the delivery of health care services to the public, both in terms of efficacy and cost effectiveness. Given current knowledge, it has become clear that the variations within a person's individual genome have an effect on disease susceptibility, disease progression and efficacy of treatment for almost any ailment. But there is considerable disagreement as to when a broad based personal genomics regime that imparts substantial health care efficacies will likely be practically and affordably achieved, not to mention how it should or could be implemented. Many experts argue that this could be many years away.

Concurrently, demographic shifts in western and many developing countries point to an ageing population and sustained increases in overall health care costs as diseases that naturally emerge in old age present themselves more forcefully in the population. Furthermore, diseases related to environmental pressures, such as the autoimmune suite of diseases as well as newly emerging and rapidly proliferating infectious diseases can be expected to continue to grow in prevalence in response to pressure put on the biosphere from environmental degradation and global warming.

So, the business opportunity, in the form of an urgent societal need, is clearly present. The challenge is to define a business model that will deliver results.

4.1. Competitive Environment

Considering the current cost of sequencing technology, the financial barriers to entry for any enterprise contemplating offering a personal genomics product are very low and will continue to get lower. Furthermore, since much of the data generated by the research community that would be required to prepare such a product has been made freely available via online databases, the barriers to entry based on proprietary information are also low.

Competition, therefore, will be based on an entity's ability to accumulate and retain expertise in the preparation of a product and its ability to penetrate the market. The winners in this envi-

ronment will be the companies that know how to create value for potential customers and how to translate that value into sales.

4.2. Product Value

While many high probability linkages between genomic makeup and clinical outcomes have been established and have led to successful targeted genetic testing regimes, the potential for a broad based personal genomics regime with clinical value in the short term remains uncertain. Researchers are still grappling with how to understand the implications of intra-genomic variations as well as the interrelationships between individual genetics and environmental factors (developmental

and external). The inherent complexity of these interactions makes it very difficult to establish high probability causal relationships between individual genetic markers or groups of markers and specific outcomes at the level of individuals.

This raises fears that promises implied by clinical decisions made on the basis of personal genomics other than in very well established situations will result in erosion of public confidence in health care institutions and, in fact, an increase in overall health care costs due to genetic tests that fail to deliver efficacy results on a case by case basis. This well intentioned fear makes for a very challenging environment for the development of a business model based on the value of personal genomics for individuals, despite its tremendous promise to improve health care in the long term for populations. Given the current state of knowledge and the nature of complexity itself, there is greater predictive power at the level of populations than at the level of individuals.

4.3. Sequencing Technology

With the cost of sequencing per unit of information dropping faster than Moore's law for computer processing, the time of affordable whole genome sequencing will eventually come, although affordability will be defined differently for different population sets. This is obviously encouraging for the future of personal genomics conceptually but health care benefits will only accrue at the rate at which researchers are able to interpret the data.

For a business model based on a specific platform

of sequencing technology, however, a rapidly changing cost structure environment imparts a risk of technological obsolescence. A product based on one level of capability can become obsolete as soon as a better one enters the market. This presents a challenge for any entity engaged in personal genomics but it is one that can be met with a business model that takes this reality into account.

4.4. Bioinformatics Deficit

With the advances already made in genomic data accumulation capability, it has become clear that a bottleneck has emerged in interpretive ability. In addition to the struggle to conceptually understand complex interactions of genes and cellular processes and how they emerge as clinical and disease state outcomes, there is also a deficit in the mathematical tools needed to aid in the analysis of those interactions and outcomes and in the number of individuals with the expertise to use them.

The private sector biotech industry has seemingly realized this as we are seeing new bioinformatics ventures being announced every month. Universities have realized this as well and are starting to respond but it will take time to graduate students with the required skills. Therefore, we can expect this deficit to remain a problem for many years.

The amount of computer processing capacity required for the task of analyzing complex genomic and cellular interactions is vast. This certainly can be a constraint but it appears to be one that has a solution. The vast computing capacity

installed by companies like Google and Amazon, not to mention the huge data processing facility being built by the National Security Agency, will be increasingly made available to scientists. In fact, Amazon already leases out excess capacity that they have built to handle peak retail season sales during the rest of the year. Cloud computing and other platforms of distributed processing will also increasingly come to the aid of genomic complexity needs.

In the coming years we should expect steady advances in interpretive ability and in the development of tools that can be used by any entity that is engaged in the business of personal genomics.

4.5. Research Regimes

The genomic research community has benefitted tremendously from the development of whole genome sequencing platforms and GWAS are now being routinely employed on small sample sets. Actionable results from this capability are only starting to emerge and as the cost of whole genome sequencing declines, larger sample sets will be possible for the same cost of research.

But as the cost of whole genome sequencing becomes cheaper, the cost of acquiring and handling samples will become the limiting factor. These costs are mostly logistics based so are somewhat intractable.

So, the research community will increasingly have the luxury of genomic sampling breadth (number of base pairs analyzed) but will continue to suffer from a lack of genomic sampling depth (number

of samples). The importance of genomic depth may be somewhat underappreciated. It will be in the identification of rare alleles within large data sets that many of the great insights on interactive complexity in the future will be realized.

A personal genomics business model that provides access to genome sampling depth will be highly valuable for the research community.

4.6. External Knowledge Deficit

There is always an imbalance in knowledge between the purveyors of a product and their consumers, but in the case of personal genomics, the imbalance is extreme. Furthermore, since personal genomic data will, in some cases, have direct medical implications, this imbalance has potentially severe consequences. This consequential imbalance has always existed with the provision of medical services, but in this case, even medical practitioners, unless specifically trained in genetics, suffer a knowledge deficit with respect to genomics.

This condition should compel any entity offering a personal genomics product to assume a heightened responsibility to inform consumers of their product's value propositions in an accurate manner in order to minimize misinterpretations and avoid undue concerns. Claims made with respect to product performance must be made carefully.

4.7. Public Versus Private

There is an inherent tension between the public

sector, engaged in the provision of public well-being, and the private sector, engaged in the generation of profits for shareholders. In the health care sector, this tension arguably has the most critical potential consequences. However, this tension is mitigated when goals are aligned and the degree to which the goals are aligned will determine to the degree to which tension is reduced.

Platforms for public-private partnerships are rapidly expanding in the life sciences fields. The large Pharmaceutical companies, in an effort to respond to patent expiration, weakened drug pipelines, and rising clinical trial costs, are looking for ways to reduce risk. They are doing so by establishing joint ventures with small biotech companies and also increasingly by reaching out to establish partnerships with publicly funded research centers. Meanwhile, public research institutions are establishing mandates to work with the private sector to commercialize promising research.

Given the state of the global health care regime, where costs are expected to increase due to demographics and newly emerging health problems, this is a critically important development. The particular propensities of public and private organizational structures and mandates need to be combined synergistically in order to mitigate the risks and time horizons that will be involved in meeting the challenge.

4.8. Focus on Translation

Many health care regimes have adopted a philosophy of having to justify research initiatives

on a translational basis; the so-called “bench to bedside” approach. The attempt is to streamline the time sensitive process of bringing research into actionable products or procedures that have demonstrated health care consequences. No doubt this philosophy is linked to the trend of increasing public-private partnerships.

While this is certainly a laudable effort and one that surely will have some positive results in terms of focusing the attention of the research community on applications, there is a risk that longer term basic research and research that has less easily defined immediate outcomes will be sacrificed to some extent.

Personal genomics, as an academic pursuit as well as a platform for a potential business model, will rely on intense research on the complexity of genetic and cellular interactions to sustain itself to the point where it will start to have an enormous impact on public health efficacy and costs. One would hope that shortsightedness would not stifle this effort considering the wide ranging implications of understanding this complexity, but an overzealous application of a translational philosophy must be considered a risk in terms of the amount of resources applied to this effort.

4.9. Use of Data

Any proposed personalized genomics business model will have to address very seriously the issue of ownership and application of the data it generates. There are real dangers that the data could be used in a discriminatory fashion against individuals, whether controlled by public institu-

tions or private companies. One of the most obvious and perhaps most sinister of uses could be by insurance companies to discriminate on the basis of genetic propensity for disease. The value of this knowledge, in aggregate, to insurance companies would be enormous so the temptation to sell the data to this industry might be considerable.

Legal regimes are starting to grapple with this issue (Thailand has a Privacy of Personal Information Act) but they have not been extensively tested for voracity in the case of personal genomic information. Specific legislation that addresses the use of personal genomic information directly by establishing guidelines for use and openness could, and perhaps should, be enacted.

Perhaps even more of a concern than institutional abuse would be abuse by single individuals against other single individuals where one party has access to the other party's personal genomic data. Individuals could be protected under law from this practice, but it would be much more difficult to enforce.

Any personal genomics enterprise, whether public or private, must have a very clear and consistent ethical standard on the use and protection of genomic data and it must be communicated openly, both internally and externally, so that it is accessible for scrutiny. A failure to conform to strict guidelines, legal or ethical, could very easily result in the downfall of the enterprise.

4.10. Public Scrutiny

Even with airtight guidelines and practice in the use of genomic data, a personal genomics business will be exposed to public scrutiny. The larger and more pervasive the business model is, the greater the scrutiny will be. This trend will probably intensify before it abates.

Although some concern from the public is justified, the greater concern from the perspective of the business model stakeholders will be unwarranted paranoia. At this moment in history, public trust in all institutions is at low ebb. Furthermore, due to the very poor public understanding of science and of genetics in particular, and the all too clear human propensity for conspiracy thinking fuelled by internet enabled confirmation bias, paranoia can easily spin out of control. The Edward Snowden NSA leak story still topical today has only heightened public sensitivity to information privacy.

The public concern for privacy of personal information in general will abate with time but concern for privacy of genomic information will lag in this process due to the poor public understanding of genetics.

The only way for an entity engaged in a personal genomics business to effectively mitigate against public opinion turning sour is to face it head on with policy and business practice openness and aggressive education-oriented public relations.

5. Assertion of Principles

In the opinion of this Consultant, in consideration of the myriad of challenges posed by the business environment, the following should be the main principles that guide the formation of a personal genomics business model that can and should be implemented in Thailand.

5.1. Big Data Paradigm

Broadly, Big Data refers to the capabilities enabled by computer processing power that are being developed to derive information, predictive and interpretive, from very large data sets that cannot be derived from smaller data sets.

5.1.1. The Paradigm

The term “Big Data” has, in the past few years, become firmly established in the consciousness of the informed public. We have seen how companies like Amazon, utilizing algorithms that analyze past purchases, can predict the products that its millions of customers will likely be interested in buying in the future. We have seen how the National Security Agency in the United States can amass communication records from tens of millions of its citizens and, with varying degrees of success, identify potential threats to national security using algorithms that look for patterns of behavior in those records.

These and other examples of how institutions with enormous databases can extract predictive power from pattern recognition software have raised anxieties amongst members of the public related to the use of that power. Echoes of George Orwell’s 1984 reverberate in minds that

raise concerns that the power will be used by governments to oppress its people in some way. Dictatorships rely on the control of information, after all. People fear that Big Data will be used against them personally, individually. And it is usually government’s use of big databases that raises greater concerns than the use by private sector institutions.

Interestingly, however, when the public is polled about their privacy concerns related to data mining capabilities, there is a noted demographic discrepancy. The Millennial Generation, those individuals aged between 18 and 30, the “Facebook” generation, is the demographic that is least concerned. Millennials don’t fear Big Data, they generally embrace it. They are correct to do so.

What the Millennial generation understands is that the big data world that is emerging is going to be a much better one for everybody. While the potential for abuse of data directed against individuals does exist, the potential for creating value to benefit societies as a whole far outweighs these concerns. Those that are overly concerned about individual privacy are missing the bigger picture. The Big Data paradigm isn’t only about amassing data; it is also about the ease of access to it. It is the interconnected and distributed nature of data capabilities that will render large scale abuse impossible.

Regardless of privacy concerns, Big Data capabilities will continue to be developed. Any enterprise that is engaged with large numbers of people should be investing in the ability to collect data, whether the specific uses of the data are well defined or not. The ability to store huge amounts of data exists now; the ability to manipulate and interpret it is advancing rapidly; but the ability to collect it takes time.

5.1.2. Big Data and Public Policy

Contrary to so much popular opinion, it will be the use of Big Data by governments that will provide the greatest value for societies. Big Data techniques will allow governments to predict the outcomes of policy making more effectively and measure the outcomes of policy making more accurately. It is not at the level of single individuals where specific outcomes of policy will become more predictable, it is at the level of populations as a whole. In any complex system, such as human societies, Big Data analysis informs us how the system behaves. Nuances that can only be identified from huge data sets will become informative.

There is no realm of public policy making more in need of a Big Data approach than health care. Policy effectiveness facilitated by such an approach will eventually ease the burden of expected increasing health care costs dramatically. Medical data collection in any format, provided that it can be amassed and correlated, will be useful, but one format for data collection with particularly promising implications is genomic data.

5.1.3. Genomic Big Data

The human genome is about three billion base pairs long and variability exists within the human species in about 0.1% of it. Each individual has a unique set of variations among those roughly three million points of variation. To reiterate a point made in Section 4.5, when considering a population to be sampled in order to understand its genomic variation, it is useful to make a distinction between genomic sampling breadth and genomic sampling depth. Whole genome sampling on a small sample set provides sampling breadth while partial genomic sampling on a huge sample set provides sampling depth.

Since whole genome analysis for a huge sample of the population is not economically feasible, the next best thing, from a Big Data perspective, is to have breadth and depth in separate approaches. Comparisons between the results of both approaches will allow powerful, high confidence inferences to be made about the population as a whole.

Whole genome analysis on small sample sets is being done in Thailand by the research community, but what is lacking is genomic sampling depth. A personal genomics business model that can generate a very large number of customers would provide such depth.

This will result in the following capabilities.

Representativeness

A very large sample size, in the tens of thousands, will provide data that is truly representative of the

Thai population as a whole, even if discriminatory biases emerge in the process of reaching customers. Low frequency alleles will be quantified with a high degree of confidence.

Identification of Outliers

With a very large sample size, very rare alleles will be discovered that might have been missed with a smaller sample size. Sometimes a lot can be learned about any system by the identification and characterization of very rare variables.

Unexpected Outcomes

Very large data sets often allow analysis to uncover aspects of, or patterns within, populations that cannot be identified with smaller data sets. The identification of these properties can lead to valuable interpretive outcomes that would otherwise be unanticipated. Unexpected value emerges from the accumulation of large data sets.

5.2. Statistical and Emergent Clinical Utility

Clinical utility, as used here and in the literature, generally refers to interpretations that can be translated directly into high probability positive treatment outcomes at the level of individual patients. Interpretations that, according to clinical studies, only slightly increase the probability of a positive outcome for any given individual are considered to be of low clinical utility.

However, when low probability utility is applied to entire populations, the impact from the

perspective of the system as a whole in terms of cost savings and cumulative impact on human lives can be considerable. This is just an additive property. But since populations are complex systems (in fact populations of genomes are complex systems comprised of complex systems) they exhibit emergent properties. They behave in a non-linear fashion. The impact of implementing interpretations that are considered of low utility at the level of individuals across a population will result in higher total utility than would be expected additively.

Furthermore, as the research community continues to study genetic interactions and make medical interpretations, clinical utility from genomic data will emerge in unexpected places. Interpretation will catch up to the data. It is impossible to predict the form the utility will take, but it is certain that new utility will emerge.

5.3. Integration

Any personal genomics endeavor is essentially in the business of trading in information. It acquires information, interprets information, and communicates information. In fact, it would be difficult to identify any other business platform that could be considered more purely about information. And the acquisition of information involves much more than collecting DNA from customers. It requires access to many sources of information external to its own operations; sources that cannot be maintained as proprietary. And it requires expertise in order to interpret the information.

Therefore, another guiding principle of this business model should be integration. The model should be designed in such a way as to be integrated as much as possible with sources of information and expertise beyond its own perimeters.

5.4. Transparency

Considering the stakes of personal genomics for societies, positive and potentially negative, the business model should be transparent. The goals, practices, policies, and claims of value made by the enterprise should be open to scrutiny.

5.5. Education

Any venture that provides a product or service where the means by which value is created are difficult for consumers to understand is potentially exposed to being misunderstood. Misunderstanding can lead to loss in consumer confidence. This is certainly the case for any personal genomics business.

Therefore, it would be in the long term interest of the venture and its customers for there to be a steady transfer of information related to the creation of product value from the product provider to the consumer.

6. Business Model Objectives

In consideration of the business environment and guiding principles, the main objectives of the personal genomics business model should be as below. These objectives, if successfully achieved, will act collectively to further the larger objective of improving the health system in Thailand for the benefit of the Thai population as a whole.

6.1. Database Generation

The primary objective of the business model is to generate a large data set of partial genomes from Thai citizens in the form of a product that collects DNA from customers and analyzes it for selected genetic markers, whether single nucleotide polymorphisms, insertions, deletions,

or copy repeats. Markers should be selected on the basis of the value that the knowledge of their existence imparts for customers, the genomic research community, and the Thai health care system as a whole.

The metadata from all samples should be made available to the research community and to health care policy makers and planners within the public

sector. In metadata format, the data would be anonymous. No customer identities would be linked to individual marker sets.

The number of markers analyzed for would be limited due to cost, so this database initially would offer a dramatic increase in genomic sampling depth rather than genomic sampling breadth. Tremendous value will be derived from the combination of sampling depth from the database and sampling breadth achieved from whole genome studies.

6.2. Clinical Utility and Consumer Value

In the short term, actual clinical utility at the level of individuals will be limited by the degree to which high probability linkages between markers, or small groups of markers, and specific clinical outcomes have been established by the research community. Some of the markers selected will have immediate clinical benefits for treatment of specific conditions, but they will represent only a subset of the total set of markers selected.

In the longer term, as the research community establishes better clinical linkages between genetic markers and treatment outcomes, it is anticipated that the ability of the product(s) offered by the business model to provide direct clinical utility for individuals will steadily increase.

At the level of the population, statistical clinical utility will be achieved on a cumulative basis and in unexpected ways. Analysis of the metadata will result in the improved ability of researchers to better understand the Thai health condition and become a tool for health care planners to better link resources with needs.

So, while clinical utility should be considered an objective of the model, the broader, more fundamental, objective should be the creation of consumer value. Providing clinical utility would be just one way of creating such value. There are many ways to create consumer value that do not have any obvious clinical implications.

6.3. Profitability and Sustainability

As with any commercial venture, the business model must be commercially viable. It must be able to recover capital investment by generating positive cash flows within a reasonable period of time. It must also be sustainable. For a personal genomics business model, this means being able to continuously offer value to consumers and stakeholders in a market characterized by rapid change, both in terms of the sequencing platforms available for product delivery and the knowledge available for interpretation. This will require a structure specifically designed to effect rapid adjustments to product design and marketing strategy.

7. Product Positioning

The personal genomics based products currently available in the market tend to be targeted for narrow purposes. They claim to deliver utility to solve narrowly defined problems experienced by a small subset of the population.

In keeping with the driving objective of generating a large database of partial genomes, the personal genomics product offered by this business model should be a broad based, multipurpose product that can be marketed to the whole population. Markers for sequencing would be selected for a variety of purposes reflecting a variety of ways that value can be delivered to different segments of the market.

It is anticipated that the duration between sample taking and provision of results will be several days or longer so the product should not be positioned to compete directly with targeted genetic tests currently available to patients that can return

results for singular purposes immediately. Rather, the product should be positioned as being complementary to these targeted tests.

As a multipurpose product to be marketed widely to generate a large database, sales volume will necessarily be large relative to other genomics products on the market. Therefore, the business model will derive economies of scale in two ways. The larger volume of sales will drive down unit costs and allow a lower price to be offered to the market. And the multipurpose utility will allow it to capitalize on overlapping value perception. Customers may be initially compelled to buy the product for one purpose, but will appreciate the value offered for other purposes. There will be synergies between the differing value propositions offered by a multipurpose personal genomics product.

8. Primary Market Segmentation

Broadly envisioned, there are two main segments into which the market for the product can be divided. These two groups will require quite different marketing and distribution strategies. Further market segmentation will be discussed in Section 13.3.

8.1. General Public

The primary market segment should be considered the general public; that is, members of the public not experiencing an immediate health concern for which genetic testing might help. Potential customers from within the general public could be compelled to buy the product for any number of reasons, such as:

1. Generally interested in genetics
2. Interested in learning about features of their own genome
3. Interested in advice on making health related lifestyle choices
4. Interested in learning what specific health risks may apply to them
5. Concerned about potential inherited risks
6. Concerned about any potential genetic diseases they may pass on to their children
7. Interested in having a genomic profile for reference in case of future medical needs
8. Willing to participate in a Thai genome database project as a matter of public consciousness

Product composition and marketing strategies should be designed, along with other consider-

ations, in order to appeal to the specific interests of members of the public revealed by market research initiatives. Sample taking logistics will have to be designed in order to access as much of the population as possible throughout the country.

8.2. Clinical Patients

This segment refers to individuals that have an actual clinical need for which genomic information can help immediately in treatment or recovery. Further subdivision of this market segment would therefore depend on the specific immediate clinical applications of the product based on the markers to be sequenced for.

Sample taking to reach this segment would take place in clinical settings at the recommendation of the patient's physician. Therefore, the marketing for this segment should be primarily directed at the medical practitioner community and would require considerable knowledge transfer.

Both public and private sector hospitals and clinics should be targeted. Private hospitals would be expected to have better in house sequencing capabilities individually than hospitals in the public sector, so may not be as receptive to a product that offers utility they feel they could or should be able to offer to their patients themselves with

quicker results. However, depending on the particular clinical benefit in question and the hospital in question, they may not have the bioinformatics capabilities to create the utility themselves or may not be able to purchase it from the market.

Small private clinics that specialize in areas where clinical utility offered by the product is relevant, however, would be less likely to have sequencing capabilities, so may be more interested in the product.

8.3. Crossover

Of course, almost everyone is healthy most of the time but has occasional need for medical

treatment. The boundary between the two market segments, therefore, is fluid. Individuals that have previously purchased the product and thus have a record of their genomic data on file would have this information immediately available to physicians should they find themselves with an immediate clinical need.

This crossover effect also provides a platform for generating clinical utility in the future. A certain proportion of healthy customers of the product will inevitably develop diseases for which having genomic information could be useful, in an aggregate sense, for researchers, even if no immediate benefit can be accrued from the data in terms of immediate treatment.

9. Business Model Integration Structure

This section describes the structure of the relationship between the Commercial Entity, as the provider of the product, and stakeholders in the public sector.

9.1. Embedded Commercial Entity

A Commercial Entity (a private sector company), subject to the freedoms and constraints of any private sector enterprise, should be created to be the provider of the product and the driver of the endeavor as a whole. It should be embedded into the existing public health care and genomic research systems in the sense that the relationships between the Commercial Entity and certain public institutions should be established prior to the onset of operations of the company.

This will create a stakeholder community involv-

ing elements of the public sector that share the Commercial Entity's interest in implementing a personal genomics model in Thailand. The development of a large database of genomic metadata representing the Thai population will be of interest to genomics researchers and public policy planners and the clinical utility that will be realized over time will be of interest to any party concerned with health care efficacy and effectiveness in general.

A counterargument could be made that such a model could be deployed from within the public

sector without the need for a private company to participate. In theory that is true, but there are many arguments that support the notion that a private sector entity, by its very nature relative to a public sector entity, would be more likely to succeed as the economic driver of the model. Manifestations of private sector management conditions relative to public sector management conditions include:

- I. Faster decision making – less bureaucracy
- II. Easier to raise money – less tied to budgetary constraints, contribution from profits
- III. Easier to attract talent – salary policy unconstrained
- IV. Greater leadership stability – not affected by political cycles
- V. More goal oriented – goals more narrowly defined
- VI. More flexible – not constrained by policy above its control
- VII. More easily incentivized – profit motive

These advantages all have relevance in a business environment such as the one faced by a personal genomics business, where conditions are in a state of rapid change. The ability to respond quickly and effectively to new information, new technology, and new market realities is a key success factor.

9.2. Commonality of Stakeholder Objectives

The stakeholder communities under this model

can be grouped into three broad categories:

- I. Public Medical Service Providers
- II. Public Medical Researchers
- III. The Commercial Entity

Public Medical Service Providers in this section refers to the subset of the government that is engaged in the policy making, planning, and implementation of publicly funded health care in Thailand.

Under the big data paradigm, where it is accepted by all stakeholders that the primary objective of the business model is to compile a large genomic database and that clinical utility will emerge increasingly over time, there will have to be agreement that the relationships between stakeholders should be constructed in such a manner as to maximize the volume of sales.

This will be easily accepted by the research stakeholder community, whose participants intuitively understand the value of data, but not so easily accepted by the medical service provider community. It will be the challenge of those that may attempt to implement this business model to make the argument that a large database of genomic information will lead to increasing clinical utility over time and to improved provision of medical services.

9.3. Profit Motive

Many individuals in the public sector will instinctively be skeptical that the creation of a private sector entity as the economic driver of

this business model will lead to positive results despite the advantages outlined above. There will be suspicions that profit motive will run counter to public interest and/or the interests of the other stakeholder communities.

However, provided that all stakeholders share the common main objective of generating a large database, an objective that will always be in the interest of the Commercial Entity, this potential conflict can be mitigated. Finer details of how the business model should be constructed, to follow in later sections, will deal with this concern in greater depth.

9.4. Public Sector Funding

Since it is anticipated that the majority of sales will come from the general public market segment, the volume of sales will be very price sensitive. The clinical market segment, where patients will be compelled to purchase the product under physician recommendation, there will be less price sensitivity but it will still exist. Therefore, relatively minor reductions in price can be expected to result in significantly increased sales volume. Market research should be conducted to try to quantify this relationship.

Provided that the big data paradigm is accepted, the public sector should be willing to fund this business model to some extent. In essence, it should be willing to pay for the metadata that will be generated by the business model. It should be willing to enable the Commercial Entity to be sustainable at a lower product price in order to generate a greater sales volume. It should con-

sider such funding as an investment in the future of Thai health care in the same way that it does for any physical asset that promises the same benefit.

The ideal means of funding, from the perspective of the sustainability of the business model would be a form of subsidy on a per unit sold basis. This would go directly to the variable cost profit margin for the Commercial Entity so would be directly reflected in the product price and would directly result in increased sales and a deeper database. It is understood that since sales volume would be unknown, the amount of total funding to be committed annually by the public sector would also be unknown. This is anathema to the public sector budgetary process, but the contractual agreement with the Commercial Entity that would define the basis of payment for the metadata could include a mechanism that establishes a cap on total funds due from the public sector in a given period of time.

The total amount of funding required for the sustainability of the business model would emerge from a detailed economic analysis of the business model and market research on public price sensitivity. Structures of funding other than those based on units sold could be considered, but for the rest of this report it will be assumed that a partial subsidy of the product from the public sector in exchange for the metadata is an accepted element of the model.

A detailed discussion of where within the public sector this funding would come from is beyond the scope of this report, but it is assumed that the following entities could potentially be involved, as all would presumably be interested in the benefits

of the metadata.

- I. Ministry of Public Health
- II. National Health Security Office
- III. National Science and Technology Development Agency
- IV. Ministry of Education

It is recognized that the inherent uncertainty in the specific outcomes that will accrue from the metadata, let alone the difficulty in quantifying the value of those outcomes, runs counter to usual means by which government agencies agree to funding proposals. It is therefore assumed that the proposal would have to be made to the very highest levels of government. It would probably have to be promoted as a national project worthy of unprecedented institutional collaboration.

9.5. Stakeholder Perspectives

For the purposes of this section, the stakeholder communities have been expanded to the following four categories by splitting medical services providers into public health care planners and medical practitioners:

- I. Public Health Care Planners
- II. Thai Research Community
- III. Medical Practitioners
- IV. The Commercial Entity

Each of these stakeholder communities will have a different perspective on the value of this integrated personal genomics business model.

9.5.1. Public Health Care Planners

The mission statement of the Ministry of Public Health is as follows:

- I. Determine national and international health policy and strategy, concordantly with ongoing changes.
- II. Develop efficient and equitable integrated health service system for both normal situation and emergency with emphasis on basic rights, specialized service and emergency medicine, surveillance system, disease prevention and control and health threats.
- III. Promote participation of all sectors to raise health consciousness, promote health and improve health behaviors.
- IV. Develop health management system and mechanism to meet the quality standard, in line with Sufficiency Economy philosophy.
- V. Determine health research and knowledge management direction policy.

If we can assume that this represents the general objectives of the health care planning stakeholders considered here, then the business model has much to offer.

Apart from the long term incremental cost savings and efficacy accrued to the health care system due to healthy customers making better health decisions and sick customers benefitting directly from more informed care from practitioners, the benefit in receiving the metadata lies in understanding allele frequencies within the Thai population and how they are distributed geographically.

Once sample sizes grow into the thousands, frequencies will become statistically robust. Precisely know allele frequencies, as they become better linked probabilistically to clinical outcomes at the population level and as their geographical distribution becomes clear, will allow health care planners to make more informed decisions regarding drug list coverage, resource allocation, training regimens, investment planning, and undoubtedly other functions.

Health care planners, via the particular institution(s) involved in funding the enterprise, may find it justifiable to participate actively with the Commercial Entity in promoting the product, both to the general public and to practitioners. In fact, the MoPH or another public entity, may want to take over the product brand and promote it as a government health care initiative, viewing the Commercial Entity as a subcontractor for management of the model. The Commercial Entity should not necessarily object to this provided its role is suitably defined and protected.

9.5.2. Thai Research Community

Like scientific researchers the world over, the Thai research community involved in genomics research should support any initiative that enables them to produce more voluminous, better quality research that will meaningfully contribute to global progress in their field of study. A large database of genomic markers will greatly facilitate this.

Due to the commercial nature of the model, the researchers involved will have access to the meta-

data data without having to acquire funding to gather it themselves; or in the case that research funding agencies participate in the funding of the model, at a much reduced cost. The raw data should lead to finer grained research initiatives and publishing opportunities.

In addition to opportunities accrued from having the metadata, researchers will have the opportunity to study the genomic foundations of specific diseases and reactions to medications by making connections with practitioners treating patients that have purchased the personal genomics product. How these clinical linkages can be established will be described in Section 11.9.

9.5.3. Thai Medical Practitioners

The objectives of medical practitioners might be varied and difficult to define, but one would assume that standard of care is a commonality.

The perceived benefit of having access to patients' genomic information for clinical purposes will vary. It is probably reasonable to assume that those that are already more educated in the implications of genomics will appreciate the standard of care implications more than those that are less educated. An effort to educate practitioners beyond access to a patient's raw data would help in expanding the participation of doctors.

A consequence of this model is that it will incrementally lead to a more educated population with respect to genetics and genomics in general. This will promote more intelligent interactions between doctors and patients. However, some doctors might feel threatened by this, perceiving it

as a challenge to their authority, especially if they are weak in genetic knowledge. This effect can be eased by educational efforts but certainly not eliminated, so it is inevitable that some practitioners will resist. However, the model does not need anything close to 100% practitioner participation in order to succeed and resistance will recede with time.

In addition to being potential users of the personal genomics product results, through access granted by individual patients that have purchased the product, medical practitioners (hospital administrators as well as doctors) would be expected to be front line sellers of the product to patients. Enabling this would be the task of marketing strategy deployed by salespeople working for the Commercial Entity. Providing hospitals a profit might be required, but it will be a task made easier with official endorsement from public health care planners.

9.5.4. Commercial Entity

The primary objective of any Commercial Entity is to be profitable and to provide a reasonable return on equity within an acceptable period of time. A secondary objective of this entity should be to conduct the business in a sustainable way by ensuring that specific goals and tactics are in close alignment with the goals of the other stakeholders in the business model. In fact, the public funding element of this model could effectively be viewed as a means of putting pressure on the Commercial Entity to ensure that those goals do remain aligned.

Being embedded in the public health care and medical research communities and being subsidized accordingly from the start greatly enhances the likelihood of commercial viability. The low price high volume market approach that this model proposes would provide a competitive edge that would be very difficult for competitors to match.

Once the initial contract between the Commercial Entity and the government institutions that have agreed to subsidize the product in exchange for the metadata expires, the Commercial Entity could face competition from another commercial venture hoping to take over commercial responsibilities. Therefore, it would be in the interest of the Commercial Entity to ensure that goal alignments with other stakeholders remain robust. The initial selection of markers will facilitate this but it shouldn't end there. The Commercial Entity, having developed expertise in the interpretation of metadata, should routinely promote to health care planners the potential health care policy implications of what the data has wrought.

While it will be important that the product composition choices generate data appreciated by the other stakeholders, the Commercial Entity's primary concern must be that product value is appreciated by potential customers. According to the big data paradigm, the metadata generated will have more intrinsic value for the health care system as a whole than the personal genomic data will have for individuals cumulatively. But this doesn't mean the product doesn't have enough value to be sold to customers. Ways of enhancing product value to consumers will be discussed in Section 11.

9.6. Collective Benefits of the Model

Individual stakeholders in this model all have interesting perspectives on the merits of this model, but the real power is in the benefits that will emerge from its integrated nature.

9.6.1. Defendability

By having the metadata sold to research and public health planning communities as part of the inherent structure of the business model, the enterprise would have a cost advantage versus potential private sector competitors. This is in addition to the advantage in economy of scale due to an anticipated large volume of sales.

Beyond the interests of the Commercial Entity itself, this competitive edge would lend stability to the model that should be appreciated by all stakeholders. While potential replacement of the Commercial Entity by a competing faction would have to be a challenge engaged by the Commercial Entity itself, it would not necessarily threaten the business model as a whole. The competitive advantage inherent in the model would remain.

9.6.2. Diversity of Interests

One of the concerns related to a model that integrates private as well as multiple public institutional interests might be that these interests could come into conflict such that progress would be impeded or that one group of interests could come to dominate the others causing cooperation to wane.

This is a valid concern but it is important to make the distinction between levels of objectives. Since agreement on the primary objective of generating a large database would be required by all stakeholders for the model to be implemented in the first place, and considering that as a commercial model it must be profitable to survive, competing interests should not be problematic at the level of decisions related to model sustainability.

Where competing interests would potentially conflict would be at the level of product composition – the decisions of what markers to include in the product and for what purposes. But as a personal genomics product that would analyze for hundreds of markers, there would be a wide platform for the inclusion of many sets of markers to achieve many informational objectives. All that would be required would be an agreed process for establishing the markers to be included in the product. The final arbiter of those decisions will always be whether the product sells and contributes to the sustainability of the model as a whole.

So, rather than being concerned about the potential of competing interests, one should consider the diversity of interests to be an advantage of the integrated design.

9.6.3. Institutional Cooperation

Most government institutions have objectives and responsibilities that overlap to some degree with those of other government institutions. This can result in cooperation and positive feedback in the best of situations but often results in duplication of efforts, or in worst cases, conflict leading to dysfunction.

If this model were to be successful, facilitated by the shared need for commercial viability, it might promote positive institutional cooperation in other endeavors. It could open up channels of communication and facilitate the identification of specific shared interests. It could ultimately become a model for other public-private partnership initiatives.

9.6.4. Commercial Expertise

The proliferation of public-private partnerships and the promotion of commercialized research is a significant trend in the life sciences and biotechnology arena globally and is an objective in Thailand. One of the impediments to this is the disconnection between a research way of thinking and a commercial way of thinking.

This business model, with a private sector entity as its economic driver, would be a vehicle for the proliferation of commercial expertise and orientation into the public sector.

9.6.5. Development of Technical Expertise

It is recognized that there is a global deficit in bioinformatics expertise. Our ability to collect genomic data far exceeds our ability to manipulate it in ways that will lead to meaningful interpretation of the complexities of genomic and cellular interactions and ultimately to clinical utility. This is a global deficit but is even more acute in Thailand.

Since bioinformatics expertise would be a required core competency of the Commercial Entity in this model, it would have to acquire it and develop it.

Because of the integrated nature of the model, this acquired expertise would proliferate throughout the system and beyond. The Commercial Entity could act as a training ground for bioinformatics. Internships could be established and managers could lecture at Universities.

Successful implementation of the model would also, by definition, expand technical expertise and every other aspect of its operation, from sample taking procedures to database systems management.

9.6.6. Commercial Spinoffs

It is envisioned that the volume of customers for this business could be very large. This could present opportunities for Thai businesses that act as suppliers to the model to grow or for new Thai businesses to be formed to seize opportunities not being addressed locally.

The generation of technical expertise specifically related to the operations of the business model could result in new non-competing or even complementary businesses being formed by former employees or associates. This would especially be expected from those who have gained bioinformatics expertise. Employee turnover could be a problem for the Commercial Entity but from the perspective of Thailand's life sciences sector as a whole, this should be considered an advantage of the model.

9.7. Challenges

Apart from the usual challenges that any new

business would have getting started and in daily operations, there are a number of challenges specific to this kind of business.

9.7.1. Creation of Customer Value

It has already been asserted that value for the research community and for health care planners is inherent in the creation of the metadata and that clinical value will steadily build, but the more pressing challenge would be to create value for potential customers in the general public; those that have no immediate clinical need.

It should be stressed emphatically that consumer value is perceived value. It is not necessarily defined the same way that value would be defined by researchers or health care planners, or even by doctors. This does not mean that consumer value is of less significance or that deceit would be involved. Every consumer defines their own criteria for value and it would be up to the Commercial Entity to identify consumer value in aggregate. In fact, since this model would have a Commercial Entity as its economic driver and sales to customers would generate the revenue (minus the subsidy), perceived value to consumers should be the primary consideration when designing the products. Markers should be selected that can generate information that can be translated into value for the customer.

This doesn't only refer to markers that impart value related to health concerns. Indeed, one of the criticisms often made for a consumer directed personal genomics business model is that consumers will not want to buy a product that will

only give them bad news. What is more important is the way in which the information is presented. What stories can be told and how do those stories relate to other people? This is real consumer value. This will be expanded on in Section 11.

9.7.2. Control of the Data

From the perspective of the Commercial Entity, the metadata would be sold to the health care planning and to researcher communities in exchange for the product being subsidized. Public sector authorities can determine how widely the metadata should be distributed and the Commercial Entity can be under contractual obligation limiting what it can otherwise do with the data. It is the opinion of this Consultant, in the spirit of the Big Data paradigm, that the anonymous metadata should be made available to anyone. Nevertheless, it would be reasonable for the Commercial Entity to expect a 3-5 year contract under which sale of the metadata to the public sector (i.e. continuation of the subsidy) is guaranteed under certain conditions of its distribution.

To protect the potential privacy concerns of individual customers, the identities of customers need not be attached to their data sets - just a bar code number obtained at the point of sampling. In cases where the product is sold to patients in a clinical setting for clinical purposes, customers can (and should) choose to release their results to doctors. At this point, privacy issues enter the realm of usual doctor-patient confidentiality. For clinical studies that might emerge from the data whereby patient records compiled by doctors would need to be linked with genomic data,

additional consent would be required.

As will become clear during the discussion of product delivery, the Commercial Entity would have the technical capability to identify customer identities. The company would be prevented from sharing this information with anyone by legislation under the guidelines of the Personal Data Protection Act. Note that “personal data” in this Act is defined as data that can be used to personally identify individuals, so the metadata created by this model and delivered to the public sector entities would not apply. Furthermore, exceptions to the rules for purposes of public health are indicated throughout the Act. In any case, expert legal opinion regarding the implications of the Act and its precedents should be sought.

9.7.3. Public Reaction

It is anticipated that this personal genomics business model will likely have a very high public profile in Thailand. In the current media environment, characterized by mistrust of institutions and the recognition of the power of data mining techniques used by private companies and governments, public reaction would have to be monitored very closely. A poorly written article by a paranoid journalist could have disastrous results.

Privacy of personal information concerns would have to be addressed and communicated vigorously. Public relations expertise would have to be a competency of the enterprise, either employed in house or contracted externally. A damage control protocol should be established for cases

where misinformation proliferates.

9.7.4. Practitioner Knowledge

As discussed above in the section on Stakeholder Perspectives, some degree of resistance to the model from the practitioner community can be expected due to lack of knowledge. This only affects the clinical market segment, but since the product would have to be sold directly by doctors to patients in these settings, it is a concern. Furthermore, since the long term clinical utility of this model will rely on linkages being made between clinical outcomes and patients’ genomic data, practitioner participation will ultimately be required.

With time, as younger doctors that are better educated in genetics gradually replace older ones, the resistance will abate, but this will be a slow process. Therefore, the Commercial Entity would have to establish a means by which interpretive information is regularly transferred to doctors. This will be discussed further in Section 11.8.

10. Platforms

The basic platforms for product delivery should be the following.

10.1. Saliva Based DNA Samples

Sample taking should be performed using the Oragene 510 saliva based system, offered by Canada-based company DNA Genotek, or a system with similar capabilities. It yields an average of 55 micrograms of DNA, enough for dozens or even hundreds of tests, and residual samples can be preserved at room temperature without degradation for years.

A saliva based sample eliminates the need for blood serum samples allowing for self-administration. The room temperature stability allows for samples to be transported without time pressure concerns and stored indefinitely for additional use. This opens up marketing, sales, and distribution opportunities tremendously.

Sample vials can be labeled by bar code or RFID, which will allow for process control and customer anonymity. There would be no need for any information to be provided by the customer.

That said, it may be desirable to ask customers to provide some minimal information just to provide metadata analysts with some controls. Sex and ethnicity can be deduced from control markers included in the marker set to be analyzed, but perhaps age, which could not be deduced from markers, should be provided. Location of birth or of current region of residence might be information worth having as well. A way for customers to

easily provide this information at the point of sale could be designed into the label.

10.2. Laboratory

It is assumed that the sequencing for this business model would be conducted at the genetics laboratory at Ramathibodi Hospital using the Ion Torrent Sequencer supplied by Life Technologies™. The capacity of this sequencer, if run 24 hours day, 365 days a year, would be about 100,000 samples annually, provided that sample preparation and PCR capacities are aligned. This certainly would be more than enough, even after allowing for some usage of the sequencer for other needs.

A single run can process 96 samples simultaneously. To minimize sequencing costs per sample, most of which is in the consumption of reagents, a full complement of 96 samples should be accumulated before a run is performed. Otherwise, the profit margin of the product will be compromised. This has implications for turnaround time – the time between sample taking and presentation of results. The laboratory will have to wait until 96 samples have been received before conducting a sequencing run.

This could result in substantial delays in the early phases of product implementation, which could negatively impact on future acceptance of the product. The Commercial Entity may wish to bear

the cost of partial runs in the beginning just as a means of avoiding negative perception of product delivery performance.

The laboratory would be paid by the Commercial Entity for sequencing and related costs on a basis to be negotiated.

Other sequencing technologies that might be able to achieve the same or better results for the same or lower cost should be considered. The option would also be open at any time for the Commercial Entity to purchase and operate its own sequencing lab.

10.3. Website Based Product Delivery

Raw data from the sequencing lab would be sent electronically to the Commercial Entity for interpretation and preparation of presentation to the customer. This would be done automatically by algorithms recognizing individual markers and combinations of markers, which would trigger formats, graphical representations, and other tailored content. Product presentations would be made available to customers on a personal

webpage accessible through the main website of the Commercial Entity.

Customers would access their personal webpage using the user code that they would peel from the label of the sample vial at the point of sale and sample taking. It would be linked to the bar code on the vial and not be visible until peeled off. A password would accompany the user code and the customer would be prompted to change the password upon first login.

Customers would be required to visit the website for the first time on their own initiative. If results are not yet posted, they would be given the option to receive notification by email or text message when they become posted. At this point, the customer would have relinquished their anonymity voluntarily within the database at the Commercial Entity but not beyond there. It would be made clear to customers that the information would go no further and that anonymity would remain in place during compilation of the metadata. The contents of the personal webpages are described in Section 11.5.

11. Product Composition

This section describes the nature of the personal genomic products the entity should offer to the market, including the selection of markers and how the results of sequencing should be presented to customers.

11.1. Selection of Markers

Based on the Ion Torrent Sequencer and a rough idea of the cost for reagents, it is assumed that an initial product offering could contain between 500 and 1000 markers. Life Technologies™, the manufacturer of the Sequencer, also supplies the reagents. Apart from an initial one-time cost for preparation of the required reagent kit, the cost of the kit would increase linearly with the number of markers selected.

The selection of markers for the initial product will be a critical process. The usefulness for further research, for public policy making, and for product marketing efforts must all be considered. Markers in high linkage disequilibrium indicating haplotypes should be prominent to maximize information potential. Markers that show no current useful correlations based on existing research, but are in exomes or regulatory regions of genes that play critical cellular roles, in metabolism or immune response for example, could be considered for future research potential. Control markers for gender and ethnic origin should be included in order to facilitate metadata studies.

Deciding on the specific targets for marker selection should be a collaborative effort between representatives of the Commercial Entity, the research community, and health care planners. It will require extensive review of the literature.

Most of the marker data required to select product markers will be available from open source databases but some expenditure might be required to purchase certain studies. The purchase of external expertise might be required.

It is assumed that the government agency or agencies that have committed to funding the business model would require the right of final approval of marker targets, in terms of the expected information that will be provided in the metadata as well the potential for clinical utility, before the product could be offered to the market.

11.2. Modules

In order to facilitate the process of marker selection and, indeed, to channel genomic interpretation, particularly from the perspective of creating perceived customer value, it will be necessary to divide the markers into modules. Some markers may have membership in more than one module.

It is proposed that the following six modules should be included in the initial product.

11.2.1. Genealogy

National Geographic's Genographic Project provides haplogroup and paternal/maternal ancestry migration patterns for customers. Their latest

product, Geno 2.0, analyzes for 150,000 markers. It also identifies Neanderthal and Denisovan markers and provides an output indicating the percentage that each customer's genome contains ancestral DNA from these two hominids that interbred with homo sapiens prior to extinction.

Markers that would be selected for this module would be a tiny subset of what Geno 2.0 provides, but since it would be tailored to the Thai population, perhaps enough confidence could be generated from fewer than 100 markers. For maternal ancestry, mitochondrial DNA would have to be incorporated in sample preparation procedures.

There would be no obvious clinical benefits from this module but for researchers involved in studying ethnic diversity and admixture patterns, and linkages between ethnic composition and disease susceptibility, the data would be very useful. From a marketing perspective, this module could be promoted to entice potential customers interested in personal genetic ancestry and human evolutionary history in general.

11.2.2. Recessive Allele Screening

The Silicon Valley based company, Counsyl, offers a recessive allele carrier screen marketed primarily to prenatal clinics and their patients and directly to consumers via the internet. It tests for 400 markers and identifies about 100 recessive genetic diseases.

Counsyl's product is constructed to cover all ethnicities in the US, including Ashkenazi Jews who have important risks associated with sev-

eral genetic disorders. A Thai product that is constrained for recessive alleles known to be represented in Thai/East Asian populations could perhaps be constructed out of 100-200 markers. Note, however, that recent studies have shown that the existence of recessive disease alleles are more ethnically and geographically widespread than previously thought. Also, since it would be expected that some ethnically non-Thais living in Thailand would be customers of the product, it might be useful to include some markers associated with more severe genetic diseases not thought to be found in Thais.

The utility of this information for customers, particularly those entering child bearing years, is obvious and a marketing strategy targeting this market segment should be straightforward to create. Prenatal clinics/wards would be obvious clinical locations where the product could be promoted and sold. The utility of a sample size in the many thousands that identifies with high confidence recessive allele frequencies for dangerous genetic diseases should be highly appreciated by those involved in public health policy planning.

The following is a list of the recessive allele diseases that Counsyl's product tests for:

- ABCC8-Related Hyperinsulinism
- Achromatopsia
- Alkaptonuria
- Alpha-1 Antitrypsin Deficiency
- Alpha-Mannosidosis
- Andermann Syndrome
- ARSACS

Aspartylglycosaminuria	Galactosemia
Ataxia With Vitamin E Deficiency	GJB2-Related DFNB 1 Nonsyndromic Hearing Loss
Ataxia-Telangiectasia	Gaucher Disease
Autosomal Recessive Polycystic Kidney Disease	Glucose-6-Phosphate Dehydrogenase Deficiency
Bardet-Biedl Syndrome, BBS1-Related	Glutaric Acidemia Type 1
Bardet-Biedl Syndrome, BBS10-Related	Glycogen Storage Disease Type Ia
Biotinidase Deficiency	Glycogen Storage Disease Type Ib
Bloom Syndrome	Glycogen Storage Disease Type II
Canavan Disease	Glycogen Storage Disease Type V
Carnitine Palmitoyltransferase IA Deficiency	GRACILE Syndrome
Carnitine Palmitoyltransferase II Deficiency	Hb Beta Chain-Related Hemoglobinopathy
Cartilage-Hair Hypoplasia	Hereditary Fructose Intolerance
Choroideremia	Hereditary Thymine-Uraciluria
Citrullinemia Type 1	Herlitz Junctional Epidermolysis Bullosa, LAMA3
CLN3-Related Neuronal Ceroid Lipofuscinosis	Herlitz Junctional Epidermolysis Bullosa, LAMB3
CLN5-Related Neuronal Ceroid Lipofuscinosis	Herlitz Junctional Epidermolysis Bullosa, LAMC2
Cohen Syndrome	Hexosaminidase A Deficiency (Tay-Sachs)
Congenital Disorder of Glycosylation Type Ia	HFE-Associated Hereditary Hemochromatosis
Congenital Disorder of Glycosylation Type Ib	Homocystinuria
Congenital Finnish Nephrosis	Hurler Syndrome
Costeff Optic Atrophy Syndrome	Hypophosphatasia, Autosomal Recessive
Cystic Fibrosis	Inclusion Body Myopathy 2
Cystinosis	Isovaleric Acidemia
D-Bifunctional Protein Deficiency	Joubert Syndrome 2
Factor V Leiden Thrombophilia	Krabbe Disease
Factor XI Deficiency	Limb-Girdle Muscular Dystrophy Type 2D
Familial Dysautonomia	Limb-Girdle Muscular Dystrophy Type 2E
Familial Mediterranean Fever	Lipoamide Dehydrogenase Deficiency
Fanconi Anemia Type C	Long Chain 3-Hydroxyacyl-CoA Dehydrogenase
Fragile X Syndrome	Maple Syrup Urine Disease Type 1B

Medium Chain Acyl-CoA Dehydrogenase
 Megalencephalic Leukoencephalopathy
 Metachromatic Leukodystrophy
 MTHFR Deficiency
 Mucopolipidosis IV
 Muscle-Eye-Brain Disease
 NEB-Related Nemaline Myopathy
 Niemann-Pick Disease Type C
 Niemann-Pick Disease, SMPD1-Associated
 Nijmegen Breakage Syndrome
 Northern Epilepsy
 Pendred Syndrome
 PEX1-Related Zellweger Syndrome Spectrum
 Phenylalanine Hydroxylase Deficiency
 Polyglandular Autoimmune Syndrome Type 1
 Pompe Disease
 PPT1-Related Neuronal Ceroid Lipofuscinosis
 Primary Carnitine Deficiency
 Primary Hyperoxaluria Type 1
 Primary Hyperoxaluria Type 2
 PROP1-Related Combined Pituitary Hormone
 Prothrombin Thrombophilia
 Pseudocholinesterase Deficiency
 Pycnodysostosis
 Rhizomelic Chondrodysplasia Punctata Type 1
 Salla Disease
 Segawa Syndrome
 Short Chain Acyl-CoA Dehydrogenase Deficiency
 Sjogren-Larsson Syndrome
 Smith-Lemli-Opitz Syndrome
 Spinal Muscular Atrophy

Steroid-Resistant Nephrotic Syndrome
 Sulfate Transp.-Related Osteochondrodysplasia
 TPP1-Related Neuronal Ceroid Lipofuscinosis
 Tyrosinemia Type I
 Usher Syndrome Type 1F
 Usher Syndrome Type 3
 Very Long Chain Acyl-CoA Dehydrogenase
 Deficiency
 Wilson Disease
 X-Linked Juvenile Retinoschisis

11.2.3. Pharmacogenomics

Depending on the severity of the condition and the immediacy of the requirement for genetic test results, some clinical needs might be better served by targeted tests that can deliver results very quickly rather than a product that would take several days or more to deliver results.

Therefore, rather than to select adverse drug reaction markers on the basis of selected diseases where research has demonstrated a high degree of confidence between markers and predicted adverse reactions, perhaps the approach should be to focus on the genes that are known to generate proteins involved in the ADME process for most exogenous compounds, such as Cytochrome P450 enzymes, secondary metabolizers, membrane transporters, plasma proteins, and HLA gene products. The intent would be to identify specific alleles that are known to have implications in terms of metabolism efficiency in the ADME process for a range of drugs and then provide the customer with a list of the drugs that are known or

suspected to be affected by those alleles relative to wild type.

According to the PharmGKB database, there are about 1000 SNPs, insertions, deletions, and CNVs that have been identified in the Cytochrome P450 genes alone, so the 200-300 markers that could be included in a pharmacogenomics module would be a snapshot. But, with qualifying criteria such as drugs that are currently used or might be used in Thailand, and disease prevalence, a useful set should be identifiable.

Marketing this module to the public, however, would be more challenging than for the first two modules. Care must be taken not to unduly raise concerns that cannot be adequately addressed. Results should be presented to customers that identify drugs that the patient should be concerned about based on definitive science (even if not available in Thailand) and in cases where the science is only suggestive, customers can be prompted to check the website for updated information. Links to actual research results can be provided on the website.

For researchers, the lack of breadth in markers provided in the product would be partially compensated for by depth in sample size. The data provided could be considered complementary to GWAS. For public health policy makers and clinicians, cross references between pharmacogenomics markers and ethnic markers may prove to be very useful in addition to the obvious implications for drug adoption and prescription policy as clinical outcome linkages are better established.

11.2.4. Cancer Susceptibility

In late May of this year, a slate of coordinated papers was published in a number of journals that identified dozens of newly found cancer risk markers. Many hundreds of genes have now been identified that contain cancer markers, few for some cancers but dozens for some others. Cancer types for which susceptibility markers have been identified include the following:

- Acute leukemia
- Bladder cancer
- Breast cancer
- Cervical cancer
- Chronic lymphocytic leukemia
- Colorectal cancer
- Endometrial cancer
- Gastric cancer
- Glioblastoma
- Head/neck cancer
- Hodgkin's lymphoma
- Liver cancer
- Lung cancer
- Melanoma
- Non-Hodgkin's lymphoma
- Oral leukoplakia
- Oligoastrocytoma
- Ovarian cancer
- Prostate cancer
- Renal cell cancer
- Testicular cancer

For a module that may only be able to devote 200-300 markers for cancer susceptibility, it probably makes sense to focus on the 5-10 cancer types that most severely affect the Thai population and select the markers that have shown the highest correlations with occurrences.

Of all the proposed modules, cancer risk might be the most controversial with respect to the expected reaction from consumers. Other than some standouts like BCRA1/2, the associations are generally weak and concerns about patient over-reaction are valid. Again, care in how risk markers are presented to customers must be taken to minimize this reaction. Many potential customers may prefer not to be given this information and there should be an option for them not to receive it in their profiles (though the data should still be included in the metadata). For those that do want it, however, information sources should be provided that help to create a balanced perspective.

From the perspective of the research community and health planners, considering the prevalence of this disease now and increasingly in the future, any data on cancer markers in the Thai population that can be linked now or in the future to cancer occurrence should be more than welcome.

11.2.5. Other Disease Susceptibilities

Cancer has been granted its own module because of its severe impact on society but another module could cover a range of other diseases where genetic markers of susceptibility have been found or are suspected. Disease categories include:

Cardiovascular disease

Dermatology

Endocrinology (including obesity, diabetes, osteoporosis, infertility)

Gastroenterology (including cirrhosis)

Neonatal disease

Neurology (including epilepsy, Creutzfeldt-Jakob, Parkinson's, Alzheimer's)

Psychiatry (including Autism, Bi-polar, Depression, OCD, ADHD, Schizophrenia)

Pulmonary disease

Renal & Urologic disease

Rheumatology (including Arthritis, Crohn's)

As with cancer, there are hundreds of genes that have alleles that have been implicated as susceptibility markers to choose from so perhaps 10-15 diseases prevalent within the Thai population and perhaps 200-300 markers should be chosen. Expected growth rates of some of these diseases due to ageing and lifestyle changes should be considered in the selection process. Degenerative neurological diseases and auto-immune diseases are obvious candidates for marker selection.

The marketing and research implications for this module would be similar to the cancer module, although depending on the severity of the condition being examined perhaps patients will generally be less fearful of learning of non-cancer susceptibilities and be less likely to opt out (another reason for cancer to have its own module).

11.2.6. Infectious Diseases

A screen for viral/bacterial infection should be included as a module. This might be very useful for the detection and population-wide measurement of infections that lay dormant for a period of time but can cause problems later in life (not to mention the occasional catching of an imminent infection that hasn't presented yet).

Furthermore, there are markers that have been identified that indicate variable susceptibility to contracting infectious diseases. They could also be included in the module. Such markers have been identified for:

- Malaria
- HIV/AIDS
- Leishmaniasis
- Leprosy
- Meningococcal disease
- Parasitic infections
- RSV Bronchiolitis
- Sepsis
- Trachoma
- Tuberculosis
- Viral hepatitis

Perhaps 50-100 markers (susceptibilities plus external agent DNA/RNA) could be selected based on the particular infectious agents that are common in Thailand.

This should be an easy module to promote to customers since most infectious diseases are treatable if identified. The benefits of early detection for health care providers, planners, and

society as a whole are obvious as it is generally less of a burden on the health care system to treat infections early.

11.3. Product Refinement

Product refinement, in terms of adjusting the actual markers to be sequenced based on developing perspectives emerging from research and assessed customer reaction, should be something that the Commercial Entity should routinely consider. However, it could only occasionally be implemented since it would require a newly designed reagent kit. Due to the preparation charge levied by the supplier, frequent product refinements would be costly, as would the disuse of reagent kits that have been delivered but abandoned in favour of new ones. However, if the supply chain is properly managed, the product could be revised a couple times a year if necessary. Obviously, the impact of any changes on research initiatives tied to the metadata would have to be recognized.

11.4. Website: A Genetics Portal

The website of the Commercial Entity would be the access point for customers to acquire their personal genomic data. Customers would use the anonymous code and password they obtained from the saliva sample vial to log on to reach their own personalized webpage.

The philosophy of the website design should be to create much more than just an access point for customers to receive their genomic data. It

should be created to be an all-purpose information source on genetics for the public: a genetics portal. It should provide links to online sources of information such as media reports on new study results as well as tutorials on basic entry level genetic science. Most of this information will be in English so the Commercial Entity should employ a capability to translate these articles into Thai or at least to write summaries in Thai accompanying the links to the English articles.

The portal should also provide original stories reporting on genetics research in Thailand. They should be personalized, highlighting the accomplishments of specific teams of geneticists working in public sector facilities.

Furthermore, as the metadata starts to accumulate, the website should report on some general statistical patterns that emerge and ultimately on ways that public health planners and researchers will be using the metadata to further the cause of improved public health in Thailand.

All of this reporting should be accompanied with high quality graphics (maps, charts, photographs) to grab and keep the reader's attention.

These features would have the dual purposes of educating the Thai public in genetics, thus generating public interest, and promoting sales of the company's personal genomics products. There will be positive feedback between these two purposes.

11.5. Personal Webpages

Customers of the products will have their own personal webpages that they log on to. The

genetics portal philosophy of the general website should be extended to how information is presented on personal webpages. The attempt should be to build customer loyalty to the brand. Existing customers should be made to feel a sense of membership in the great project of building a database to further the cause of public health and Thai genetics research.

Each webpage would be personalized, but would be automatically generated by algorithms that recognize selected markers or sets of markers (haplotypes) to build content from the raw data. The highest standards of graphic design should be maintained with the intention of presenting information in visually interesting manner.

Each individual webpage should consist of a cover page with links to a data page and a page for each of the six modules.

11.5.1. Cover Page

The cover page should supply basic information concerning privacy policy and legal conditions. It could also provide more detailed information on sequencing methodology than would be provided on the main website. It would be standard for all customers.

The cover page should also give the customer the option to provide the company with his/her email address and/or phone number so that the company can contact him/her with updates. If the customer logs on before the results have been posted, the first notification would be to tell the customer that the results are ready. Subsequent updates would be related to new content postings.

It should be made clear to customers here that by providing an email address or phone number the customer will be exposed to being identified but that the company is prohibited by policy and/or law to provide that information to any other parties and that no identities will be attached to the metadata.

11.5.2. Data Page

The data page would simply provide a listing of the sequencing results indicating genome locations and allele designations. It could be made more interesting for the customer by also showing, in graphical format, which genes (or regulatory regions) each of the markers belong to and where on the chromosomes these genes can be found.

It is a human universal to want to compare oneself to others. So, for each allele the customer should be presented with a frequency number representing:

- I. Frequency within the metadata
- II. Frequency within Thai or Asian sub-populations known from external sources
- III. Frequency within the global population known from external sources

11.5.3. Genealogy Module Page

Analysis of genealogy markers should be able to identify the paternal and maternal haplogroups that each customer belongs to. This module should be able to provide an automatically generated paternal and maternal ancestry map showing

the locations where haplogroups originated and the time that they occurred. The graphical result should show two migration routes starting from the original migration out of Africa about 70,000 years ago to Thailand today. There may be uncertainties along the way due to lack of information (not enough markers analyzed for) but a rough indication will suffice. The map should be interactive so that the customer can learn more by clicking on specific haplogroup origination locations.

The module should also indicate the estimated percentage of Neanderthal and Denisovan DNA each customer has in their genome, including comparisons with the metadata population and sub-populations known from external sources. Links to sources providing general information on what is known about these two hominid species should be provided.

11.5.4. Recessive Allele Screening Module Page

Presumably, many or most customers will be found not to be carriers of any of recessive alleles being screened for. For these cases, just some general statistics about recessive allele frequencies in Thailand could be provided.

But for customers who are identified as recessive allele carriers, detailed information about the disease in question should be provided. They should be advised to have their spouse checked for the same recessive allele before having children.

If any unfortunates are identified as having two copies of a genetic disease allele but are

not aware of their condition because it hasn't presented yet or does not present strongly, they should be advised to seek medical advice.

11.5.5. Pharmacogenomics Module Page

For each protein/enzyme producing gene involved in the ADME process for which markers have been selected to characterize, the customer should be provided with a description of which two allelic versions they have. The implications with respect to metabolism efficiency (poor, intermediate, extensive, ultra-rapid) should follow from this along with some basic, graphics intensive, information on how each of the proteins/enzymes in question function in the process of drug metabolism.

The customer should be presented with a watch list of drugs that have been shown by research to produce adverse reactions linked with the specific alleles they carry. In each of these cases, some commentary on the robustness of the predictive ability provided by the research should be added. The customer should be advised to provide their doctor with this information in the event that they have a condition that might require treatment using any of the drugs on their watch list so that alternative drugs or dosage adjustments can be considered.

All of this content can be generated automatically on a customer's webpage by algorithms that recognize the specific markers for each customer.

11.5.6. Cancer and Other Disease Module Pages

All customers will presumably carry some markers

that have been implicated in cancer and other disease susceptibilities. They should be identified for each customer but it wouldn't be necessary to produce specific content for each marker individually. The content in these modules should be driven by disease type.

For each disease selected for marker identification in the product, a statistical treatment should be applied to the relevant susceptibility markers that a customer carries that results in an overall risk assessment based on accumulated research. The risk assessment should be put in perspective with comparisons to actual prevalence of the disease. For example, it should be made clear that while a high risk assessment for a particular customer might suggest that they are three times more likely to develop a particular disease than the average, if only 2% of all people develop the disease then their actual risk assessment does not mean that they are more likely to develop it than not.

Again, care should be taken not to unduly frighten customers, but some information on the disease in question should be provided as well as links to information on ways that risk can be mitigated in terms of dietary and lifestyle choices.

11.5.7. Infectious Disease Module Page

Depending on which agents are selected for detection (Herpes simplex virus?), it is likely that in most cases, no infectious agents will be identified. For these customers, some basic information on how bacteria and viruses proliferate and how the immune system works to combat these infections can be presented for general along with some data on bacterial and viral prevalence in Thailand.

For customers that have been identified with bacterial or viral infections, they should be provided with additional information concerning treatment options.

11.6. New Information Updates

Building content will be an ongoing process for the Commercial Entity as the database grows and as new information is acquired from the research community. So a customer's personal webpage will be continuously updated. There should be a notification feature on the customer's cover page that directs the customer to where updates have been posted.

For customers that have opted to provide an email address or phone number, automatic emails or text messages should be sent out to alert the customer to any update. This could apply to updates on personal webpages as well as to new articles appearing on the main website. Customers could be given the ability to select what kinds of updates they would like to receive notifications about.

11.7. Customer Feedback

The website should have a built in feedback facility that allows customers to address questions they have or to submit comments. The intent would not be to answer specific medical questions by recommending treatments, but rather to identify customer concerns in order to improve how the data is presented or otherwise improve the business model. It should include an FAQ section and should use automation software to minimize

administrative burden.

11.8. Access to Practitioners

For customers that have purchased the product in response to a doctor recommendation for an immediate clinical need and for customers with a clinical need that have purchased the product previously, it will be necessary for there to be a link between the patient's webpage data and the doctor.

There should be a practitioners-only zone accessible from the main website. Doctors should have to sign up for access to it and the Commercial Entity should have to verify the doctor's identity before access is granted. Once logged on, the doctor should be able to enter the patient's user code, provided with consent by the patient, to bring up the patient's data.

Apart from a means of accessing patients' genomic information, the practitioner's zone should be a facility for the Commercial Entity to provide doctors with information to help in the interpretation of the results. This could entail specifically written reports as well as access to technical papers. It should also include contact information so that doctors can consult directly with experts, under employment by the Commercial Entity or not, that have agreed to be listed as such.

11.9. Access to Patients for Clinical Studies

This model also provides a means for genetics researchers to find candidates for further study.

From the metadata, researchers might discover a subset that have a particular minor allele, or group of associated alleles that they wish to study further, either for genetic association purposes or clinical outcome purposes.

On behalf of researcher requests, the Commercial Entity could post on the personal webpages of the identified individuals (by code, still anonymous) a request for participation in a study. Those that agree to participate could be put in contact with the researchers and the usual process of compensation for participation in clinical trials would commence.

Alternatively, practitioners engaged in the system that treat patients for certain conditions that genetic researchers wish to study could be contacted similarly via the practitioner-only zone or by direct email contact. After patient consent is received, patient medical history and genomic data could be linked for researchers to evaluate and possibly follow up on with clinical trials.

11.10. New Product Development

The initial product, supported by sufficient marketing efforts, has the potential for a volume of sales in the tens of thousands of units per year, but will eventually start to slow down as a result of market saturation. Even if marketing efforts directed at the clinical market segment gradually succeed in overcoming practitioner resistance, it is likely that growth there for the initial product will not be able to overcome slowing sales to the healthy general public segment.

Furthermore, as sequencing technology continues

to improve from the perspective of cost per unit of information generated, the Ion Torrent platform will eventually become obsolete. This will expose the business model to competing ventures that have more to offer. Therefore, new product development should be an activity embraced by the Commercial Entity as soon as the initial product has been introduced to the market.

11.10.1. Other Broad Spectrum Products

Provided that the sequencing technology employed initially in this model has not been superseded by more cost effective technology, the company should proceed quickly to design new broad spectrum products analyzing for a similar number of markers but for more focused purposes. Essentially, these products would be expansions of the modules in the first product.

Customer feedback and utility would have to be assessed, but the two modules that would most likely make the most sense to expand and offer as new products would be the pharmacogenomics module and the disease susceptibility modules simply because of how much marker data exists. But, if there is customer and practitioner interest, all of the modules could potentially be expanded and offered to the market. Care would have to be taken when deciding when to introduce these new products so as not to cannibalize sales of the first product and thus compromise the depth of the metadata generated by it.

Since residual DNA from customers that have purchased the initial product will be in storage, there will be no need to acquire new samples

from them. The product price could reflect this and existing customers could simply purchase the new product online by credit card. Turnaround time would be quicker.

These new products should initially be offered through the personal webpages to existing customers to capitalize on high interest users and then be offered at a later date to the general public and through clinical settings.

These secondary products would be expected to generate smaller databases than the first, but what is lacking in sampling depth would be compensated for in increased sampling breadth in the total accumulation of metadata. Provided that the initial product isn't cannibalized, there will be data mining synergies from having a large population of genomes that cover a narrow range of markers for many purposes in addition to smaller populations of genomes that cover a wider range of markers for narrower purposes.

11.10.2. Reagent Kits

Currently, no hospitals in the private sector are known to own the Ion Torrent Sequencer. However, if any do purchase this technology, the Commercial Entity could sell them the product in the form of reagent kits supplied by the reagent supplier along with the vials. Essentially, they would be buying the bioinformatics, interpretation, and presentation expertise of the Commercial Entity but would do the actual sequencing themselves. The price would be adjusted accordingly. The raw data from the sequencing would just have to be sent to the Commercial Entity in the proper con-

figuration for inclusion in the web based format for customers.

11.10.3. New Platforms

Eventually, technological development in sequencing capability will render the platform used here obsolete. Developments must be monitored closely by the Commercial Entity and the time will come when the sequencing platform will have to be changed. The Commercial Entity may decide to purchase the new technology itself or the laboratory at Ramathibodi may decide to do so, or perhaps the two institutions may decide to do so collaboratively. Presumably, new reagent arrangements would have to be made as well. Given that by definition this will result in more markers being sequenced for the same cost, the switch in platform would also require the development and implementation of new product compositions.

It is envisioned that expanded sequencing capabilities will eventually lead to an affordable high throughput or whole genome capability that will rapidly be purchased by clinical institutions everywhere allowing for immediate results. At this stage, a model that requires samples to be sent to a central location will not be viable for the clinical market and may even become threatened for the general public market. The long term strategy for the company should be to prepare for this eventuality while ensuring that its bioinformatics expertise remains unrivalled. The long term future of the Commercial Entity will most likely be in the provision of bioinformatics services.

12. Process and Logistics

Since the target market is so diverse, including various clinical settings as well as segments of the general public at large, the logistics of selling, distributing and retrieving sample vials, will necessarily be complex. The Commercial Entity would need to employ state of the art process control and tracking software to maintain the integrity of the model.

12.1. Points of Sale

The points of sale would be varied depending on the market segment being targeted. Details of market segmentation will be discussed in Section 13.3.

12.1.1. Clinical Market

For specific clinical settings where the product would serve a specific clinical need, the point of sale would be the doctor's office. The product would have to be marketed based on its clinical utility directly to doctors or to the purchasing agents of hospitals. So in effect, practitioners would become the sales force for the product in these settings.

Depending on the nature of the sales agreement, sample vials would be distributed to these locations as outright sales or on a consignment basis. Print based promotional materials directed at doctors and at patients should accompany the vials.

12.1.2. General Public Market

The primary ongoing means of selling to the general public would be through the website. Customers could purchase by credit card and the

sample vial would be mailed to them.

For customers concerned about anonymity, however, this method would reveal customer identity. For this reason and to widen sales potential, other avenues of access to the product should be established and publicized on the website. These could include:

- I. Office of the Commercial Entity
- II. Hospitals and other clinical settings that have been sold the vials for clinical purposes
- III. Partnered institutions that have public access
- IV. Special events and other limited time locations

These will be discussed further in Section 13.3., but in each of these cases, where customers pick up and pay by cash for the vials in person, anonymity would be preserved.

12.2. Sample Vial Collection

Once saliva has been deposited in the vials by the customer, the vials will have to be returned to the lab for DNA sequencing.

For customers that have purchased the product online and received a sample vial by mail, it would have to be sent to the lab by mail. The package

received by the customer, therefore, should contain a return envelope with the lab address printed on it. Postage could be prepaid but in that case the cost would have to be accounted for in the product price.

For customers that have purchased the product physically at any location, the vials would be sent to the lab in bulk by courier by the institution or personnel managing the point of sale. For limited time locations, unused vials would have to be returned to the Commercial Entity for re-distribution elsewhere.

Keeping track of the locations of vials would be an important function of the Commercial Entity but should be manageable using a bar code system and tailored software.

12.3. Raw Genomic Data

The sequencing lab would conduct a sequencing run once a full complement of 96 samples is received on a first come first served basis and the results would be transferred by linked software with the server at the Commercial Entity.

The output of the raw marker data would be in a format determined by the software of the sequencing technology provider so it would have to be made compatible with the system of algorithms and content generation used by the Commercial Entity to ultimately produce what will appear on customers' individual webpages. It would presumably take considerable effort to program this ability by internal and possibly external expertise employed by the Commercial Entity.

Once the system is prepared and debugged, however, the flow from sequencing results to webpage content provision should be largely automatic. Quality control measures would have to be robust in order to catch errors and malfunctions. Some purposely built in steps requiring human intervention in the process might be desirable, if not necessary.

12.4. Cash Flows

Financial transactions related directly to the sales of the product (not including capital, fixed, employee, and utility costs, etc.) would be as follows.

12.4.1. Cash Flow In

- I. Online payments received from customers ordering the product for delivery by mail
- II. Payments received from customers purchasing the product directly from the Commercial Entity
- III. Payments received from institutions having purchased vials outright for resale to customers
- IV. Payments received from institutions with vials in consignment upon sale to the customer
- V. Payments received from the government institution(s) contributing the subsidy

To determine the amount of subsidy contributed by the funding institution(s), a method of reporting and verifying sales would have to be established.

12.4.2. Cash Flow Out

- I. Payments to the saliva sampling vial supplier
- II. Payments to the sequencing reagent supplier
- III. Payments to miscellaneous other suppliers
- IV. Payments to the sequencing lab for other costs involved in sequencing
- V. Payments to institutions as commissions for sales to customers (if necessary)
- VI. Payments for postage and/or courier services for transportation of vials (if necessary)

12.5. Inventory Management

The cash flow management system would be linked to the tracking system for the bar coded vials. The company would have to know where every vial in the system is located and whether it has been used in the process of a sale and thus has generated income. The vial inventory status options would be:

- I. In inventory at the Commercial Entity location yet to be distributed
- II. In inventory under consignment at points of sale
- III. Sold to an institution but yet to have returned customer DNA
- IV. In process at the lab awaiting DNA sequencing
- V. In storage with residual DNA at the lab after sequencing

12.6. Information Flows

In addition to the specific physical flows of vials and DNA, the flow of sequencing data from lab to customer, and the flow of cash from various points of sale into the company and out to suppliers of goods and services, it is useful to consider also the flow of information. Information, in the sense being used here, is anything that imparts knowledge. The flows of information, therefore, are defined as any communication that transfers knowledge.

Considering that the products that will be offered under this business model are precisely about compiling, interpreting, and transferring knowledge, the information content is rich. The following are the specific information flows of this model, considering also the wider stakeholder community, and indicating the functions that facilitate the information transfer.

12.6.1. Information Flow Into the Commercial Entity

- I. From the global research community (product composition and presentation)
- II. From the Thai researcher community (research objectives)
- III. From the Thai health care community (clinical target markets)
- IV. From the Practitioner Community (clinical needs and outcomes)
- V. From Potential Customers (market research, sales pattern analysis)

VI. From Actual Customers (customer feedback)

VII. From the lab (sequencing data)

12.6.2. Information Flow Out of the Commercial Entity

I. To the Thai research community (research opportunities from metadata)

II. To the global research community via the Thai research community (published research)

III. To the Thai health care system (clinical outcomes)

IV. To Thai health care planners (trend and frequency analysis from metadata)

V. To the practitioner community (genomic interpretation)

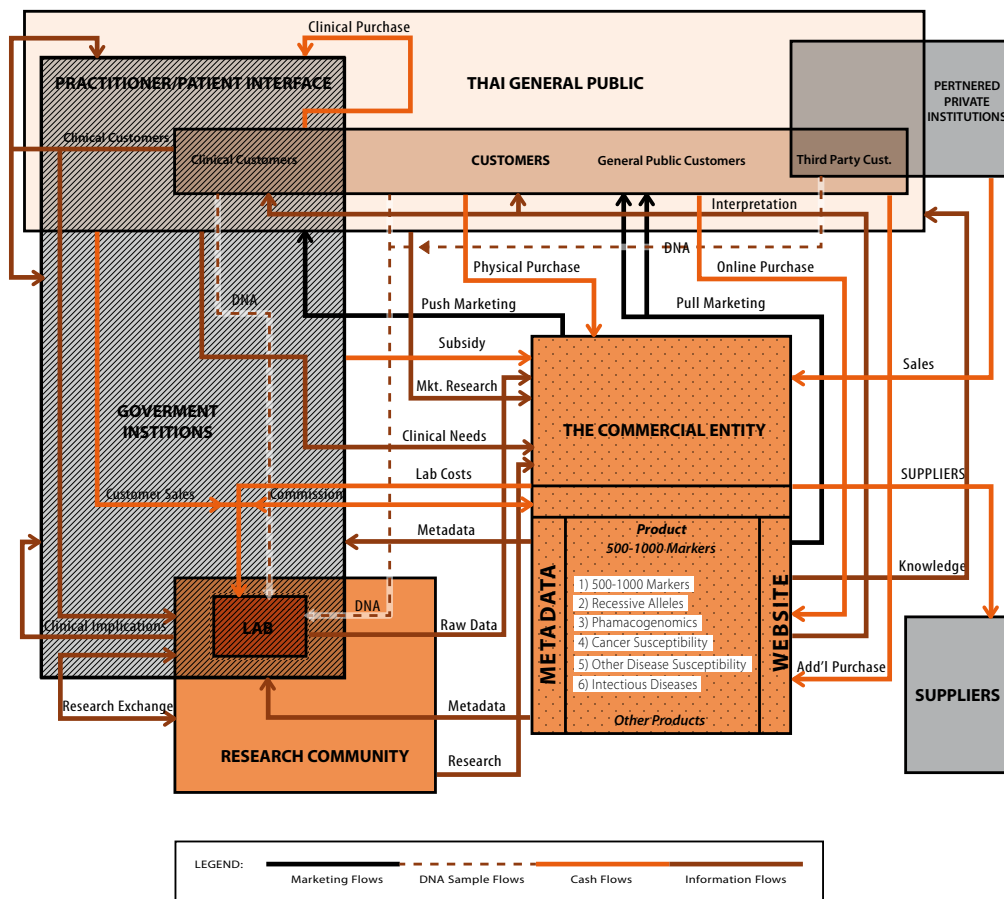
VI. To all customers (increased knowledge in genetics)

VII. To customers with clinical needs (clinical implications of genomic interpretation)

VIII. To Thai society (generation of expertise)

12.7. Flow Summary

The figure below is a graphical representation bringing together all of the flows between stakeholders discussed above.

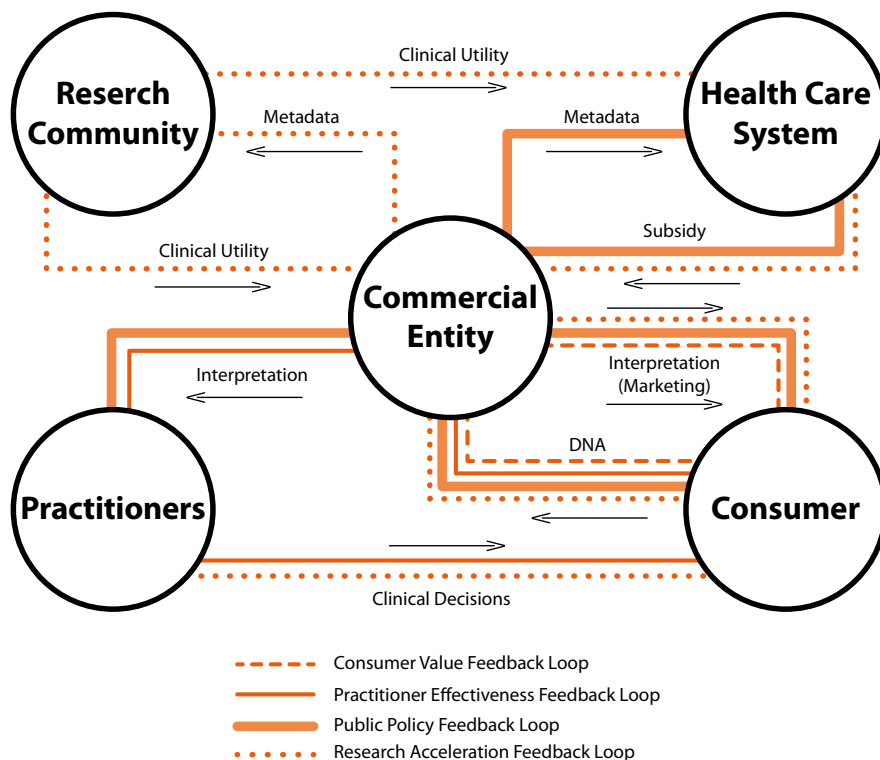


12.8. Positive Feedbacks

Positive feedbacks are features of any complex system that exhibits emergent properties. A positive feedback is any linkage of causality that results in an effect on the original causal agent that promotes the original causation, thus accelerating the entire linked process. Enzymes are the primary class of complex molecules in cells that are responsible for the positive feedbacks that have allowed the machinery of life to evolve. Indeed, enzyme activity, along with replication and energy provision (metabolism), are the core building blocks of functionality that were required for life on earth to emerge.

By direct analogy, any human cultural endeavor, including the application of a business model, relies on positive feedback to grow. Positive feedback, in the form of information transfer between human brains, is what allows the whole of the endeavor to exhibit properties greater than the sum of its parts. It is the driver of human creativity.

As an institutionally integrated model essentially trading in the transfer of knowledge, this personal genomics business model is, by its nature, rife with positive feedback loops. There are potentially many ways of defining the feedback loops that exist in this model as the lines of cause and effect are not in reality linear, but it is useful to attempt to do so in order to understand the value of the integrative structure of this model. The figure below attempts to illustrate four main feedback loops.



For clarity, some definitions are required for this representation as they may differ slightly from how they have been used elsewhere.

The “**Heath Care System**” refers to the system as a whole in terms of its ability to function effectively in the provision of health care to Thais as managed by various institutions involved in this mandate.

“**Practitioners**” refers to the institutions and individuals that directly intersect with patients in the provision of health care.

“**Consumers**” refers to the totality of customers of the personal genomics product.

“**Researchers**” refers to the institutions and individuals involved in the conduct of genomic research and its implications for health care.

In the feedback loop descriptions below, each link in the loop is isolated and the nature of the connections discussed so that it becomes clear how the feedback propagates. Note that realized value and perceived or expected value operate the same way in the propagation process.

12.8.1. Consumer Value Feedback Loop

Commercial Entity → Consumers

The Commercial Entity provides consumers with the promise of value via marketing efforts and realizes that value in the interpretation of genomic data for customers. The promise and realization work in parallel to establish the linkage.

Consumers → Commercial Entity

The Commercial Entity derives informational value from consumers cumulatively by assessing

the trends and patterns in sales distribution and customer reaction. This latter process starts with initial market research used to guide composition of the product and would remain ongoing throughout operations.

Closing the Loop

Provided with consumer reaction and sales data, the Commercial Entity is able to improve its ability to provide value, promised and realized, to consumers, thus increasing sales. Increasing sales allows the Commercial Entity to improve the value it offers consumers. This establishes the positive feedback and closes the loop.

12.8.2. Practitioner Effectiveness Feedback Loop

Consumers → Commercial Entity

The Commercial Entity derives potential clinical value from the genomic information obtained from each customer’s DNA and in the interpretation that it generates. This operates individually and cumulatively.

Commercial Entity → Practitioners

When customers’ genomic profiles are shared with practitioners in clinical settings, whether the product was purchased in response to an immediate clinical need or prior to a need arising, the interpretive value created by the Commercial Entity is transferred to the practitioner. Value is accrued by the clinical decisions that are made in response to the interpretations.

Practitioners → Consumers

When clinical decisions based on genomic inter-

pretations result in positive clinical outcomes, value has been transferred directly to customers individually and consumers cumulatively.

Closing the Loop

The realization of positive clinical outcomes will prompt practitioners to more readily recommend that their patients purchase the product, thus increasing sales and facilitating the process of interpretive improvement. Accumulated clinical success will allow the Commercial Entity to more successfully market the product into clinical settings and to the general public. This creates positive feedback and closes the loop.

12.8.3. Public Policy Feedback Loop

Consumers → Commercial Entity

As the number of customers accumulates, the Commercial Entity builds a deeper database. This increases the intrinsic value of the metadata.

Commercial Entity → Health Care System

When the Commercial Entity transfers the metadata to the health care system, its interpretation will lead to health care planning and implementation decisions with expected value that will eventually become realized value.

Health Care System → Commercial Entity

It is the expected value of the metadata that will have allowed the business model to have been established in the first place by the agreement by certain government institutions to fund the project under the guise of purchasing the metadata. As the metadata is accumulated and analyzed,

health care planning initiatives will be identified resulting in an increase in expected value. This will provide justification for the funding having been previously agreed to and for its continuation. Once positive results from these initiatives can be measured, value will become realized prompting further justification.

Commercial Entity → Consumers

By agreeing to fund the business model by purchasing the metadata from the Commercial Entity in the first place and in continuing to do so, the Commercial Entity is enabled in its efforts to offer the product to consumers at a lower price than it would otherwise. This translates directly into increased value to consumers.

Closing the Loop

Increased value to consumers, whether perceived or realized, will be reflected in increased sales and a deeper database. A deeper database, by definition, will create metadata with greater value, thus creating positive feedback and closing the loop.

12.8.4. Research Acceleration Feedback Loop

Consumers → Commercial Entity

As the number of customers accumulates, the Commercial Entity builds a deeper database. This increases the intrinsic value of the metadata.

Commercial Entity → Research Community

When the Commercial Entity makes the metadata available to the research community, it will provide numerous opportunities for research for numerous purposes. Some uses will be purely

academic while others will have direct clinical objectives. Other research will focus on patterns of genomic distribution and genetic linkages will have implications for health care planning.

Research Community → Health Care System

Analysis of the metadata focused on reaching conclusions that impact the health care system as a whole, or impact any elements within the system, will lead directly to health care planning and policy decisions intended to improve the efficacy and effectiveness of the system.

Research Community + Health Care System → Commercial Entity

In ongoing communications with individuals engaged in research and health care management, the Commercial Entity will be able to assess the

implications of the metadata it has generated. This will enable the Commercial Entity to make improvements in product design, interpretation and presentation of genomic results, and marketing efforts.

Commercial Entity → Consumers

Improvements in product design, interpretation, and marketing will enable the Commercial Entity to create greater value, perceived and realized, for consumers.

Closing the Loop

Increased value to consumers will be reflected in increased sales and a deeper database. A deeper database will create metadata with greater value, thus creating positive feedback and closing the loop.

13. Marketing and Distribution Strategy

Since the driving objective of this business model is to generate a deep database of partial genomes from a product with diverse utility, a substantial multifaceted marketing effort will be required. The Commercial Entity would have to be sufficiently capitalized to allow for a marketing budget that would be up to the task of creating public and practitioner awareness of the product prior to funds being made available from internally generated cash flow.

Implicit in the notion of a substantial marketing effort is the expectation that public awareness of the enterprise and its claims of value will be greater than has been achieved by any other personal genomics effort in the past. To ward off negative public perception, careful attention should be paid to the promotion of a positive image for the company and the enterprise as a whole.

13.1. Market Research

Market research should be a regular function of the Commercial Entity. It will be required for the

initial stage of product development and will be critical throughout operations for providing guidance in the process of new product development and positioning. The analysis of sales patterns

by market segment and distribution method will provide much useful information in this regard but an ability to assess broad public reaction beyond what sales information and immediate customer feedback can provide will also be important.

Market research intended to identify potential perceptual impediments that could arise within the public should be conducted by a contracted market research firm during the product development phase and beyond in order to guide the preparation and implementation of marketing strategy.

13.2. Messaging

Since a high degree of public scrutiny would be expected and considering the diversity of value propositions being offered by the product, the Commercial Entity should devise themes that should consistently be reflected in all marketing efforts that involve communication with consumers. These themes should be considered as elements of the product's brand image. Market research would inform this process, but based on current expectations, the following themes are suggested.

13.2.1. Trustworthiness

Since it can be anticipated that some paranoia related to the accumulation of personal genomic data will result from the introduction of this business model, trustworthiness of the enterprise should be a theme. This can best be achieved with openness with respect to the purposes, structure,

and policies of the enterprise, as well as the voracity of the product claims made by the Commercial Entity. The public-private teamwork aspect of the model, involving multiple stakeholder communities, should be leveraged in building public trust.

13.2.2. Public Consciousness

The grand project nature of this model should be a theme. Rather than downplaying the uses of the metadata, they should be promoted. The effects that the availability of the metadata will have on the Thai research community and policy planners in their combined effort to improve health care in Thailand over the long term should be stressed. Customers should feel that they are participating in a national project to better the country.

13.2.3. Genetics is Fun

Specific health benefits should be promoted in a targeted manner, but in order to combat the perception that personal genomics information will only give the customer bad news, a theme of marketing efforts should be to project an expectation that the customer will receive interesting information that will enrich their lives. This theme has already been addressed in the module design and presentation discussions and should apply also in promotions.

13.3. Market Segmentation

Because the product would be multipurpose and would be meant to be sold to healthy members of the general public in addition to patients with

immediate clinical needs, it will be necessary to attempt to segment the market in order to devise targeted marketing strategies that will maximize sales. The challenge in segmenting the market is to improve the ability to reach as many potential customers as possible while at the same time retaining a cohesive image of the product in the marketplace.

13.3.1. General Public

In Section 7.1, the following reasons why a healthy consumer might consider buying a personal genomics product were identified:

- I. Generally interested in genetics
- II. Interested in learning about features of their own genome
- III. Interested in advice on making health related lifestyle choices
- IV. Interested in learning what specific health risks may apply to them
- V. Concerned about potential inherited risks
- VI. Concerned about any potential genetic diseases they may pass on to their children
- VII. Interested in having a genomic profile for reference in case of future medical needs
- VIII. Willing to participate in a Thai genome database project as a matter of public consciousness

For the purposes of devising targeting strategies, these reasons might be consolidated into the following three types of consumer, recognizing that

they would not be mutually exclusive:

Knowledge Focused

These are people that are interested in having information for sake of being more informed generally. They might be specifically interested in genetics or science more broadly and might be interested in learning about what personal genomics can do for public health, individually and collectively. They would be more inclined to purchase the product to see how their own genome compares to others in the population and would probably be more likely to participate in the grand project of collecting and using the metadata for public good out of a sense of public consciousness.

Self-Improvement Focused

These are people interested in maintaining a healthy lifestyle. They would be interested to know what their genome can tell them about how to incrementally improve their future health prospects in terms of diet or medications. They would want to know what they should avoid in case of health problems in the future.

Concern Focused

These are people that are specifically concerned about impending health issues for themselves or for loved ones. Their concerns might be real or imagined. They might have had a troubled health history personally or have identified certain types of illnesses that seem to occur frequently among family members. They may be the type of person that routinely seeks out medication for every ailment they encounter or the type that seems to frequently react poorly to medicines when prescribed.

For marketing strategy decisions such as where to place advertising, what information to be conveyed about product value, and where to establish points of sale, these three segments of the general public could be approached differently.

13.3.2. Clinical Settings

The specific clinical settings within the wider practitioner community that are to be targeted for marketing efforts would be chosen based on the actual clinical utility offered by the product as well as how that need is being served by other genetics based products available to the practitioner. If a competing, more cost and/or time effective, product is already available to the practitioner in a particular clinical setting, the interests of all parties might be better served by focusing on other clinical settings.

Potentially, any clinical setting for any purpose could be considered a separate market segment. Since practitioners would be the targets of marketing efforts in these settings, the practitioner community at the level of hospital administration should be engaged. However, for the purpose of reaching specific communities of specialists for which the product has particular value, individual clinical settings could be targeted for attention. Settings in both public and private health care realms could be targeted.

Prenatal Settings

The Recessive Allele Screening module would be of particular interest to doctors treating patients planning to have children.

Maternity Settings

Parents may be interested in having their newborns tested for recessive alleles as well as for information on disease susceptibilities.

Chronic Disease Treatment Settings

The specific markers chosen for inclusion in the Pharmacogenomics module, and thus the drugs for which information is to be presented for customers, would guide the selection of which chronic disease treatment settings should be selected for targeting by marketing efforts.

Oncology Settings

Typically, it would be too late for oncology patients to benefit from the cancer susceptibility module, but the product could be marketed to relatives and other loved ones of cancer patients. This rationale could also apply in settings related to the treatment of other suites of diseases for which susceptibility markers are included such as cardiovascular, autoimmune, or psychiatric diseases.

Nutrition and Wellness Settings

The information provided by the Pharmacogenomics and Susceptibility modules could be of interest to patients that visit the nutrition and wellness clinics that take a holistic approach to health care. These approaches are proliferating, particularly in the private sector. However, many such enterprises are engaged in fraud by promoting alternative medicines that make claims not substantiated by science. They should be avoided so as not to tarnish the product by association.

13.4. Advertising

The Commercial Entity should conduct an extensive advertising campaign to be rolled out in waves according to the company's financial position and sales projections. An advertising company should be engaged to produce the graphics and make the placements in accordance with the company's messaging and targeting objectives.

13.4.1. General Awareness

Online

Ads could be placed on high volume Thai websites and/or websites heavy in science and health care subject matter. The ads should be attention grabbing with the main purpose being to link viewers to the main company website.

Billboards

Advertising on billboards and other signage platforms such as public transportation sites (busses, BTS, MRT) can be an effective means of building general awareness. Since viewer attention tends to be fleeting, the main objective should be to prompt the viewer to remember the brand name and website address.

Video

Promotional videos could be produced and placed on television and other video advertising formats such as office building and shopping center elevators and public transportation locations. Video content should focus on communicating the broad messaging objectives, informing the viewers of the basic value propositions of the product, and indicating where the product can be purchased.

13.4.2. Targeted

Print

Ads could be placed in magazines that have a distribution audience considered to be in line with the general public market segments discussed above. Popular science, health, and fitness related publications would be candidates. Ad content should be more informative in nature than in wider access ads and tailored to the expected reading audience.

Journals

Thai medical and genetics journals should be targets for ad placement directed at the practitioner community. Content should focus on clinical utility and the value of the metadata and should provide contact information that will lead the reader to sources of more information.

Conferences

The Commercial Entity should have an active presence at life sciences and medical conferences held in Thailand and regionally in the form of sponsorships and booth placements. Company representatives should accept speaking engagements when commercial presentations are allowed. Additionally, the product will receive promotion by default when researchers involved in analyzing the metadata report on their findings.

13.5. Sales and Distribution

This section is supplemental to the discussion of logistics in Section 12. The objective in distribution strategy should ultimately be to provide access to the product for every Thai.

13.5.1. Website

The main point of access for customers will always most consistently be the website. Customers will be able to order sample vials online, receive them by mail and return them to the lab by mail. All locations where customers can purchase the product and submit samples in one stop, discussed below, should be listed on the website, categorized by region and specific location.

13.5.2. Partnered Institutions

Distribution partnerships with private institutions should be negotiated to provide wide point of sale access to consumers beyond the reach of what can be achieved by the website. Consumers that are concerned about privacy and are thus reluctant to order the product online can be satisfied by being able to buy the product anonymously at a physical location provided by the distribution partner.

The criteria for selection of potential distribution partners should be:

- I. Wide geographical distribution of physical locations
- II. Efficient internal logistics infrastructure
- III. High throughput of interaction with the public
- IV. Regular personal contact between staff and the public
- V. Held in high degree of trust by the public
- VI. Active public service philosophy

Ideally, selected distribution partners should be willing to engage with the enterprise without compensation out of a sense of public service in exchange for good will, but this may be unrealistic in most cases so a sales commission or at least cost compensation might be required.

Some training of staff at the points of sale would be required, but considering the ease of use of the sample vials, it would be minimal. Promotional materials informing consumers of the nature and value of the product should always accompany the vials at all points of sale.

The duration of distributor partnership agreements should be contractually established, but it is likely that the effectiveness of a distributor would wane over time, especially if the distributor's primary goal is to achieve public good will. Constant assessments of the effectiveness of current distributorships and evaluation of potential new distributorships should be an ongoing function of the Commercial Entity.

The following are some suggestions of institutions that could be approached to act as distribution partners.

Hospital and Clinics

A distinction is made here between clinical settings at hospitals and clinics, where customers would purchase the product in response to a clinical need as recommended by doctors, and non-clinical settings. In non-clinical settings at hospitals and clinics, consumers would be prompted by print advertisements to purchase the product and submit their sample over the counter without a doctor's involvement.

Presumably, due to policies regarding the sale of commercial products, public sector hospitals would be prohibited from participating as distribution partners, although this prohibition might be waived if they are already selling the product in clinical settings.

Private sector hospitals, however, might be more amenable to such an arrangement. Private sector companies that own and operate a chain of hospitals or clinics would be the most attractive targets for cooperation due to their wider access and internal logistics operations.

Commercial Entity sales staff would be responsible for selling the product to hospitals for non-clinical settings in concert with their efforts to sell the product into clinical settings.

Thai Banks

Thai banks would, in many ways, be the ideal distribution partners. They have hundreds of branches, thousands cumulatively, reaching every corner of the country and virtually everyone has at least occasional reasons to visit a bank branch physically. They have internal logistics operations to move money around, are heavily staffed, and have centralized organizational structures. Although subject to some public derision, they are trusted in terms of security.

An additional benefit provided by banks is that they could sell the product to their customers on a payment installment basis, whereby customer accounts could be debited monthly for a period of, say, six months (plus interest, if necessary). This would expand access to consumers that cannot afford a one-time payment for the product.

Promotional signage would have to be placed at all branch locations and one or two staff members would have to be given responsibility for interacting with customers interested in purchasing the product. The partnering banks would be expected to promote the product in parallel with their other ongoing promotional activities.

Ideally, all of the major Thai banks should be persuaded to participate in the distribution and collection of vials as a matter of public service. This may not be realistic, as some banks may simply not be interested or may wish to retain exclusivity in order to capitalize on public good will exclusively. However, a distribution arrangement with even one bank would provide tremendous public access for the product. Partnered banks would receive positive publicity on the Commercial Entity's website and in its advertising efforts.

Presumably, the Commercial Entity would just be responsible for delivery of the vials to a central distribution location operated by the bank and the bank would distribute to their branches using their internal logistics system. Used vials would be returned routinely to the bank's central distribution location and forwarded in bulk daily directly to the lab for sequencing.

Pharmacy Franchises

Nationwide franchised pharmacy chains such as Boots and Watsons could be approached for distributor partnerships. The health care link makes them natural partners and they have product supply systems that could handle the distribution and collection of vials.

In this case, point of sale product advertising

might not be necessary. The product could simply be placed on shelves in an appropriate location. When customers purchase the product, the pharmacist would simply accept the sample containing vial and send it to the lab. Alternatively, customers could mail it in to the lab on their own.

Other Franchises

Other, non-health related, franchise operations could be considered in order to take advantage of access to potential customers and internal logistics capabilities. For these companies, the purpose of participation would be promotional.

An obvious candidate would be Starbucks. They are known to be routinely interested in public consciousness campaigns and might be interested in participating on these grounds. Their premises are always clean and orderly.

There are other widely distributed franchise operations that could be considered as well, although fast food chains should probably be avoided.

13.5.3. One Time Events and Locations

In addition to the establishment of distributorship partnerships with institutions, the Commercial Entity should engage in one time sales drives at specific locations and events around the country that exhibit a high density of public traffic.

High quality portable booths should be designed for this purpose. Company employed sales staff should be responsible for managing this activity but, depending on location and frequency, external companies that provide setup and staffing

services for promotional booths could be engaged. At least one company employee, however, should probably be present, at least until confidence in the services company's competence is achieved.

In all of these cases, physical delivery of the vials to the point of sale and return to the company would be the responsibility of sales staff managing the booth.

Commercial Fairs

Commercial fairs operate throughout Thailand all the time to provide sales opportunities for retailers and for rental income for retail space owners. They typically last from two to seven days. They are often open to any retailer, but often they have themes. Often they are located in convention halls and are connected to other events involving speakers or presentations. Fairs that are themed along the lines of science and health could be sought for the placement of booths to sell the product. The integrity of the brand should be considered when selecting these opportunities.

Shopping Centers

Shopping Centers routinely rent out retail space in lobby areas on a temporarily basis and often they are themed. Booths could be set up in these locations on a basis similar to at commercial fairs.

Office Complexes

Temporary retail space beneath and between interconnected office complexes could also provide opportunities for booth placement. The target market in these locations would be office workers at lunch hour or after work rather than shoppers. A booth could travel around from complex to complex, spending no more than a couple days at each.

Employee Health Initiatives

Large corporate entities often engage in health related employee initiatives in an effort ultimately to reduce sick days and improve employee productivity. The product could be promoted to such large entities for this purpose. Sales staff from the Commercial Entity could spend one day with a booth at the corporate office location selling the product to employees at a discount covered by the employer.

13.5.4. Company Owned Retail

The Commercial Entity's head office location would initially be the only permanent, internally owned, retail location for the product.

After some experience selling at temporary retail locations out of booths, a review of the results might prompt the Commercial Entity to consider a more permanent retail location. Most likely the best location would be a high end high volume shopping center in Bangkok. It is certainly questionable whether enough sales volume could be maintained at such a location to justify the rent and permanent staff costs, but retail contracts are usually just one year in duration so it could initially be considered a one year experiment.

Ideally, the retail operation should be profitable on a stand-alone basis, but some provision for public awareness advertising value might be allowed. Other health related products could be sold in order to boost sales revenue and commercial viability of the operation. If successful, retail operations could be expanded to other locations.

13.5.5. Clinical Settings

As discussed, for the clinical market segment, the model requires that doctors would be the sellers of the product directly to patients. But knowledgeable Commercial Entity sales staff, supported by targeted product awareness advertising efforts, would have to sell the product to the practitioner community. Hospital purchasing policy will vary from hospital to hospital, but most likely centralized purchasing staff as well as individual doctors within the clinical settings being targeted will have to be engaged.

This will surely be a challenging effort, as most doctors will have little or no experience interpreting genomic results. Sales staff will have to be well trained in how to convey the benefits of the product. Repeated follow-ups will surely be required before most sales are concluded.

The first objective for sales calls to doctors should be to sign them up for access to the practitioners' area of the website and inclusion of their email addresses in the mailing list. This will give them access to the interpretations created and posted by the Commercial Entity and allow them to receive email notifications of updates relevant to their area of expertise. Hopefully, the combined efforts of sales staff, access to the website, and product awareness advertising will build to the point where word of mouth between doctors starts to result in a sustained increase in sales of the product into clinical settings.

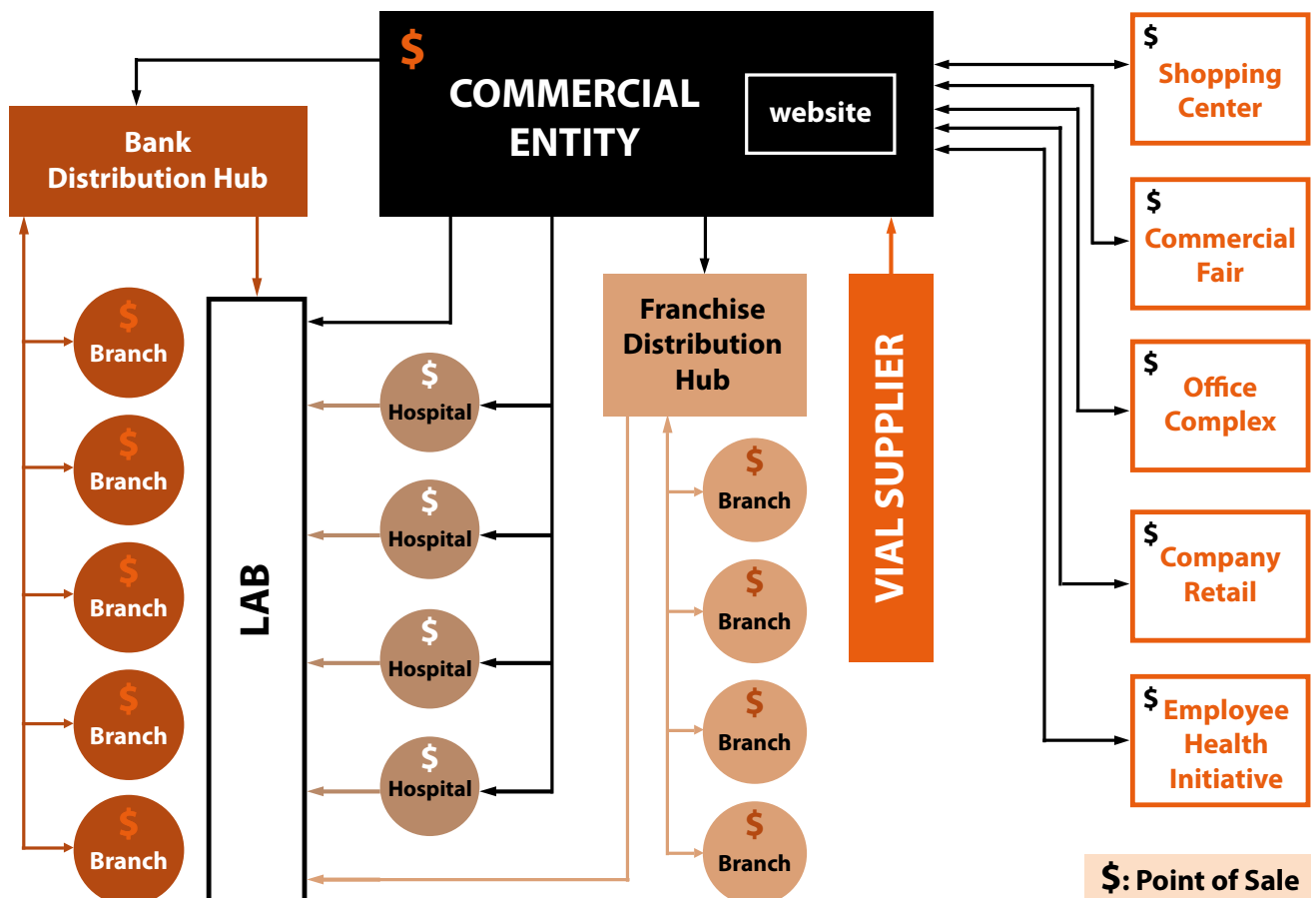
Another option could be to use established medical distributors to sell the product to practitioners. The advantage they would have would be in the

personal relationships have already established with doctors, which would give them easier access for meetings. However, this option is not recommended. Distributors would have to be compensated well to develop loyalty to the product and the Commercial Entity would have difficulty controlling the messaging they convey to doctors. The distributors would most likely know a lot less about genomics than even the least educated of doctors.

As for physical distribution of vials to clinical settings, an evaluation of costs should be conducted, but most likely delivery could be managed by the Commercial Entity nationwide by courier services. Used vials containing samples could be likewise couriered by the partnered hospitals to the lab for sequencing.

13.5.6. Physical Sales and Distribution Chart

The following is a graphical representation of the pattern of sales and distribution for the product. Where the colours of distribution lines match the colours of the institutional boxes, it indicates responsibility for the distribution.



13.6. Point of Sale Promotion

Accompanying all vials at points of sale should be signage to advertise the product and brochures available for customers to read prior to purchasing the product and/or to take home. Promotional materials should be tailored (to some extent) according to the expected market segment, whether

clinical or general public, expected to be reached at the point of sale.

Included in the brochure should be a clear explanation of the procedures for depositing saliva into the vials, for peeling off the identification code label, and for accessing the customer's personal webpage from the website.

14. Commercial Entity Composition

This section describes the recommended nature of the Commercial Entity in terms of its capital and equity structure as well as the specific functionalities it would need to possess in order to be successful in the context of the integrated model.

14.1. Objectives

The composition of the Commercial Entity should be such that it will promote the realization of the objectives of the business model discussed in Section 6. It should be able to effectively build a database of partial genomes by marketing products that provide value to consumers in a sustainable and profitable manner. It should be constructed with the technical capabilities to achieve these objectives in concert with the other stakeholders in the business model.

In keeping with the justification for having a Commercial Entity as the economic driver of the model, the company should be able to effectively respond to the specific market conditions facing a personal genomics business globally and locally.

14.2. Capitalization and Equity

Depending on the initial budget for marketing, startup capital requirements should be modest. Since sequencing would be outsourced to Ramathibodi Hospital, startup costs will be limited to working capital (including marketing costs), computer hardware, and office equipment. Furthermore, given the high priority status granted to life sciences and biotechnology ventures by various government agencies tasked with promoting the science and technology sector in Thailand, grants, tax breaks, lease deferments, and special category loans should be readily available.

However, due to the relatively long process of product development and infrastructure preparation involved in bringing the Commercial Entity from conception to realization, the working capital requirements will be substantial. A core of full

time employees will be needed for this process and it could take at least six months and possibly a year or longer before any revenue is generated and some time thereafter before the company becomes cash flow positive.

Seed financing, perhaps in several branches, will be required for this process and the method chosen will have implications for the eventual equity structure.

14.2.1. Alternatives

There are various alternatives that could be considered for access to startup capital. Each have implications for ownership structure and therefore control of the company. Any two or more of these alternatives could be combined.

Public Institutional Ownership

It has been proposed here that the ideal method of public funding for the model would be a subsidy on a per unit sold basis so that the product can be sold at a lower price to consumers. In the course of discussions with public institutions in this regard, one or more of them may express interest in providing the startup capital and thus retaining ownership, in part or in whole, of the Commercial Entity.

Private Institutional Ownership

One or more private companies could be approached to provide capital. An argument could be made that there could be synergies to be gained if the Commercial Entity is owned by an enterprise already engaged in a genetics or medical services related business.

Senior Management Ownership

A consortium of individuals interested in creating and managing the Commercial Entity could be assembled to provide startup capital through combined personal investment.

Debt Financing

The banks could be approached to provide startup capital loans. This option, however, would only be possible in combination with another avenue of financing as banks would not be willing to provide 100% of capital requirements. They would probably require that considerable financial risk is being borne by individuals involved in management.

Venture Capital

Venture capital firms could be approached to provide startup capital. Normally, such firms would require some management investment before considering participation. In this case, ownership would be distributed among management and investors in the venture capital fund. Venture capitalists investing in high tech startups, however, typically require an inflated risk premium on return of equity.

Angel Investor

An angel investor is a single individual that is willing to invest in an enterprise for the majority of the capital requirements while retaining a lesser proportion of the equity, the balance being retained by management. In effect, angel investors invest in the capabilities of the management team.

14.2.2. Distribution of Equity

In section 9.6.2, it was asserted that the diversity

of interests involved in this business model is an inherent advantage rather than a source of conflict and in sections 9.7.2 and 9.7.3, the issues of control of the customers' personal data and the potential for adverse public reaction over privacy concerns were discussed. These perspectives should be paramount when considering the ownership structure of the Commercial Entity.

Regardless of legislation and/or company policy, the potential for abuse of personal genomic data cannot be eliminated entirely. Even if protections against such abuse are robust, the potential for loss of the public's trust in the company's ability to maintain the integrity of personal data, whether real or imagined, will remain. If loss of public trust becomes widespread, the enterprise will fail. The equity structure of the Commercial Entity, therefore, should be constructed in such a manner as to enhance public trust.

In the opinion of this Consultant, the best way to accomplish this is for the equity of the company to be widely held. Ownership should be maximally distributed so that concentration of power is kept under strict limitations. The company should be constituted, from the first acquisition of seed capital financing, with these limitations defined in terms of a maximum amount of equity that can be held by any single individual and a minimum number of equity holders that must be maintained. Institutional ownership should be avoided in recognition of these conditions.

Furthermore, a portion of the equity should be distributed to employees of the Commercial Entity. The distribution can be in proportion to seniority within the company, but all employees,

ideally, should have an ownership stake. This will foster loyalty, creativity, and teamwork.

So, in final composition, the owners of the Commercial Entity should be a combination of its employees and a pool of non-institutional external investors. This structure will necessarily lead to transparency in company policy and business practices as shareholders will have rights to information. It should also mitigate the potential for adverse public reaction related to misuse of power as the highly distributed equity structure of the company would be open for anyone to see. The company could even be promoted in advertising as being for the people by the people.

14.2.3. Capital and Equity Model

In order to achieve maximal equity diversity and distribution, it is proposed by this Consultant that TCELS fund the creation of a crowd sourcing seed capital website to solicit funds from the general public. This mechanism for the funding of startup companies is growing fast in the USA and will become a major paradigm in venture capital access in the future, especially for technology rich enterprises. Note that this model for raising capital, if successful in this case, could be applied to other TCELS funded ventures ready for commercialization.

Existing web based seed capital ventures should be further studied for guidance, but the general principles should be along the following lines:

- I. A prospectus should be presented online for potential investors to consider

II. A limited amount of time should be set between introduction of the prospectus and the onset of the share purchasing process

III. Individuals can purchase no more than a certain maximum number of shares but several share block sizes could be offered

IV. The total amount of capital to be raised should be capped at a predetermined amount and when that amount is reached no more purchases should be allowed

V. Purchases should be accepted on a first come first served basis

VI. A time limit should be imposed on the process

VII. If the total capital requirement is not reached in the prescribed time and/or other methods of initial fund raising become necessary, investors should be allowed the opportunity for reimbursement

VIII. Share purchases should be translated into equity on a clearly expressed basis, recognizing possible future financing requirements and equity given to eventual employees

IX. In the event that additional rounds of share offerings are anticipated, initial purchasers should be rewarded in some manner for assuming the risk of early investment

X. All shareholders should have access to a full accounting of expenditures from raised capital and be given updates on developmental progress

XI. Purchases should only be accepted from Thai citizens or the proportion of foreign equity should be restricted

For the personal genomics business model, with an anticipated lengthy process of product development prior to the onset of revenue generation, at least two rounds of capital fund raising should be conducted. The first should be introduced to cover the expected costs of conducting the research required to fully develop the product and related software capabilities to the point where it is considered to be ready for implementation. The second should be meant to cover the costs of capital equipment and additional working capital to bring the venture to a position of positive cash flow.

Provided that the first round of financing using the seed funding website model proved successful, the same mechanism should be used for the second round. The basic principles would be the same as in the first round, with the following differences:

I. The total amount of capital to be raised would probably be significantly greater so the maximum allowed individual investment (in share blocks) should be higher

II. Investors from the first round should be given the first opportunity to increase their stake before the field is opened up to new investors

III. Investors from the first round should be rewarded by increasing the book value of their initially purchased stocks

IV. Since by this point the decision to proceed

will have been made, there would be no need for a mechanism of reimbursement

There should be a backup plan for additional financing should the second round not be able to generate sufficient funds.

This financing model is admittedly a radical idea that would have to be checked legally, but there are many obvious benefits to having a diverse investor pool like this, not the least of which would be an engaged, knowledgeable group from which to raise additional funds at a later stage, if necessary.

In fact, one way of enhancing that ability would be to manage an in-house share trading program whereby shareholders that perceive a higher future value of their shares could buy shares from those less optimistic. Share concentration would increase and the investor pool would shrink but the base would be so wide to begin with that some loss of investor diversity could be tolerated. In fact, arguments could be made that an ideal investor pool should consist of no more than several hundred individuals whereas the initial investor pool might be considerably larger. Nevertheless, strict limits on investor concentration should be maintained. The upside of this share trading platform would be a more optimistic and energized investor pool that would be more willing to repeatedly invest in the enterprise as it progresses.

14.3. Management Structure

The proposed management structure of the Commercial Entity is designed to allow it to most ef-

fectively operate within the internal and external business environments described above.

14.3.1. Advisory Board

An Advisory Board should be formed consisting of five or six individuals with the combined range of expertise necessary to perform strategic and some senior management functions as well as major long term decision making. They should all be given equal equity positions in exchange for advisory duties. Modest salaries might be considered for some Board members that are expected to contribute additional time. One of the Board members should be the Managing Director, who would also receive a full salary. The Board should meet no fewer than twice a month, probably more often in the early stages. The role of the Advisory Board would be crucial during the phase of product development prior to the start of formal operations.

The main areas of expertise that would need to be covered by Board members are:

- I. Conceptualization – Big picture perspective, long term vision, lateral thinking
- II. Genetics – Concepts, global trends, technology, human and technical resource analysis
- III. Informatics – Statistical analysis and presentation, data manipulation
- IV. Health Care Management – Structural knowledge, resource capabilities/limitations, medicine
- V. Finance – Financial structures, compliance,

taxation, cash flow management

VI. Internet Company Management – Hardware and software, programming, internet site development, data management

It is not meant that there must be a one to one relationship between these areas of expertise and individual Board members. There should be overlap and combined expertise.

The main functionalities of the Board should be:

- I. Strategic planning
- II. Global trend analysis
- III. Key relationship management
- IV. Policy planning
- V. Financial structural integrity
- VI. Regulatory compliance
- VII. Public Relations

14.3.2. Managing Director

The Managing Director, responsible for day to day operations and also a member of the Advisory Board, should be someone with experience running internet startups, preferably science related ones. From a day to day operating perspective, the Commercial Entity in the model resembles an internet startup more than any other kind of company. The integrity of data management and control will be a critical function of the Managing Director.

The Managing Director must also have human resource management experience and skills as he/she will be primarily responsible for hiring staff

and creating a productive working environment.

14.3.3. Company Employees

The main broad areas of expertise that will need to be covered by personnel are:

- I. Informatics (bioinformatics and information systems)
- II. Genomics
- III. Marketing/Sales
- IV. Finance

The specific functionalities that will have to be covered would be (in alphabetical order):

- I. Accounting
- II. Cash flow management
- III. Compliance
- IV. Genomic data analysis
- V. Literature research
- VI. Logistics management
- VII. Marketing strategy
- VIII. Product design
- IX. Sales
- X. Sales trend analysis
- XI. Systems management
- XII. Website design (content and presentation)

As with the Board, it is not meant that each functionality should be individually staffed by a single

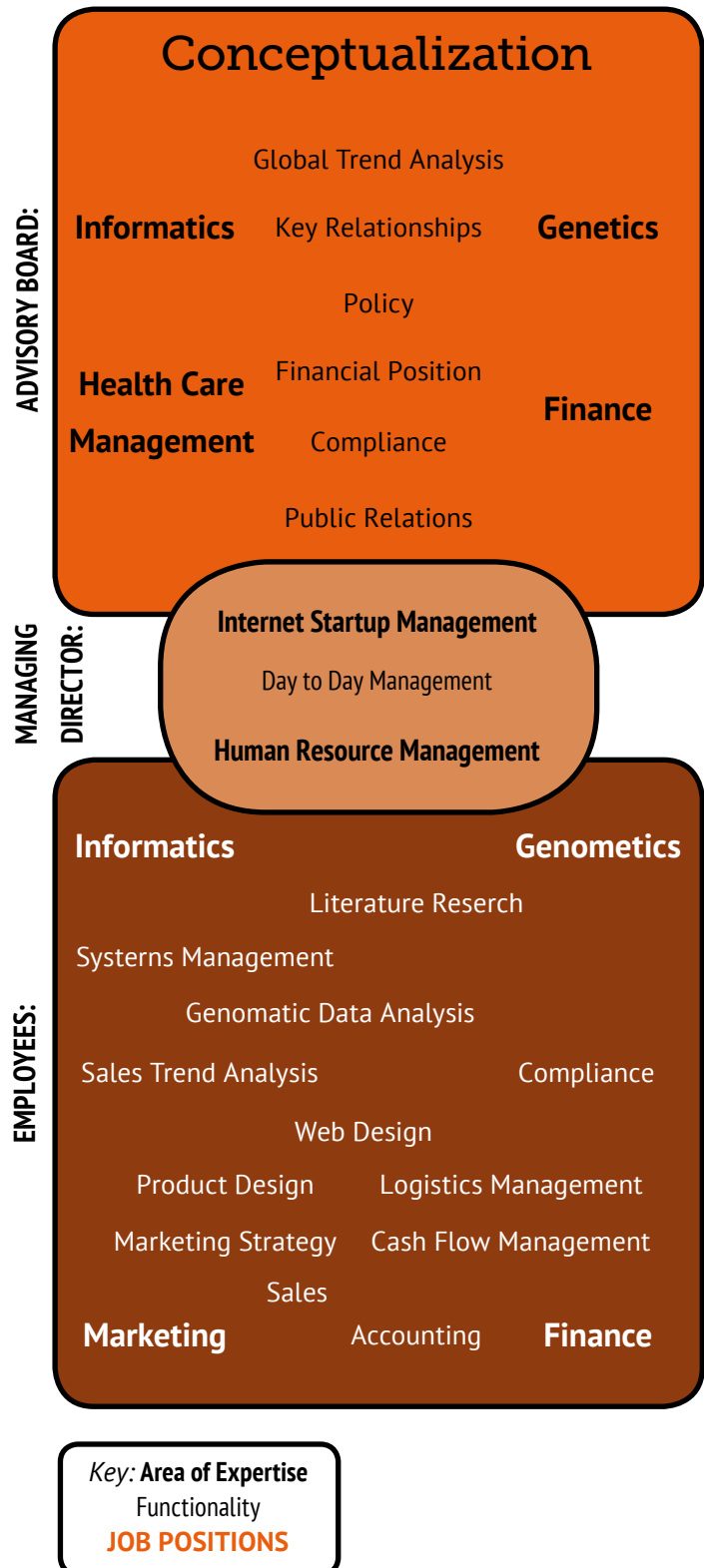
employee. Considerable effort should be made to hire employees with diverse skills and to cross functionalize job descriptions, although there will be some natural divisions.

In the beginning, if the budget doesn't allow for a full complement of staff, some of these functionalities can be outsourced.

All employees should be given a small ownership position in the company (upon completion of a probation period) which provides them with profit sharing compensation in addition to salary. The cumulative employee ownership position (not including Advisory Board members) could amount to as much as 20-30% of total equity. This will build loyalty and reduce the likelihood of inter-disciplinary rivalry.

14.3.4. Organizational Expertise and Functionality Chart

The following chart illustrates the placement of expertise and functionalities required for the Commercial Entity. In the Employee box, functionalities have been placed in positions according to degree of relatedness to the four main areas of expertise in the corners.



14.4. Retained Outsourced Functions

A number of functions required by the Commercial Entity should be outsourced to specialized firms on a retained basis. Eventually, it may become cost effective to incorporate some of these functions into the company.

14.4.1. Legal Representation

In addition to usual matters of business establishment, the Commercial Entity will need legal representation in order to evaluate potential liabilities related to the accumulation of personal information. This will be required from concept evaluation and product development through to ongoing operations.

Interpretations offered by the Commercial Entity will be acted upon by practitioners and in some cases, due to the complexities of human biology, outcomes will not be as desired. The Commercial Entity will need to be adequately protected from potential legal challenges in this regard.

14.4.2. Market Research

Market research should be an ongoing activity of the Commercial Entity in terms of analyzing sales patterns and assessing feedback from the practitioner community and from direct customer contact. But assessing broad public reaction to the business model and to its promises of value would be more difficult for the Commercial Entity to accomplish in an unbiased manner.

A market research firm should be retained to perform this function. It would be primarily required during the phase of product development, but an assessment of public opinion should be performed periodically as deemed appropriate.

14.4.3. Advertising

The Commercial Entity should formulate its own target market definitions and messaging objectives but should employ an advertising agency to create content, make recommendations on ad placements, and submit evaluations of effectiveness. The two entities should work closely in the development of content to ensure that messaging tactics are in line with objectives.

14.4.4. Distributors

As discussed in Section 13.5, the Commercial Entity would need to establish distribution partnerships and employ point of sale facilitators in order to establish wide geographical access to the product.

In all cases of outsourced distribution, close monitoring of vial inventory would have to be maintained and some training of outsourced staff would have to be conducted.

14.4.5. Public Relations

Due the potentially high degree of public exposure this business model would be expected to generate, the company should employ public relations expertise. Due to the diverse, unpredictable,

and potentially immediate nature of the needs for this function, it would make sense to employ a public relations firm that has broad capabilities rather than to rely entirely on internally developed capabilities.

That said, senior management should always retain public relations awareness when engaging in strategic decision making and public relations expertise should be consulted regularly.

15. Implementation Process

The following is a list of the key steps that should be undertaken to bring the business model into reality, from concept adoption to product launch.

15.1. Selection of Development Committee

A group of four or five individuals with the skills required to accomplish the tasks necessary to bring the business model from concept to reality should be assembled, perhaps under the auspices of TCELS. The criteria for selection should be roughly as was outlined for the Advisory Board in section 14.3.1. TCELS should also appoint several employees to act as support staff.

The responsibilities for each member should be clearly assigned, as should the relationship that each member will or could have with any future entity that might be. This group could eventually become the Advisory Board for the Commercial Entity, although some mechanism for addition to and/or elimination from the Board should be defined.

Committee members should meet at least bi-weekly.

15.2. Completion of Formal Business Plan

A complete implementation ready financial busi-

ness plan should be completed by or under the auspices of the Development Committee.

Provided that adequate resources are made available, this should take no more than two months.

15.3. Discussions with Relevant Government Institutions

The Development Committee should prepare a carefully considered plan for approaching the relevant institutions. It is assumed that these institutions for discussions related to the public sector subsidy in exchange for the metadata.

The Development Committee should enter into discussions with these institutions with a proposed structure of funding and cooperation and a clear metadatabased assertion of short, medium, and long term benefits that will accrue from the business model for each institution. Specific opportunities for research should be proposed and the means by which metadata could be analyzed to identify health care policy initiatives should be described. The goal of these discussions should be to reach broad agreement between all parties on

funding and structure in the form of a Memorandum of Understanding (MOU).

This process could run concurrently with the preparation of the formal business plan, although it might be expected to take longer to finalize.

15.4. Registration of Company

Provided that a satisfactory MOU is obtained, a Commercial Entity should be registered with the Development Committee members (presumably) as management principals.

15.5. Initial Seed Financing

At this stage, an initial injection of capital will be required to fund the next several steps. The Capital and Equity Model outlined in section 14.2.3 should be employed to do so. The conditions of the share offering, in terms of share block sizes, time limitation, and total capital to be raised should be based on the specific needs of the company at this stage of development.

It's difficult to estimate how long it would take to reach the predetermined capital requirement, but if the amount is set at no more than two or three million Baht, which should be more than enough to move the project ahead, it might occur very quickly, especially if some minimal promotion accompanies the launch of the seed capital website.

15.6. Preparation of Tentative Product Design

Tentative product module designs should be constructed for the initial purpose of conducting

market research. This will require intensive literature searches and must result in the selection of markers for sequencing, decisions on how marker sets should be compiled and converted into useful standardized conclusions, and decisions on how these conclusions should be presented in webpage format for customers.

This could be accomplished using existing bioinformatics and genomics expertise under various government Ministries, by issuing grants for graduate students, by hiring external bioinformatics consultants, or any combination of the three. The cost for this would be covered by the initial seed financing. It would not be required to have the content generating algorithms developed at this stage, only the presentation formats.

This effort should be as concentrated as possible (all individuals should be working full time) with the aim of it taking no longer than four months. The process should be organized and ready to start by the time enough seed financing is received.

15.7. Market Research

Once mock product designs are ready, they should be test marketed for public acceptance/resistance and pricing point viability by a market research firm. A Thai owned market research firm, At Vantage, has been contacted by the Consultant and has responded with a two module proposal. Module 1, priced at 345,000 Baht conducts qualitative research and module 2, priced at 300,000 Baht, conducts quantitative research. Both would be worth doing and the cost would be covered by the initial seed financing.

Both modules have 8 week timelines and they could be performed concurrently.

15.8. Agreement with Government Institutions

Provided that the business model generally, and the requirement for government subsidy specifically, is validated by market research, a more formally agreed arrangement with the relevant public institutions will be required. The formula for the calculation of the subsidy and the administrative procedures for generating it will have to be agreed and all of this will have to be committed contractually with the Commercial Entity.

This should be an outcome prompted by the receipt of market research validation and should emerge from the process of ongoing discussions with the relevant government institutions.

15.9. Second Round of Financing

A second round of financing will be required at this stage to raise enough capital to bring the company into operation and to an expected point in time where sustained positive cash flow generation can be achieved. If the first round of financing using the seed funding website proved successful, the same mechanism should be used for the second round.

It is anticipated that the second round would be larger than the first in terms of capital to be raised, size of share blocks, and number of investors. Investors from the first offering should be given limited access priority to acquire shares in the

second round before the offering is opened to others. Shares purchased in the first round should be increased in value as a reward to first round purchasers for having assumed the risk of early stage investment.

There should be a backup plan for additional financing should the second round not be able to generate sufficient funds.

Key positions necessary for the initial phase of operations, the period between second financing and product launch, should be hired. These would include people involved in product development, website design, marketing strategy, infrastructure development, and financial management.

15.11. Purchase of Assets

Office space and physical equipment should be purchased.

15.12. Product Refinement

Using the insights gained from the market research process, in-house genomics, bioinformatics, information systems, and website design personnel should work towards producing a final product. This will involve final selection of markers for each of the modules, translation of raw genomic data into useful categorizations, the creation of written and graphical presentations, development of content generation systems, and website/webpage design.

15.13. Logistical Infrastructure

Physical procedures such as the moving around of vials and samples as well as procedures of data handling should be implemented and tested. Test samples should be sequenced at the lab and brought into full webpage presentation mode for process evaluation.

15.14. Marketing Plan

A detailed marketing plan should be finalized.

For marketing to the general public, printed materials will need to be prepared, advertising space booked, messaging and public relations positions considered, and distribution partnerships negotiated. For marketing to clinical settings, practitioner communities should be engaged and educational methods and materials prepared.

Marketing efforts have been placed somewhat arbitrarily in this location on the time line. In fact, full engagement would have to begin right after the second round of financing and conducted co-incidentally with all other activities. Indeed, development and implementation of marketing initiatives would be an ongoing function.

15.15. Full Complement of Employees Hired

By this point, it should be relatively clear what additional employees will be required for product launch and they should be hired.

15.16. Soft Launch

The soft launch is a partial introduction of the product into the market. A subset of the target market segments should be selected for initial approach and narrow marketing campaigns should be deployed and a selected subset of the clinical target markets should be engaged. Only a limited distribution of saliva vials to select locations would be initiated and advertising should be limited to online presentation.

15.17. Testing and Adjustment

The period between soft launch and hard launch would be a time of intensive measurement of the results of the processes that have been introduced into the market and feverish work to repair failures and deficiencies. This could take anywhere from several months to a year or longer in the event of catastrophic failure.

15.18. Hard Launch

After management is confident that the bugs in the system have been worked out, a hard launch should be scheduled, accompanied by the desired press releases, media coverage, and promotional events. Marketing and distribution would presumably start to roll out towards full implementation at this point and the company would hope to move quickly into normal operations mode.

16. Conclusion

The general consensus among health care experts is that personal genomics, as a concept to be broadly applied in health care regimes, does not provide enough demonstrated efficacy to be widely adopted. It is believed that while some highly predictable clinical outcomes related to genetic characterization have been established, cumulatively they don't yet justify the implementation of a broad spectrum testing regime from a cost-benefit perspective.

Proponents of this view argue that more research resulting in high probability predictive ability will be required before a broad spectrum personal genomics approach should be widely adopted. They claim that the value propositions of personal genomics are too weak.

From an immediate clinical, patient centric, perspective, it is hard to disagree. Most individual patient needs are probably currently best served by targeted genetic tests for specific purposes where clinical utility has been well established.

It has been argued here, however, that a broader perspective should be considered; that other value propositions in addition to cumulative clinical utility should be counted. These additional sources of value, discussed throughout this business model proposal, can be reduced to two categories:

- I. Demonstrated and expected value of meta-data from genomic sampling depth
- II. Immediate and future clinical and non-clinical value that will emerge from knowledge transfer

When the value, to the research and health care planning communities, of metadata compiled from a very large database of Thai partial genomes is considered, along with the value, to consumers and institutions, of information compiled and communicated are considered, the prospects of a broad spectrum personal genomics platform look much better.

The business model described in this report has been constructed with these additional sources of value very much in mind. The following features of the model have all been incorporated precisely to facilitate the creation of value in these categories.

- I. Institutional integration
- II. Public-private cooperation
- III. Public subsidy in exchange for the metadata
- IV. Distributed interests
- V. Genetics portal philosophy
- VI. High profile marketing campaign

To fully appreciate how value is created from these features, however, one needs an adopt mindset informed by complex system and information network dynamics. One needs to recognize how the synergies and feedbacks that emerge from highly interconnected systems translate into value, even if the precise nature of the value is impossible to quantify or even to anticipate in advance. One needs to accept and embrace the Big Data paradigm.

Indeed, if this personal genomics model or something similar to it is to be implemented in Thailand, it will require that the politically motivated and publicly funded institutional regimes involved in genetics research and health care provision accept this perspective. They must adopt a long term perspective of value and consider a deep, broad spectrum personal genomics database to be a public investment in Thai health care. Achieving this will admittedly be a daunting challenge.

But conceptually, this Consultant is convinced that the model would generate impressive results in a myriad of ways throughout the health care system. Whatever the model lacks in immediate clinical utility is more than compensated for by the totality of value it would generate systemically and in anticipated future clinical value. There would be many challenges, as identified throughout the report, but they all have solutions that can be applied provided that enough resources are committed to the project. Therefore, it is asserted that if political and institutional buy-in can be achieved, the process for implementation of the model could possibly begin immediately.

The main potential impediment to immediate implementation, other than political, would be economic. It remains to be determined whether the model could generate enough revenue from sales volume to become financially sustainable. Is the model economically viable? The opinion of this Consultant, based on partial cost information, is that the answer would be either yes or almost but not quite. Therefore, it is recommended that a detailed financial analysis be performed to assess economic viability.

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