

Sciona

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July 20, 2006

I. Company Background

Sciona was formed in the United Kingdom in the summer of 2000 with the goal of bringing the benefits of the Human Genome Project directly to the consumer. The initial meeting that led to the formation of our company was held on June 26, 2000, coincidentally, the day that former president Bill Clinton and British Prime Minister Tony Blair announced that the first draft of the human genome was now complete. At this initial meeting, the cornerstones of the philosophy of Sciona were laid down:

- **The knowledge resulting from the enormous public and private investment should be used to benefit the average person on the street**
- **Each member of the public should be able to learn directly about his or her own genetic information**
- **The goal of the company is to use the information to provide health care information focused on health and wellness, rather than treatment of illness**
- **It is the duty of the company to deliver this information in an ethical and responsible manner**

Sciona decided to focus on the growing body of knowledge of the impact of genetic variation on response to dietary and environmental factors. This was a deliberate decision to focus on health and wellness based applications, and to focus in an area in which there was a significant body of research that substantiated the links between dietary and environmental factors and genetics. Our goal in founding the company was to use the power of genetic information to help people maintain their health, a fundamental change from disease management based health care.

The founders of Sciona believed that delivering information directly to the consumer was an essential step in helping to drive this change toward using genetics to support health and wellness. Sciona became the first company in the world to provide this type of genetic information and advice, and so as the pioneers in this field, we felt a duty of care to provide a service that was credible,

scientifically-based, ethical, and which maintained the highest standards of privacy protection. The founders of Sciona worked to make every aspect of the business meet best practice, with the goal of establishing standards for what is now a rapidly growing industry, to ensure protection of the individual consumer.

To ensure that our company conformed to the highest standards, we engaged the services of top leaders in the field:

- **Ethics** – before the first product of Sciona was developed, we worked extensively with a highly respected Ethics consultant from the Ethox group in Oxford, United Kingdom. This consultant reviewed the first products that were developed by Sciona, and provided invaluable feedback on the language that was used, and how the information was communicated. Sciona funded a PhD project to examine the ethical and societal implications of genetic testing. Sciona also participated in an extensive review of emerging biotechnology companies with a focus on ethics, entitled *Bioindustry Ethics* by D. Finegold, C. Bensimon, A. Daar and others, published by Elsevier in 2005. We have subsequently used consultants based in North America, and have recently completed the formation of a formal Ethics Advisory Board. Sciona has been highlighted as a company that has established ethics as the necessary foundation for any company in genomics in recent press articles.
- **Privacy Protection** – the original founding team of Sciona included experts in computer software and internet security, so we were able to build an infrastructure that provided the highest degree of protection for the safeguarding of each individual's personal and genetic information.
- **Scientific Review** – Sciona has a Science and Business Advisory Board, with leading experts in the fields of gene-diet interactions, also referred to as nutrigenomics and/or nutrigenetics, as well as industry leaders in health care and food industry. The board has reviewed our products, our publications, and our research and development projects extensively.

II. Sciona's Products and Services

Sciona offers a nutritional lifestyle information service directly to the consumer. Sciona does not manufacture, produce or sell dietary supplements or any other food-related products, nor does the company obtain any revenue from sales of products from any of our commercial partners. Our business activities are solely based on the provision of nutritional lifestyle information. Our information service consists of the following:

1. The consumer purchases a kit, containing cheek cell collection swabs, a Lifestyle Questionnaire, and a return mailer envelope, through a variety of distribution channels, including health care practitioners, internet, direct sales agents, and pharmacies.
2. The kit is designed for the consumer to use in the privacy of his or her own home. The individual uses the cheek swabs to collect cells from the inside of his cheek, then fills out the Lifestyle Questionnaire, and returns the swabs and questionnaire to Sciona. The questionnaire includes a consent form, which must be signed by the individual before the samples can be processed. Also note that individuals must have reached the legal age of consent in the country of origin, usually 18 years of age, for the sample to be processed. Sciona does not process samples from children.
3. Samples are received by Sciona, and the personal data from the questionnaire is recorded as well as the bar codes on the sample tubes containing the cheek swabs and on the questionnaire.
4. The sample tubes which have no personal identifying information on them, simply a bar code, are then delivered to the independent laboratory which carries out the genetic analysis for Sciona on a contract basis.
5. The questionnaire is scanned by Sciona. The questionnaire output is put into an electronic file, which is merged with the electronic data output from the laboratory. These two data sets are matched by the bar codes. The information is then delivered via secure electronic means to Sciona's proprietary Rules Engine, which produces a report for each individual. The report is delivered either directly to the individual or to the individual's health care practitioner, if the individual has so requested by signed consent.

Sciona Report

Sciona's nutritional advisory report in its current product configuration includes information on 19 genes, 24 variations in these genes and 18 particular nutritional and lifestyle factors. The report has been written in language that is intended to be easily understood by the consumer; however, technical information such as the exact genetic variation has been included so that individuals or health care practitioners can refer directly to the genetic information if required. The report describes how the interaction of these genes and nutritional factors can play a role in different areas of health; including heart

health, bone health, antioxidant and detoxification function, inflammation, and insulin sensitivity. Many of the 19 genes have an impact on more than one of these health areas, so this information is also shared with the consumer.

Each of the 19 genes selected for the current product has a clear gene-diet or gene-environmental relationship that has been demonstrated in peer-reviewed scientific publications. Gene-environmental relationships may include physical activity, body mass index, or tobacco smoking. Each gene may play a role in more than one of the areas of focus for Sciona's nutritional advisory report.

Each of the 5 health areas that is covered by the current report includes the following elements:

- Table with genes and variations identified
- Action map graphic element combining genetic profile with nutritional analysis
- Bar graphs in which the individual's current estimated nutritional intake is measured against a goal intake of nutrients

Finally, the report contains a section with additional tips and advice on where to find rich sources of particular nutrients and how best to prepare foods to maximize the nutrient value of these foods. Sciona does not sell any products in connection with the report.

Looking into more detail on the health areas covered and the nutritional and environmental relationships, the report consists of information on the following areas:

Heart Health: This section of the report focuses on 14 variants of 13 genes, which have a role in the following:

- Lipid metabolism - responsive to saturated fats and cholesterol in the diet
- B-vitamin metabolism and homocysteine remethylation - responsive to levels of B vitamins in the diet
- Antioxidant function and inflammation - responsive to levels of antioxidants, omega 3 fatty acids, tobacco smoking, and physical activity
- Vascular tone - responsive to physical exercise, omega 3 fatty acids and smoking

Bone Health: This section of the report focuses on 7 variants of 4 genes, which have a role in the following:

- Calcium and Vitamin D absorption - responsive to dietary calcium and dietary vitamin D plus exposure to sunlight, smoking and caffeine consumption
- Bone structure and remodelling - responsive to omega 3 fatty acids

- Overall bone integrity - responsive to Body Mass Index (BMI) and physical exercise

Antioxidants and Detoxification: This section of the report focuses on 7 variants of 6 genes, which have a role in the following:

- Phase II detoxification - responsive to dietary allium and cruciferous vegetables
- Antioxidant function - responsive to levels of antioxidants in the diet and tobacco smoking
- Nitric oxide generation - responsive to omega 3 fatty acids and smoking

Inflammation: This section of the report focuses on 7 variants of 6 genes, which have a role in the following:

- Pro-inflammatory cytokine production - responsive to omega 3 fatty acids
- Antioxidant function and phase II detoxification - Responsive to levels of antioxidants in the diet, dietary allium & cruciferous vegetables and smoking
- Overall inflammatory profile - responsive to BMI

Insulin sensitivity: This section of the report focuses on 6 variants of 5 genes, which have a role in the following:

- Levels of insulin secretion and glucose release into the blood stream - responsive to dietary glycemic load
- Glucose and lipid metabolism - responsive to dietary glycemic load and ratio of unsaturated to saturated fatty acids in the diet
- Sensitivity of cells to insulin - responsive to dietary omega 3 fatty acids
- Vascular flow - responsive to physical exercise and BMI

These reports do not diagnose any disease but are focused on nutritional and lifestyle status to promote general health and wellness.

Sciona Rules Engine

Each report that an individual receives from Sciona is generated by a proprietary software system developed by the Research & Development Team at Sciona, in collaboration with a bespoke software development company, Solcom, Ltd. The software consists of a series of algorithms in which genetic variations are scored according to their biological impact and the resulting genetic score is put together with nutritional analysis from the Lifestyle Questionnaire provided by each consumer. Then the Rules Engine provides the integrated information in the form of visual feedback, as well as instructional language to help the consumer make nutritional and lifestyle choices. The software architecture is a Microsoft SQL relational database, into which genetic and other data for each individual is delivered by secure electronic methods. The output of the rules engine is a

locked pdf file which cannot be altered electronically, together with CSV (comma separated variable) files and log files which are used for quality control purposes and customer tracking information. Reports are delivered to a secure printer for production, and the electronic files are encrypted and stored on physical medium, with multiple layers of encryption to ensure maximum security of information. The rules engine is currently being validated to GAMP4 standards (Good automated manufacturing practice, a quality standard for software functionality), with completion expected in approximately 3 months time.

Scientific background

The Sciona nutritional lifestyle information service has been developed through an extensive survey of peer-reviewed literature from the fields of nutrition research, biochemistry, epidemiology and molecular biology, and the genes which have been selected have had to meet our internal selection criteria:

- a. The gene-diet or gene-environmental relationship must have appeared in multiple reports in credible, peer-reviewed journal articles.
- b. The genetic variation cannot be a rare form found in less than 1% of the population
- c. There must be some nutritional or environmental factor which has been shown to have an impact on the effect of the genetic variation

In order to build upon the knowledge available in the public domain, Sciona has invested in collaborative research with academic groups interested in exploring gene-diet and gene-environmental relationships.

Research collaborations:

University of Southampton, UK:

The influence of genes on the ability of Vitamin E supplements to reduce inflammation in healthy people and patients with rheumatoid arthritis.

University of Reading, UK:

Study 1: Examine the impact of genotype on fasting and postprandial lipid metabolism and vascular function and on responsiveness to fish oil fatty acids in pre- and post- menopausal women.

Study 2: Examine the impact of fasting and postprandial lipid metabolism in both men and women.

Micro2DNA:

Integrated polymer-based micro fluidic micro system for DNA extraction, amplification, and silicon-based detection for point of care genetic testing

and information use by health care practitioners. EU/FP6 - Specific Targeted Research Projects (STREP)

University of London School of Pharmacy:

PhD project to examine ethical and regulatory implications of genetic testing.

University of Portsmouth:

Genetic predisposition to cytokine-mediated fatigue in ultra-endurance athletes and chronic fatigue syndrome patients

III. Sales and Distribution of Sciona's Products

Sciona's nutritional advisory service is sold and marketed through a variety of distribution partners:

1. Health Care Practitioners
2. Pharmacies
3. Direct Marketing Organizations
4. Internet Distribution

Through its distribution channels, Sciona sells kits containing the cheek cell collection swabs and questionnaire, Sciona orchestrates the processing of the samples, and produces the personalized advisory kits.

IV. Quality

The laboratory work for Sciona is outsourced, and the company maintains close scrutiny on the results and performance of the laboratory testing supplier. Each batch of samples which are run by the supplier includes a set of blinded controls supplied by Sciona for processing. The supplier is not aware of the nature of the blinded samples, and so when the results are supplied back to Sciona, these blinded controls are used as a measure of reproducibility and reliability of the laboratory results. The laboratory supplier also uses internal controls chosen by the supplier, and pass/fail criteria have been set in which both internal supplier controls and Sciona blinded controls must be in concordance before any set of results is cleared for report production.

V. Conclusion

Sciona is safely, effectively and ethically providing important genetic information to consumers concerning their nutritional well-being, contributing to their health and wellness. Sciona is not involved in diagnostic or disease-related services or information. Sciona believes that the nutritional genetic information provided can best assist consumers if it is available to the consumer through direct access to the service.