Novel Platforms for Genetic Analysis: An Assessment of Rapid, Portable Diagnostic Devices

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Pioneered simultaneously in Denmark and the United States in the early 1990s, consensus conferencing is a relatively new tool for consulting the public on a wide range of issues. A consensus conference involves members of the lay public and gives them the central role in assessing a problem area. Participants rarely have subject expertise that is directly relevant to the topic being explored and contribute by making their views known in the form of concerns, values, and everyday experiences. The underlying purpose of a consensus conference is to provide a means by which ordinary (lay) members of society can be involved in a purposeful way in making their views known to regulators, industrial actors, scientists, and politicians.

Consensus conferencing often involves an examination of science and technology issues and is seen as a way to reinvigorate democratic decision making by including the public "upstream" in the development of science and technology, rather than after-the-fact. Additionally, it is a tool for building trust and for creating a more open and transparent dialogue.

In Canada, consensus conferencing has been used previously to explore topics like genetically modified foods, plant molecular farming, and blood safety. Other countries have used consensus conferencing on topics like nanotechnology (USA), telecommunications and teleworking (USA and Denmark), national electricity policy (Switzerland), and radioactive waste management (UK). Consensus conferencing is about building consensus. Since consensus refers to "general agreement," the results of a consensus conference are a record of group decisions, and represent positions and recommendations that participants can "live with." It is therefore fundamental to the success of a consensus conference that the process for getting to a certain degree of general agreement occurs in an environment which promotes inclusivity, participation, cooperation, egalitarianism, and a willingness to be solution-oriented.

The purpose of a consensus conference is to produce an informed debate on a limited subject and to produce statements and recommendations that reflect the nature of the deliberations. As such, this document reflects the views of 22 adult Canadians from coast-to-coast, and across all age ranges. Participants were selected in one of three ways: (1) responses from a series of advertisements in the *Globe and Mail* newspaper, (2) random digit telephone recruitment using quota sampling, and (3) "snowball" sampling to fill in demographic gaps. In general, participants were non-specialists who were motivated to understand the importance of the issues, and were not meant to reflect a perfectly random assortment of Canadians.

The topic of this consensus conference was the development of rapid, portable, low-cost diagnostic devices. Such devices are being developed in many parts of the world, and utilize micro-fluidics, electrical fields, micro-scale pumps, and fluorescence technologies to analyze biological samples including blood, urine, water, etc. Such devices have been called various names including "micro-fluidic platform technology" and "lab-on-chip technology." These devices, and the glass and silicon chips that are used with them, will provide "point of care" and "point of concern" testing that may usher in a new age of testing and monitoring.

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This technology brings the functionality of a large-scale laboratory down to the size of a hand-held unit which can perform diagnostic testing, meter, measure and mix samples, move mixtures to temperature-controlled chambers, and separate and analyze results. By taking advantage of favourable scaling properties and a small footprint, this technology promises to improve the availability of diagnostic and genetic testing, environmental monitoring, and several other clinical and non-clinical applications. Clearly, such technology has many risks and benefits associated with its use, and also raise a range of socio-economic and ethical issues.

Based on a New Emerging Team grant provided by the Canadian Institutes of Health Research (CIHR) entitled "Novel Platforms for Genetic Analysis," and led by Dr. Linda Pilarski from the Cross Cancer Institute and the University of Alberta, a team of researchers is developing a "made in Canada" version of this technology. Dr. Michael Mehta of the University of Winnipeg has conducted a series of public engagement exercises since 2003, with this consensus conference being the final stage.

The following report includes the recommendations and observations of participants in this consensus conference regarding this technology. The report is divided into two sections: (1) clinical applications, and (2) non-clinical applications.

It is expected that the report will form the basis for future public engagement on this topic, and it is hoped that policy makers, politicians, regulators, scientists and others will consider these carefully thought out recommendations. There is much richness and reflection in them, and they represent the product of a consensus process that could act as a model for future deliberations on the development of new scientific innovations in general.

CLINICAL GROUP

Recommendation 1

We recommend that the Government of Canada support this technology for the "public good," and that all reasonable efforts should be made to develop and deploy this technology in the developing world.

The group had lively debate on the risks and benefits of this technology. Opinions were strong and sometimes anchored in personal experiences. Eventually a general consensus was formed based on the need to maximize the benefits of this technology while minimizing risks. Several questions were raised, such as:

- Who defines "public good"? Which "public" is being referred to?
- How far should Canada commit to developing this technology domestically?
- How far should Canada commit to supporting this technology in developing countries?
- Which Government of Canada departments should take the lead?

Recommendation 2

We recommend that the general public be educated on this technology, and that they be consulted on specific applications of this technology.

The group reached consensus that the general public should be consulted on specific applications of this technology. The group felt that the public would need to be educated (e.g., on terminology, the technology itself, applications, and various social, ethical and economic issues) in order to maximize their engagement and contributions to the consultation process. It was clear from the discussion that participants felt that members of the general public should not be marginalized from such discussions since the public has a vested interest in this technology and its applications. Participants felt that the consultation process needs to be ongoing as the technology evolves. Participants also felt that Canadians would be ready, willing and able to participate in the public consultation process. In short, they believed that the public has a right to be heard and that Canadians have a duty and obligation to contribute to determining how to implement this technology.

Recommendation 3

We recommend ongoing review in a systematic way of the social considerations of applications of this technology.

The group reached consensus that the technology was going to continue to evolve and that issues would continue to emerge over time. Participants did not believe that public consultation of social considerations was a one-time endeavour, but rather that the government should continue to consult the public on a regular and ongoing basis. The group identified a range of social considerations flowing from the use of the technology. These included:

- Environmental Concerns: The group felt strongly about the potential impact of this technology on the environment. The disposal of these devices (and chips) was perceived to be a significant issue and discussion focused on designing this technology to be recyclable. It was felt that this was an important issue that needs to be addressed early on in the development of this technology.
- Environmental Benefits: The group supported the use of this technology for monitoring environmental pollutants.
- Veterinary Testing: The group felt this technology could provide benefits to animals as well as humans and that research on veterinary applications should be supported.
- Quality, Accuracy, and Reliability: The group raised concerns about the quality and reliability of the technology and the results flowing from its use, and felt that there should be work on minimum standards ("gold standards"), which should be approved and regulated by government.

Recommendation 4

We recommend that provincial and territorial governments re-examine curricula in primary schools, secondary schools, colleges and universities with the view of including more comprehensive education in issues of science, technology and society. Moreover, dedicated resources should be provided to increase Canada's capacity in the area of genetic counselling.

The group recognized the need to provide support to the various sectors of the educational systems across Canada so as to ensure that citizens have an opportunity to learn about science and technology.

The group felt that it was particularly important to focus on education in genetic issues (including counselling), both for individuals to make their own decisions and for trained counsellors to assist others. The group felt that the technology was far more sophisticated than most people's current knowledge level and that this gap would continue to widen as the technology evolves.

Recommendation 5

We support the use of this technology as a diagnostic tool for early detection and effective, cost efficient treatment of illnesses.

The group reached a general consensus that using the technology for the early detection of "illness" would be a positive application on several levels. However, there was far less consensus on how to define "illness," what "illnesses" should be prioritized for testing, and who should make such decisions.

The discussion focused on cancer detection and this provided a useful framework for thinking about and debating multiple dimensions at a general and conceptual level. The group agreed that early detection of cancer is optimal. This was true of some other illnesses as well, such as viruses and childhood maladies like the measles. Less clear was how to think about and define "illness" that results from the passage of time and life itself, such as aging.

The group discussion revealed that more analysis is needed on how society defines "illness" and how causes are interpreted. For example, lung cancer from smoking was viewed differently than a rare form of pediatric brain tumor. The group acknowledged the complexity of the connections between health and illness, prevention and treatment, genetic vs. non-genetic conditions, and environmental factors. They also realized that some normative issues, such as labelling certain genetic conditions as an "illness" (e.g., dwarfism), have profound social implications.

It was of utmost importance to the group that the results of genetic testing be interpreted by highly skilled and knowledgeable genetic counsellors and that they are skilled in helping patients cope with whatever results are transmitted.

The topic of cost efficiency generated a great deal of discussion. The group was concerned about the rising cost of health care in Canada and reached consensus several times that cost efficiency should be a priority. The group recognized the large expenditures associated with developing this technology and tended to view the investment as a needed trade-off for long-term benefits. The group also recognized that priorities for developing this technology need to be established. In essence, discussion on this recommendation centered around two key terms, "diagnosis" and "illness." Several ancillary issues were folded into these terms, such as the certainty/uncertainty of developing a particular genetic condition given its presence in a person's genes. Here the line of discussion shifted from "detection" (which might have been a better term to use), to "diagnosis" (which the group tended to relate to certainty of gene expression), to a person actually developing a particular condition, and finally to intervention.

Recommendation 6

We support the use of this technology by accredited, regulated health care professionals with support systems in place for patient counselling.

The group reached consensus that the technology should be used in a health care context by "accredited," "regulated" health care professionals. The group debated the notions of "accredited" and "regulated" in terms of appropriate certification and governance, mainly from the point of view of what agencies should be responsible for testing and regulation. There was no clear solution or direction suggested but the general opinion was that some minimum level of knowledge of genetics and genetic counselling should be required. The issue of concern was not technical skill in administering the test or in handling the technology itself, but rather on how to interpret the results flowing from a test. A clear consensus was reached that support systems must be in place for patients who receive genetic testing information (especially if the news is unwelcome). The group was concerned about people receiving unwelcome news and being left with little follow-up information and interpretation on prognosis, treatment, etc. It was of utmost importance to the group that the results of genetic testing be interpreted by highly skilled and knowledgeable genetic counsellors and that they are skilled in helping patients cope with whatever results are transmitted. It was noted that our current health care system is not well equipped to handle this. The group felt this was a priority that needed to be addressed simultaneously with the implementation of the technology. The group felt that physicians (general practitioners in particular) could not fill this role adequately.

Recommendation 7

We support the use of this technology for personalized medical treatment, pharmacogenetics, and ethically approved clinical trials (with patient consent).

The group reached consensus that the technology should be implemented for personalized treatments in two main areas: (1) cancer and other illnesses, and (2) proactive preventative intervention. With respect to the former, the group felt that personalized cancer treatment is desirable. They felt that the technology could contribute to this by, for example, analyzing the genetic fingerprint of a cancer tumor and facilitating tailor-made treatment of patients. This would not only benefit the patient and his/her recovery and quality of life, but may also minimize suffering and the costs for treatments that are not effective. The group also felt that personalized treatment for proactive preventative intervention to maintain and/or improve health and well-being is appropriate. The group felt that a person should be able

to act on such information and thereby take control of their own health and well-being. In a related vein, the group reached consensus that random samples (e.g., blood, tissue, etc.) that are taken from patients could be used for the purpose of scientific research, as long as patients consented to this. The group discussed what the parameters for consent might be, such as using excess material taken from patients. The group tended to feel that anonymity should be sufficient to allow such uses to occur.

Recommendation 8

We support the mandatory use of this technology for managing pandemics.

The group reached consensus that mandatory use of the technology was justified in the event of a pandemic and that people should be required to be tested whether or not they agree. The feeling of the group was that preventing or managing a devastating pandemic supersedes the rights of people to (1) decline testing, (2) claim ownership of their sample or information, or (3) refuse to consent to the use of their sample or information. The group felt that samples, tissues, etc. gathered in a clinical setting could undergo testing and that the technology may aid in effectively dealing with an emergency situation.

Recommendation 9

We support the use of this technology for testing for predispositions towards developing diseases so as to assist in the early intervention and ongoing monitoring of individuals.

The group reached consensus that the technology should be used in a preventative fashion to test for possible or potential health problems that may emerge. The consensus was based on the group agreeing to the notion that people are responsible for their own health and well-being. They should therefore be able to obtain not only their genetic information, but also information about the ongoing status of their health, which should allow them to make informed choices about life-style changes, etc. that will improve their quality of life and/or prolong their health and life. The discussion included topics like monitoring cholesterol levels, heart function, blood pressure, etc. The group viewed these notions very positively and, in addition to improved health and quality of life, saw them as cost-effective uses of technology that could prevent people from accessing the healthcare system as frequently.

Recommendation 10

We recommend that this technology be made available in non-traditional environments as long as it is used in the presence of accredited healthcare personnel and that testing is voluntary.

The group reached consensus that the technology has a role in the boundary spanning area of non-traditional environments and debated which environments might be acceptable. The group tended to view "non-traditional" environments as those outside of the traditional clinical setting of a hospital, doctor's office, or clinic. Non-traditional environments were identified as drugstores and kiosks, for example. In this environment the group felt that accredited healthcare personnel were an essential part of testing and that the technology could be made available if genetic counselling services were provided. The group tended to see the technology and counselling/interpretation as two sides of the same coin with one having to accompany the other.

Boundary spanning environments included corporate settings with, for example, a company nurse. This environment was thought to be particularly important because of the possibility that people would be required or coerced into testing as a condition of employment, job performance, or benefit coverage. The group reached clear consensus that testing in non-traditional or boundary spanning environments must be completely voluntary with no repercussions upon refusal. The main issues to the group were who would have access to a person's information and how could such information be used against a person (even if they had consented to the test).

Recommendation 11

We recommend that this technology not be used for predetermination of heritable characteristics such as sex, eye color, skin color, or, potentially, intelligence.

The group reached clear consensus that they did not recommend that the technology be used for any purpose related to creating "designer babies." This line of discussion had a decidedly ethical and moral tone, and participants seemed to feel that it was wrong to use the technology for these purposes. This was seen as tampering with nature or usurping the role of the Creator. The group *failed to reach consensus* on using the technology on fetuses to test for potential non-life-threatening conditions. Group members were divided on

this point, with some opining that it would be positive because it would make intervention possible. Others felt that the technology should be used for life-threatening conditions only.

Recommendation 12

We recommend that the technology only be used under conditions of voluntary consent and that authorized approval for use of test results occur with full disclosure about the purpose of the test and possible end uses of the information.

The group's final recommendation focuses on the use of data in terms of confidentiality, privacy, and consent issues. In essence, the group felt that patients own their health information, tissues, and samples. The group raised questions about access to information and potential misuses or abuses. This led to a discussion of regulation and governance, and the group recognized the complexity and enormity of this topic. The group was particularly concerned about insurance companies obtaining personal information.

NON-CLINICAL GROUP

The non-clinical group recognized that their role was to identify issues that extended beyond the doctor's office or other clinical settings. However, there was much discussion in this group that did address clinical areas due to the overlap of many of the key issues.

The following is a "brainstorming list" of the non-clinical applications that the group identified and discussed:

- Biological monitoring of bodies of water and air sheds for environmental contaminants;
- Testing well water (e.g., e-coli);
- Soil testing;
- Indoor moulds, asbestos, or other indoor air quality testing;
- Veterinarian diagnostics, treatments, and care;
- Conservation, disease detection in wildlife, and species differentiation;
- Testing for BSE ("mad cow disease") and other transmissible animal diseases;
- Food safety and quality (e.g., pesticide detection), detection of additives, nutritional composition;
- Testing for genetically modified organisms;
- Pet food safety;
- Military uses (e.g., sensors for detecting biological weapons or bioterrorism);
- Forensic applications at crime scenes and referencing with data banks;
- Blood typing and monitoring of blood products for infectious agents;
- Anthropological and genealogical research, or racial profiling;
- Personal testing ('home kits') for paternity, genetic diseases, viruses, prenatal conditions, adoption, and sexually transmitted diseases;
- Private sector uses:
  (1) genetic testing for insurance purposes, the establishment of premiums and eligibility;
  (2) genetic testing for employment purposes, potential denial of health plan coverage or other benefits, or denial of employment due to genetic pre-dispositions; and
  (3) pharmaceutical company access to genetic data for drug development and private genetic clinics;
- Public sector uses:
  (1) mass testing for managing pandemics (e.g., avian flu, SARS), and;
  (2) potential testing uses in nursing homes, schools, shopping malls, public transit sites, etc.;
- Health monitoring in non-clinical settings such as outer space, and remote field stations.

Recommendation 1

We support the research, development, and use of this technology for the following reasons: portability, ease of use, reduced cost, rapidity of testing and results, and applications for broad usage around the world to provide socio-economic benefits.

The group recognized the value of pursuing the development and implementation of this technology, and emphasized the following items in a "SWOT Analysis."[1]

Strengths

- Low-cost and widely available diagnostic and predictive aspects of technology are worth pursuing
- Promotes a holistic view of medicine (e.g. links between human health and environment)
- Potential to protect public health by minimizing the spread of diseases by air travel, etc.
- Forensics: requires less biological material and produces more immediate results
- Could be used to build vaccines sooner for emerging pathogens

Weaknesses

- Potentially large disconnect between diagnosis and treatment
- Forensic (and other) data could become too widely available or misused

Opportunities

- Implement the "precautionary principle"[2] early to develop technology responsibly, sustainably, and with appropriate regulations (e.g. no unregulated use of genetic material)
- Pre-emptive and proactive uses for public health purposes
- Agricultural (e.g. water, plant, animal) testing opportunities

Threats

- Non-consensual use of existing human samples and databases
- Security opportunities (e.g. border security) become a threat with overzealous use
- Inappropriate use, abuse, or sale of genetic information to private interests

It should be noted that the first recommendation came with several cautions, as the group was concerned about the potential misuse of this technology. The recent sequencing of the human genome in particular has heightened concern about genetic research in general. The group discussed this at great length and acknowledged that this technology may present specific challenges to privacy, confidentiality, autonomy, and public trust.

The group agreed that because genetic materials are the building blocks of life, genetic information deserves special consideration and protection above and beyond other confidential information (such as identity, financial, or criminal records). The group therefore felt that a special governance framework is required in order to assure the public that this technology will be appropriately regulated and that personal information will be not be inappropriately acquired or used.

The group also discussed issues surrounding possible rewards or punishments for genetic status (e.g. discrimination based on just the possibility of future health or disease) and posed questions like:

- How does one define disease when genetic information is probabilistic in nature?
- What implications might this bring with respect to the ways in which people regard their fellow citizens?
- Who would control this information?
- Will this further lead to the commodification of the human body?

There was also considerable discussion about the fear that this technology could be used to enable eugenics.

Recommendation 2

Privacy and confidentiality must be protected in clinical and non-clinical applications of this technology, both in public and private settings.

The group recognized that privacy and confidentiality issues will be of great importance in the use of this technology, and indicated that the following issues should be considered:

- Privacy must be protected: this is a critical governance, public trust, and confidence issue;
- In whose hands will information end up and whether this is this acceptable?;
- A concept of a gatekeeper is important;
- Disclosure and freedom of information; a patient's right to know their own information;

- Provision of testing services, not outside medical/counselling supervision
- Clinical settings, with counselling, support and proper interpretation of test results being important
- Public health emergency/civic duty with regard to access and confidentiality.

The group shared an overall lack of confidence in our society's ability to safeguard the personal information of its citizens. There were concerns expressed with respect to whose hands this technology will wind up in and, in whose interest will the information be used, and who is an acceptable body with which to store or keep this information. Examples of trustworthy entities might be:

- Medical professionals
- Individuals being tested
- University researchers

There was also much discussion around the public/private sector divide and how there is little trust in either sector. That said, private sector access to personal information was considered to be even more controversial than government access. Finally, the group was curious about how the *Personal Information Protection and Electronic Documents Act*[3] could protect people from genetic "theft" and protect personal health information in general.

Recommendation 3

The principle of voluntary choice, autonomy and informed consent must be respected by all users of this technology.

The group was clear with respect to this recommendation and stated that voluntary participation is a key issue, as is both access to and disclosure of information. However, the group acknowledged that in certain emergency circumstances, public health issues might supersede such rights. Consensus was reached on the following points:

- When it comes to human genetic testing specifically, mandatory testing should not be allowed
- Voluntary choice, autonomy and informed consent must be honoured

There was a great deal of discussion regarding concerns about mandatory testing by insurance companies and employers, where individual consent becomes especially problematic. Who, ultimately, can determine who is tested or if testing should be done?

Recommendation 4

We oppose mandatory, non-voluntary uses of this technology by employers and other private sector actors.

Recommendation 5

With the exception of overriding public health concerns, we oppose the mandatory, non-voluntary use of this technology by government.

The group discussed the fact that government departments are both regulators and promoters of new technologies, pointing to concerns about conflict of interest. The group expressed the need to be cautious about public trust, leading to the need for good governance models, gatekeeper systems, and expert decision-making panels. Although no specific recommendation was formulated, the group identified that Canada needs a new regulatory agency to, for instance, make decisions about non-clinical uses of the technology. This agency would also have a role in preventing the misuse/abuse of the technology and protecting both privacy and freedom of information. The question of whether there should be no unregulated use of genetic material was raised. The group felt that both clinical and non-clinical genetic testing must be regulated, especially with regard to insurance and employment usage. In either setting, a key issue arises: who would assume responsibility (liability) for erroneous test results? Given the potential for misinterpretation and current lack of appropriate professional counselling and health service delivery, the group concluded that this technology should not be made immediately widely available to the general public. Especially in the case of human genetic testing, the technology should be restricted to health professionals only. However, the group concluded that other applications may be pursued in the near future.

Recommendation 6

Research and development be furthered to promote use of this technology in the following non-clinical areas: ecosystem monitoring and protection, animal diagnostics and care, food monitoring and safety, air and water quality.

In the realm of human testing, the group recommended that the ultimate aim of the technology should be for the greater good of society, including the developing world.

Recommendation 7

This technology should be developed and made available to vulnerable populations in a socially and culturally responsible manner.

Recommendation 8

This technology should be developed using a multi-pronged public consultation strategy that will have "real" impact on public policy and decision-making.

The group expressed that input from a large cross section of society should be sought when informing the societal decision-making process around this technology. Inclusive grassroots stakeholder input was thought to be valuable, as well as input from business, government, and other interest groups. There is a need to prioritize early applications in order to ensure the greatest success with the fewest problems and carefully regulate the dissemination of this technology. Equally important, the group felt that intra- and inter- disciplinary research should be encouraged, and that broad public dissemination and consultation are essential.

Recommendation 9

Educational strategies around this technology (and other emerging technologies) must be developed. There is a need for the development of provincial curricula at all levels.

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Endnotes

1 A "SWOT Analysis" is a strategic planning tool used for identifying strengths, weaknesses, opportunities, and threats.

2 The precautionary principle asserts the following: in the absence of scientific certainty, reasonable measures should not be delayed if the costs of not acting may be significant.

3 S.C. 2000, c. 5