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# Walking the tightrope: expectations and standards in personal genomic susceptibility testing (PGST)

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# Overview


23andMe


Navigenics®


deCODEme


PATHWAY GENOMICS™
The Value of Knowing

# Regimes of truth/regimes of hope

- Expectations help shape technological development
- And articulate discursive "regimes of truth" with "regimes of hope"[1]
- How does "what we know" relate to "what we can do"?
- PGST as an example: what is the value of a risk profile?

> "When confronted with the question of what one does when confronted with a probability statement, the absence of an obvious response allows the probability statement to harden into a reified statement of fact."
>
> *K. Sunder Rajan (2006)* Biocapital: the constitution of postgenomic life, *p. 168*

1. Brown, N. 2005. Shifting Tenses: Reconnecting Regimes of Truth and Hope. *Configurations* 13(3).

# PGST: a story of contested expectations

## Commercial uncertainties

- Regime of hope or regime of hype?
- Scepticism about clinical validity and clinical utility
  - Predictive power
  - Heritability of complex disease
  - Contribution of genetic risk not generally significant
  - Gene-gene interactions
  - Missing heredity …

overclaiming

## Regulatory uncertainties

- Are PGS tests medical devices?
  - Federal Food, Drug, and Cosmetic Act, Section 201[h]

- Regulatory action
  - Reclassification
  - Product requires pre-market approval

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# Strategies of standardisation

- PGST companies have promoted standardisation as a regulatory strategy
- Standards channel power
  - Allowing regulatees to help reshape regulatory terrain
  - Consolidating some future visions and not others[1]

Navigenics®

1. Clinical Validity
2. Analytical validity
3. Clinical relevance
4. Actionability
5. Access to genetic counselling
6. Security and privacy
7. Ownership of genetic information
8. Physician education and engagement
9. Transparency
10. Measurement

1. Rashba, E. and D. Gamota (2003). "Anticipatory Standards and the Commercialization of Nanotechnology." *Journal of Nanoparticle Research* 5(3): 401-407.

# 2008: Clinical validity and scientific standards

- Concerns about clinical validity
  - Quality of GWAS databases used by companies[1]
  - Divergences between risk scores from different companies for the same condition[2]
- PMC-sponsored working group on standards (June-December 2008)
  - Focus on risk modelling methodologies
  - Ran aground on differences between model assumptions

> "[...] we just couldn't get the three companies to agree on the standards, on what's real and what's science."
>
> *Navigenics interview*


1. Janssens, A. C. J. W. et al. 2008. A Critical Appraisal of the Scientific Basis of Commercial Genomic Profiles Used to Assess Health Risks and Personalize Health Interventions. *The American Journal of Human Genetics* 82(3), pp. 593-599.
2. Fleming, N. 2008. Rival genetic tests leave buyers confused [Online]. London: Times Newspapers. Available at: http://www.timesonline.co.uk/tol/news/science/article4692891.ece

# 2008-2009: From clinical utility to new regulatory objects

- Regulatory objects define *what matters* about a technology
  - E.g. shift from minimum lethal dose to median lethal dose in drug regulation[1]
- A parallel strategy – redefine regulatory objects for standardisation
  - Clinical usefulness
  - Personal utility
- Collaboration with regulatory agencies, e.g. NIH & CDC
  - Seminar held in December 2008
  - Reported in 2009[2]

REVIEW

The Scientific Foundation for Personal Genomics: Recommendations from a National Institutes of Health–Centers for Disease Control and Prevention Multidisciplinary Workshop

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**Abstract:** The increasing availability of personal genomic tests has led to discussions about the validity and utility of such tests and the balance of benefits and harms. A multidisciplinary workshop was convened by the National Institutes of Health and the Centers for Disease Control and Prevention to review the scientific foundation for using personal genomics in risk assessment and disease prevention and to develop recommendations for targeted research. The clinical validity and utility of personal genomics is a moving target with rapidly developing discoveries but little translation research to close the gap between discoveries and health impact. Workshop participants made recommendations in five domains: (1) developing and applying scientific standards for assessing personal genomic tests; (2) developing and applying a multidisciplinary research agenda, including observational studies and clinical trials to fill knowledge gaps in clinical validity and utility; (3) enhancing credible knowledge synthesis and information dissemination to clinicians and consumers; (4) linking scientific findings to evidence-based recommendations for use of personal genomics; and (5) assessing how the concept of personal utility can affect health benefits, costs, and risks by developing appropriate metrics for evaluation. To fulfill the promise of personal genomics, a rigorous multidisciplinary research agenda is needed. ***Genet Med* 2009:11(8):000–000.**

**Key Words:** *behavioral sciences, epidemiologic methods, evidence-based medicine, genetics, genetic testing, genomics, medicine, public health*

The accelerated discovery of genes for common diseases fuels expectations that genomic information will become an integral component of personalized health care and disease prevention.[1,2] Several companies now offer personal genomics

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1. Porter, T. M. (1995). *Trust in numbers: the pursuit of objectivity in science and public life*. Princeton, Princeton University Press: pp. 206-207.
2. Khoury, M. J., C. M. McBride, et al. (2009). "The Scientific Foundation for Personal Genomics: Recommendations from a National Institutes of Health-Centers for Disease Control and Prevention Multidisciplinary Workshop." *Genetics in Medicine* 11(8): 559-567

# Growing uncertainties 2009-2010

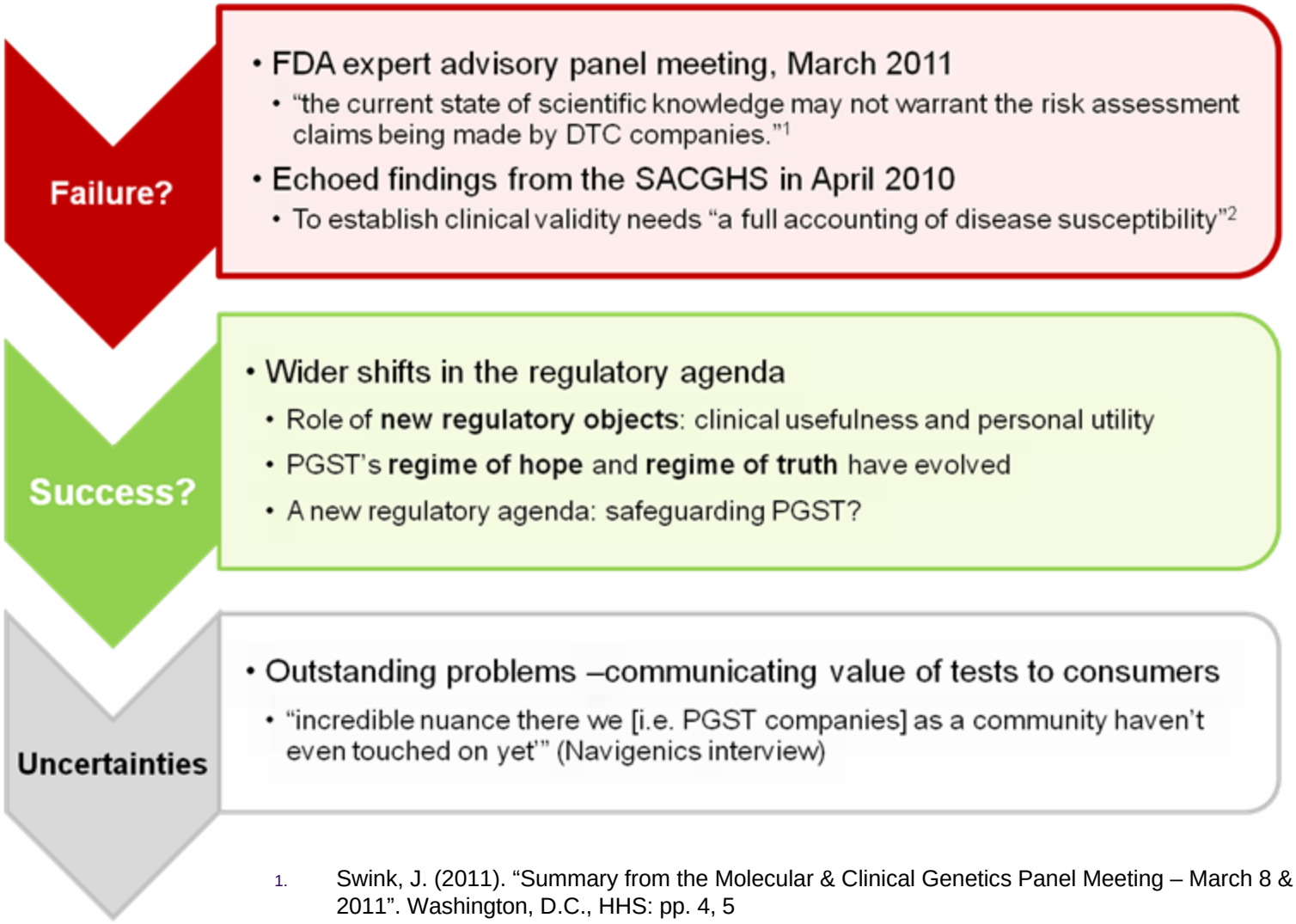
- Companies offered tests for more clinical conditions (e.g Tay-Sachs, CF)
  - 'clearly the claims [PGST companies] are making are medical claims'[1]
- July 2009: Pathway Genomics launched
  - Product shaped by uncertainties about clinical validity
- Pressure from regulators
  - Walgreens controversy, FDA letters, Energy & Commerce Ctte hearings

" [...] there's no real good validated argument that [...] if you have this gene you have a higher chance of getting breast cancer, for example. We just don't think that there's clinical evidence to support that, without all the other data behind it. So we just decided to kind of not get in that business of giving hard risk data."

*Pathway interview*

1. Carmichael, M. 2010. "DNA Dilemma: The Full Interview With the FDA on DTC Genetic Tests". Available at: http://www.thedailybeast.com/newsweek/blogs/the-human-condition/2010/08/05/dna-dilemma-the-full-interview-with-the-fda-on-dtc-genetic-tests.html

# Standardisation: strategic failure or success?




1. Swink, J. (2011). "Summary from the Molecular & Clinical Genetics Panel Meeting – March 8 & 9, 2011". Washington, D.C., HHS: pp. 4, 5
2. Secretary's Advisory Committee on Genetics Health and Society (2010). *Direct-to-Consumer Genetic Testing*. Bethesda, HHS: p. 24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