Testimony Of David Ewing Duncan Before The Secretary's Advisory Committee
On Genetics, Health, And Society
Session Of Personal Genome Services

Personal Genomic Informaton:
A Consumer's Perspective

July 8, 2008

Good Morning And Thank You For Inviting Me To Speak And Share Some Of My Experiences And Thoughts On The Topic Of Personal Genomic Testing.

I Am Here This Morning Wearing Three Hats. The First Is As A Journalist And Writer Covering The Science And Policy Aspects Of Biotechnology And Life Sciences. I Also Am The Director Of A New Program At The University Of California At Berkeley Called The Center For Life Science Policy That Launches This Fall, And Will Join Programs In Science, Business, Law, The Humanities And The Media To Cover Issues And Analyze A Range Of Policy Topics On This Topic.

Finally, I Am A Consumer Of Genomic Information Websites As Part Of An Endeavor Called The Experimental Man Project. This Is A Book That I'm Writing And An Educational Effort At Uc Berkeley That Includes A Website, Panels And Lectures, White-Paper Research Projects, And Seminars For Students.

The "Experiment" In The Experimental Man Project Is To Participate In And Analyze A Wide Array Of New Tests That Are Becoming Available To

Essentially Predict, Or Attempt To Predict, The Future Health Outcomes Of A Healthy Individual.

For The Book And Project, I Have Had Myself Extensively Tested For Not Only Genomic Information Tucked Inside Me, But Also Data On The Impact Of My Environment – Sun, Diet, Chemical Toxins – Along With Scans And Other Tests Applied To My Brain And To My Body. The Idea Is To Humanize The Science By Using A Real Person And His Family To Describe The Technologies, And To Assess Their Usefulness In These Early Days Of Personalized Medicine.

The Project Is An Expansion Of Two Articles I Wrote – One In Wired Magazine, In 2002, When I Was Tested For Several Hundred Genetic Markers; And In National Geographic, In 2006, When I Was Tested For Levels Of 320 Environmental Chemicals Inside Me.

Since Primordial Times Most Of Medicine Has Primarily Focused On Diagnosing And Treating The Sick And The Unhealthy. Now, For The First Time, Technology Is Allowing Humans To Delve Into Our Inner Workings To Gather Information On What May Lie Ahead In This Field Called Personalized Medicine.

As A Human Guinea Pig, I Embarked On The Experimental Man Project Under The Supervision Of My Personal Physician At The Univeristy Of California At San Francisco, Who Confirmed That I Am A White Male, 50 Years Old In Good Health, According To The Current Standard Of Care, With No Real Indications Of Pending Maladies, Though My Cholesterol Was Slightly High. I

Also Come From A Mostly Healthy Family That Lives A Long Time, Often Over 90 Years Old.

The Committee Has Asked Me To Answer Several Questions About My Experiences As A Consumer Of Genomics, Which I Am Pleased To Do In These Written Comments. I Also Am Happy To Answer Further Questions That The Committee Might Have. I Have Added One Additional Question, Which Inquires Which Tests I Took And My Results.

These Questions Can Be Broken Down Into Three Categories: Expectations, Tests And Results, And Reactions And Thoughts.

Under The Headline Of “Expectations” I Was Asked: “What Were Your Reasons For Pursuing Personal Genome Services?”

I Had Three Primary Reasons. One Is As A Journalist And Communicator Seeking The Best Method For Describing A Science That Is Complex And Often Eye-Glazingly Abstract For Non-Scientists To Grasp. Perhaps More Important Is A Vehcle To Report On The Implications Of The Science For Commerce, Law, Politics Abd Regulation, Privacy, The Health Care Industry, And Individuals. A Closely Related Reason Is Curiosity, In This Case About The Technologies And Information An Individual Might Learn About Genomics. This Is A Classic Early Adopter Profile: The Type Of Consumer Who Bought An I-Phone In The First Couple Of Months. A Third But Admittedly Less Important Consideration For Me Was That I Might Discover An Unexpected Insight About My Future Health, And Who I Am.

The Next Question Asked By The Committee Is: “What Sort Of Information Did You Anticipate Receiving From These Services?”

Given The Newness Of The Science And Its Power To Offer Insights To Individuals I Had Rather Low Expectations That I Would Learn Anything Significant About My Health. Mostly, I Expected To Receive Confirmation That I Am Essentially Healthy, And That My Family Is Healthy – With One Exception I’ll Explain In A Moment. I Am In That Category Of Patient That Doesn’t Think About Or Worry Much About Getting Sick. This Is In Contrast To Advisers On The Project That Might Be Termed “The Worried Well.’ One Of These Is A Prominent Geneticist And Author Who Told Me That He Would Never Get A Genetic Test He Didn’t Have To. “I’d Be Too Nervous That I’d Find Out Something Terrible,” He Told Me.

The Next Set Of Questions, About Tests And Results, Is Where I Will Spend The Bulk Of My Presentation Before Getting To My Reactions At The End.

For The Experimental Project, I Have Had About 1.5 Million Genetic Markers Tested, Mostly Single Nucleotide Polymorphisms (Snps). These Are Single Letters In Human Genetic Code – The Familiar G, C, T And A – That Vary From Person To Person, And Account For Many Of The Differences Among People. Having An A, For Instance, Rather A G Might Mean That I Have A Higher Risk Of Getting Diabetes, Or That I Will Have Blue Rather Than Brown Eyes. I Have Had Tests Run To Identify Places In My Genome Where I Might

Have Deletions Of Genetic Sequences, Or Insertions, Or Copies That Probably Shouldn't Be There. The Snps, Insertion, Deletions And Copy Number Variations Were Run On Genomic Array Chips Made By Illumina And Affymetrix, With A Few Tests Run On Other Custom Chips. Individual Labs And Companies Have Sequenced A Number Of Complete Genes, And I'm Hoping Later This Year To Have My Entire Genome Sequenced.

A Number Of Genomic Testing Services Have Run My Tests And Offered Analysis, Including Companies, University Researchers, And Others. Some Of These Tests Are Not Yet Available To Consumers.

My Journey Into My Genomic Self Began In 2001 With The Original Tests Run For The Wired Story Published In 2002. I Emphasize This In Part Because Many Of The Tests That Remain Controversial Today Were Available Seven Years Ago, Such As Apoe-4 For Alzheimer's Disease And A Number Of Genetic Tests For Cancers And Heart Disease. At The Time, Sequenom, A Company Now Best Known For Making Mass Spectrometry Equipment, Even Ventured To Provide Me A Life-Score Based On About 100 Genetic Markers They Tested. This Score Was Quite Crude, As They Fully Admitted, Although I Was Happy To Hear That I Would Have A Lifespan Lasting Until I Presumably Dropped Dead At Age 88. The Bulk Of My Testing Has Come In The Past Two Years.

The Investigation Has Collectively Cost About $16,000, Although The Bulk Of The Tests Were Performed For Me Pro Bono By The Companies And Labs, Or Were Paid For By Publications That I Write For. The Cost Of Running A Full

Genome Sequence Will Boost The Total To Well Over $100,000, Though This Cost Is Rapidly Coming Down, From Over A Million Dollars Just A Year Or Two Ago.

I Am Not Alone In Participating In This Experiment. My Family Has Joined Me In Part Of The Testing – My Parents, Who Are Quite Healthy At Age 76 And 76; My Brother, Who Is 48 Years Old And Has A Wife And Two Children; And My 19 Year-Old Daughter, One Of My Three Children. The Family Was Tested On The Illumina Humanhap 1 Million Snp Array Only, And Their Results Were Run By Decodeme, Which Supported The Project By Waiving Fees That Would Have Cost The Family $4,000 Had We Paid Out Of Pocket.

This Morning, I'm Going To Home In On Three Of The Services Recently Launched That Provided Me With Genomic Testing And Analysis: Navigenics, Decodeme, And 23andme. In Addition, Decodeme Tested My Four Family Members. Details About The Three Companies Are Discussed Elsewhere In These Hearings, Though It Is Important To Note That From A Consumer Perspective, The Sites Offer Services Both Similar And Different.

One Similarity Is That All Three Companies Use Snp-Array Chips That Test Hundreds Of Thousands Of Snps, But Offer For Diseases And Traits Analysis Of Only A Few Dozen Snps, Which Are Being Added To All The Time. The Companies All Use As Sources The Thousands Of Studies Conducted And Published By Genetic Researchers In Peer-Reviewed Journals. So Far, The Companies Have Opted To Offer Mainly Common Diseases That Affect Large

Numbers Of People, Rather Than Rare Diseases. All Three Companies Offer Risk-Factors For Individual Snps Pertaining To Diseases, And Also Lifetime Risks That Combine The Risk-Factors Of The Individual Snps. For Most Customers, The Over-All Risk Factor Is The Big Number They Are Looking At To Tell Them If They Have A Higher, Lower, Or Average Risk For Celiac Disease, Colorectal Cancer, Or Diabetes.

Navigenics, Based In The San Francisco Bay Area, Focuses Exclusively On Diseases Risk Factors, Offering Results For 17 Maladies. They Provide As Part Of Their $2500 Fee Access To Live Genetic Counselors On The Phone, A Feature The Other Two Services Do Not Offer. Decodeme, Based In Iceland, Offers Results For 25 Diseases, But Also Provides Results For Traits Such As Eye And Hair Color, As Well As Results On A Customer's Genetic Ancestry. Decodeme's Parent, Decode Genetics, Is A Publicly-Traded Company That Is A World-Leader In Conducting The Scientific Studies Used By The Other Sites. Decode Also Is A Drug Development Company. 23andme Is Headquartered In Silicon Valley And Offers Results On 78 Traits, Blending Disease With A Wide Range Of Other Traits. They Offer A Rating System That Assesses Tests They Consider Preliminary, Or Verified, According To Their Own Criteria.

I Want To Mention Two Other Online Genetic Services – San Francisco-Based Dna Direct, Which Offers Only Individual Genetic Tests In Common Use By Physicians, And Caters To Customers Who Have A Family History Of Disease Or Some Other Indication, Though Anyone Can Take Their Tests. The Corriel Institute, Based Just Outside Of Philadelphia In Camden, New Jersey,

Will Launch In The Next Few Weeks As A More Academic Exercise. They Will Run A Genome-Wide Array Of Up To 100,000 People For Free, Starting With Physicians In The Philadelphia Area. They Have Convened An Independent Oversight Committee Made Up Of Scientists, Academics, Ethicists, Patient Advocates, And Others To Choose What Genetic Tests To Offer.

I Will Briefly Describe My Results For The Three Companies For Three Diseases. The First I Choose Randomly As An Example – Age-Related Macular Degeneration. [**Explain Color Codes**]. This Ailment Thankfully Does Not Run In My Family, So I Came Out With Average Or Below-Average Risk Factors Both For Individual Snps And For Lifetime Scores. The Lifetime Scores For The Three Companies Varied By As Much As 500 Percent, But The Actual Numbers Showed A Uniformly Lower-Than-Average Risk, Which Was Reassuring. The Committee Can Ask The Companies How They Came Up With Different Average Lifetime Risks For The General Population, Which Range From 1.2% To 8.0%. You May Also Want To Inquire With Navigenics Why One Of Their Snps Gave Me A 6.98 Times Higher Risk Factor, Which Is Quite High, And Seems To Contradict The Other Results. This Result Has An Asterisk Attached To It That Says: Tk. As A Layperson, I Don't Understand What This Means.

My Results For Type Ii Diabetes Also Made Me Feel Good. I Am Mostly In The Medium To Low Risk Range, With Only One Anomaly Out Of 19 Snps Tested Among The Three Companies Being In The High-Risk Category. It Is A Bit Confusing That Out Of These 19 Snps Tested For This Disease, Only Four Appear On All Three Sites. Out Of These Four, Two Gave Me Different Risk-

Scores For The Same Snp. Four Other Snps Appeared On Two Of The Three Sites, And They All Gave Consistent Results. My Lifetime Risk Scores Were Not Too Far Off For The Three Sites, With Navigenics Giving Me A 21% Lifetime Risk Of Coming Down With Type Ii Diabetes, Decodeme An 18.8% Risk, And 23andme A 16.8%. This Was A Spead Of About 4.2%, But All The Scores Made The Same Point: That My Chances Are Lower Than The Average Caucasian, Which Has A 25% Lifetime Risk.

I Have Not Done A Thorough Quantitative Analysis Of My Results Comparing The Three Sites, But I Can Offer The Following Observations:

•The Genotyping Results (Clia Lab Tests) Were Very Consistent Among 3the Three Sites (That Is, If One Site Said Gg, The Others Did, Too).

•Risk Factor Results Provided For Snps Were Generally Consistent Where The Companies Used The Same Snp, With A Few Exceptions.

•The Lifetime Risk Factors Presented By Disease Were Not Always Consistant. That Is, If There Was More Than One Snp Used For A Disease, The Results Could Vary From Low To High Risk. This Is One Reason The Companies Use Lifetime Or Blended Risk Factors, Although Having Such A Range Of Results (**Colors**) Is Confusing.

•The Lifetime Risk Factors Provided By The Sites Were Usually Consistent, With At Least One Exception For Me.

In My Data From 2001, The Only Results Worth Mentioning Were Some High-Risks For Heart Disease, Though In Those Early Days, I Could Easily Dismiss Them Because The Science Was So New And Incomplete. Seven Years Later, As I Began Checking Out My Results, I Admit To Being Slightly Apprehensive About My Heart – Particularly When A Private Test Done By Decode Genetics Before They Launched Their Decodeme Site Suggested That I Had At Least One Relatively High-Risk Genetic Marker For Heart Attack.

Imagine The Scene, Where I'm Sitting At Home Logging On To Each Of The Three Websites In Turn As They Became Available. Naturally, I Clicked First On My Heart Attack Results – Only To Find That The Three Sites Gave Me Different Results. According To Decodeme, I Have A Lower-Than-Average Lifetime Risk Of About 42% And Navigenics Gives Me A 62% Lifetime Risk. The Average Risk For A Male Caucasian Living In North America Is About 49% -- Which Means That One Site Has Told Me I Have A Lower Risk, The Other A Higher Risk. 23andme Uses A Different Method For Calculating Lifetime Risk Which I Frankly Don't Understand. They Use One Snp That Seems To Confer A Medium Risk For Me Compared To Those Who Have The Lower-Risk Variant, And Their Life Score For Me Is A Comforting 29.9%, Compared To 42% And 62%. But They List The Average Risk For A Male My Age As Being Only 17% -- Which Is Different Than The 49% Average Risk Given By The Other Two Sites, And Suggests That I Have A 75% Higher Risk Of Getting A Heart Attack Than Their Average Person – Which Is Alarming, I Think.

In Comparison, Navigenics Says I Have A 26% Greater Chance Of A Heart Attack Than The Average Caucasian, While Decodeme Says I Have A 14% Less Chance.

As A Reporter, I Have Spent Time With Each Of The Companies Going Over These Results, And I Have Some Understanding Of Why I Had Variable Results For Heart Attack. Briefly, They Seem To Have To Do With The Following:

- Different Snps/Studies Used
- Different Methods For Determining Snp Risk
  - Decodeme Uses Relative Risk
  - 23andme And Navigenics Use Odds Ratios
- Different Methods For Determining Combined Snps Risk/Lifetime Risk: Each Company Uses Its Own Formula.
- The Companies Rely On Correlative Snps That For Most People Give Similar Results, But Not For Everyone.

The End Result For Me Is A Fair Bit Of Head Scratching As I Try To Ascertain What It Means For Me.

In Articles I'm Writing About My Project And In The Experimental Man Book, I'll Be Providing Much Greater Detail About My Results, And Those Of My Family. I Will Say Here That Perhaps The Biggest Surprise In The Family Results

So Far Has Been That My Father And Brother Have A Medium-Higher Risk For Alzheimer's Disease. My Fathe Shrugged At The News, Since He Is Completely Lucid And Healthy At Age 76, And His Risk Of Alzheimer's Is Rising Anyway As He Gets Older. The News Didn't Much Bother My Brother, Either, Since We Have No Alzheimer's That We Know Of In The Family. I Wonder Though How Others Who Aren't Of Stoic Puritan Stock From The Midwest Would Feel.

[**Mention Heart Attack].**

I Would Like To Mention My Brother… Some Of The Sites Are Talking About Testing For Rare Disorders, This Is More Serious…

Non-Disease Can Be Fun, Ancestral… Preliminary Data, Not Sure What It Means…

[**Go Over Recreational]**

One Other Feature Of All Three Sites… They Provide Raw Data… Overwhelming Information, Chart 24 Feet Long…

Then Final Questions: •Did You Alter Your Behavior In Light Of Test Results? If So, How?

– One Person – Journalist, Tested On Multiple Sites

– Not Really… Subsequent Heart Test Convinced Me To Alter My Diet

– Breast Cancer Data (High Risk Snps) For Mydaughter = Closer Care

Pluses From This Consumers Point Of View --

•Insight Into Personal And Societal Health

•Personal Empowerment

•Will Push Society (And Health Industry) To Discuss Guidelines, Ethics, Education, And Funding

•Opening Up New Avenues For Research Impacting Individuals And Subgroups

•Medical And Drug Development

Minuses:

•Early Days Of Technology

•Association Studies Not Always Applicable To Individuals

•Disease And Non-Disease Results Mixed

•No Standards For Validity, Risk Factors

•Physicians Not Trained In Genetics

•Potential To Frighten

•High Costs, No Insurance (Costs Will Go Down)

Thoughts And Suggestions:

•Consumers Should Be Free To Access Their Information And Buy Services

•Encourage Discussion

•Early Adopters Should Be Part Of The Experiment – Coriell Approach, Doctor's First

•Establish Standards And Guidelines For Tests And Information – Uniform Risk Assessments, Etc.

•Who Will Pay?

•Crash Program To Set Validation Standards, Refocus On Preventive Medicine

•Disease Markers Should Be Handled Differently; Counseling Offered

•Physicians In Companies Should Review Disease Markers, Alert Consumers Of Serious Findings

•Companies Should Provide Lists Of Local Physicians And Counselors Trained In Genetics

In Conclusion, Genetics Is Just The Beginning: Genes, Environment, Brain And Body… Environmental Man Website. The Book.

Thank You Again To The Committee And Organizers For Inviting Me To Speak.