



February 18, 2014

Cellular, Tissue, and Gene Therapies Advisory Committee
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Via email: gail.dapolito@fda.hhs.gov; rosanna.harvey@fda.hhs.gov

Dear Gail Dapolito and Rosanna Harvey,

I am writing to submit a sign-on letter for review by the members of the Cellular, Tissue, and Gene Therapies Advisory Committee Meeting in preparation for the February 25-26 public meeting to discuss oocyte modification in assisted reproduction for the prevention of transmission of mitochondrial disease or treatment of infertility.

This letter was prepared by the Center for Genetics and Society (CGS) and the International Center for Technology Assessment, a project of the Center for Food Safety. Each of the 255 signatories filled out a [form](#) at the CGS website, or sent an email asking that their name be included.

Thank you for this opportunity to express the widespread concern regarding oocyte modifications that would constitute inheritable genetic modification.

Sincerely,

Marcy Darnovsky, PhD
Executive Director

February 18, 2014

To the FDA Cellular, Tissue and Gene Therapies Advisory Committee:

We are writing regarding the upcoming public meeting on “oocyte modification in assisted reproduction for the prevention of transmission of mitochondrial disease or treatment of infertility.”

We strongly believe that clinical trials of oocyte modification for mitochondrial disease (also referred to as mitochondrial replacement techniques) should not be permitted because of the profound safety, efficacy, policy and social problems they would pose. We question the ethics of bringing children into existence by experimental techniques that have had developmentally poor outcomes in studies using both animal and human oocytes. We are also concerned about the contravention of widespread prohibitions against human germline genetic modification that approval of clinical trials would represent, and about the possible precedent such approval could set for additional human germline modifications.

Scientific understanding of the complex interaction between nuclear and mitochondrial DNA, and of the role of epigenetics on an individual’s phenotypic traits, is still at an early stage. Constructing an oocyte using one woman’s enucleated egg and the chromosomes from the egg of a second woman would be an evolutionarily unprecedented experiment that is more akin to somatic cell nuclear transfer than to conventional in vitro fertilization. Noted scientists^[i] have argued that it is unlikely that such an invasive procedure could be undertaken without causing unforeseen damage. Unintended harms could manifest at any point in the lives of resulting children; subsequent generations would be at risk as well.

We sympathize with women who place a high importance on having children genetically related to them. But we note that the number of women who would be candidates for the techniques in question is quite small. While about one in 5-10,000 people suffer from mitochondrial diseases, only about 15% of mitochondrial disease is caused solely by mitochondrial DNA mutations; the rest is associated with nuclear DNA variants and how they interact with mitochondria. Oocyte modification would be of no help in these cases.

Even for the handful of candidates for this procedure, a safer alternative exists. Because women can produce eggs with varying degrees of mitochondrial mutations, preimplantation genetic diagnosis (PGD) is proving to be effective for screening embryos resulting from in vitro fertilization to identify those with low risk.^[ii]

Finally, oocyte modification should not proceed because it constitutes human germline modification. More than 40 countries, including those with the most highly developed biomedical sectors, have adopted policies on human germline modification, and all of these have prohibited it. This emerging global policy consensus has been supported by the major international biomedical and bioethical organizations and councils. We believe that it would be unconscionable for the United States to unilaterally cross this bright technical and policy line that has been observed internationally for decades.

We appreciate the distinction between the proposed techniques and attempts to control traits associated with nuclear DNA. However, many who have carefully examined these issues recognize that allowing one form of germline intervention could make it prohibitively difficult to prevent subsequent applications intended to modify cosmetic, behavioral, cognitive or other phenotypic traits. This

understanding, and the concern it raises about a new era of eugenic engineering, is the basis for the widespread agreement to forego human germline modification.

Considering and weighing the benefits of oocyte modification for mitochondrial disease to a small number of people who want a genetically related child, the existence of alternatives for them to achieve this, and the techniques' significant safety risks and profoundly disturbing societal implications, we believe that the case for maintaining the current proscriptions on human germline genetic modification is clear. We strongly urge the FDA not to allow the techniques under consideration to move to human clinical trial.

[i] See, for example, "Nuclear transfer to prevent mitochondrial DNA diseases," J Poulton, S Kennedy, P Oakeshott, J St John, *The Lancet*, Volume 368, Issue 9538, Page 841, 2 September 2006; and "Mitochondrial Replacement, Evolution, and the Clinic and," Klaus Reinhardt, Damian K. Dowling, Edward H. Morrow, *Science*, VOL 341 20, September 2013.

[ii] "Preimplantation genetic diagnosis in mitochondrial DNA disorders: challenge and success," Sallevelt SC, Dreesen JC, Drüsedau M, Spierts S, Coonen E, van Tienen FH, van Golde RJ, de Coo IF, Geraedts JP, de Die-Smulders CE, Smeets HJ., *J Med Genet*. 2013 Feb; 50(2):125-32. doi: 10.1136/jmedgenet-2012-101172.

Sincerely,

Matthew Aakre, Helena, Montana
Stacia Abe, Lake Forest, California
Joe Aboumoussa, Knoxville, Tennessee
Enola Aird, Mothers for a Human Future, Cheshire, Connecticut
Sandra Albanese, Indialantic, Florida
Joan Almon, College Park, Maryland
Heidi Alterson, Chicago, Illinois
John Amodio, Sacramento, California
Kathryn Amodio, Sacramento, California
Angela Anaya, Buffalo, New York
Marlo Anderson, Farmington, Washington
Amy Armstrong, Virginia Beach, Virginia
Brenda Asterino, Renton, Washington
Stavros Baloyannis, Aristotelian University, Thessaloniki, Greece
Talma Bar-Din, Isha l'Isha, Haifa, Israel
Eve Barna, Weston, Connecticut
Jeanin Barsamian, Princeton, New Jersey
Judy Baum, Towaco, New Jersey
Raul Bedoy, Jr., El Dorado Hills, California
Diane Beeson, Alliance for Humane Biotechnology, Berkeley, California
Emily Smith Beitiks, Paul K. Longmore Institute on Disability, SF State University, San Francisco, California
Car Beitz, Douglassville, Pennsylvania
Gomer Ben Moshe, Kibbutz Hanita, Israel
Ruha Benjamin, Boston University, Boston, Massachusetts

Michelle Bennett, Lakeside, California
S Bennett, Manchester, Tennessee
Philip Bereano, University of Washington, Seattle, Washington
Susan Berke Fogel, Pro-Choice Alliance for Responsible Research, Los Angeles, California
Clarisa Bisenius, Sherwood, Oregon
Andrew Blye, Midland, South Dakota
Edward and Jewell Bode, Jefferson City, Missouri
Nancy Boicourt, Hillsboro, Oregon
Deborah Bolnick, University of Texas at Austin, Austin, Texas
Denise Bowers, Defiance, Ohio
Raymond Boyd, Blackfoot, Idaho
Martin Bradshaw, Decatur, Illinois
Patty Brady, Chadds Ford, Pennsylvania
Michele Brill-Edwards, Children's Hospital of Eastern Ontario, Ottawa, Canada
Ariele Brooke, El Cajon, California
Judie Brown, American Life League Inc., Stafford, Virginia
Jenna Brunnen, Winnipeg, Canada
Christine Brunner, Duncannon, Pennsylvania
Jo Burns, Marco Island, Florida
Kenneth Carder, Chapin, South Carolina
Alana Cattapan, Dalhousie University, Halifax, Canada
Archie Caughell, Fresno, California
Sheila Cavalet, Weirton, West Virginia
Eva Charles, Bentonville, Arkansas
Emily Choge, Moi University, Decatur, Georgia
Michelle Clark, Barnstead, New Hampshire
Francine Coeytaux, Pro-Choice Alliance for Responsible Research, Los Angeles, California
Mary Colling, Liverpool, New York
Joseph Collura, Auburn Township, Ohio
Maria Collura, Auburn Township, Ohio
Steven Coots, San Antonio, Texas
Mary Corcoran, Flagstaff, Arizona
Myrna Cosby, Charlotte, North Carolina
Sandra Crago, Havana, Florida
Robyn Croix, Corona, California
Lane Crouch, Mount Juliet, Tennessee
Austin Cruz, Missouri City, Texas
Melissa Curley, Virginia Beach, Virginia
Jessica Cussins, Center for Genetics and Society, Berkeley, California
Gwen D'Arcangelis, Alhambra, California
Marcy Darnovsky, Center for Genetics and Society, Berkeley, California
Liz Day, Rehoboth, Massachusetts
Donna L DeHart, Wasilla, Alaska
Daisy Deomampo, Fordham University, Bronx, New York
Michael DeSaye, Washington, District of Columbia
Donna Dickenson, University of London, Oxford, United Kingdom
Susan Didriksen, Placerville, California
Sharon DiPiazza, Seffner, Florida

Paul Dobrowolski, Saline, Michigan
Donna Domzalski, Pineville, Louisiana
Rena Drabant, Newman Lake, Washington
Justine Durrell, Alliance for Humane Biotechnology, San Rafael, California
Carol Edwards, Gateway Community College, Niantic, Connecticut
George Elliott, Virginia Beach, Virginia
Desiree Engel, Bothell, Washington
Jill Escher, Escher Fund for Autism, San Jose, California
Joan Eukitis, Loxahatchee, Florida
Hedva Eyal, Isha L'Isha, Haifa, Israel
Lizabeth Farrell, Spokane Valley, Washington
Rachel Finley, Corpus Christi, Texas
Kim Fix, Newman Lake, Washington
Gabriella Foe, New York, New York
Ryan Foley, Cumming, Georgia
Suzie Frei, Spokane, Washington
Sarah Freiboth, Oconomowoc, Wisconsin
Alexander Gaguine, Appleton Foundation, Santa Cruz, California
Charles Garzon, Center for Genetics and Society, Berkeley, California
Mary Gentry, Olney, Maryland
Mary Gonsior, Minneapolis, Minnesota
Megan Gray, Frederick, Maryland
Debra Greenfield, UCLA Institute for Society and Genetics, Los Angeles, California
Gina Gresch, Otis Orchards, Washington
Robert Griffin, Canal Winchester, Ohio
Isai Guido, Sunnyvale, California
Kathleen Hamlon, Lincoln, California
Matthew Hamrick, Virginia Beach, Virginia
Nancy Hansen, Port Orchard, Washington
Jaydee Hanson, International Center for Technology Assessment, Washington, DC
Wendy Hartl, Medford, Wisconsin
Mary Hathaway, North Augusta, South Carolina
Dave Hawes, Midlothian, Virginia
Richard Hayes, University of California, Berkeley, California
Diane Heath, Bend, Oregon
AnnaMarie Hemingway, Spokane Valley, Washington
Greg Hertfelder, Kansas City, Missouri
Elizabeth Hilton, New Haven, Connecticut
Erin Hodorff, Lola, Wisconsin
Norbert Hoog, Zeschdorf, Germany
Donna Hores, Annandale, Virginia
Gloria Hyder, Omaha, Nebraska
Linda Jack, North Bend, Washington
Anne Jackson, Gig Harbor, Washington
Tammy Jed, Livonia, Michigan
April Jennings, Orlando, Florida
Gygi Jennings, Yale University, New Haven, Connecticut
Elisabeth Jess, Batavia, New York

Jonathan Kahn, Hamline University School of Law, St. Paul, Minnesota
Ilona Kajokiene, Mykolas Romeris University, Vilnius, Lithuania
Eunice Kamaara, Moi University, Eldoret, Kenya
Dana King, Lawrence, Kansas
Kathleen Kittilstved, Spokane, Washington
Teresa Knode, Richardson, Texas
Dr. Heike Knops, Ev Kirche, Uedem, Germany
Jon Knowles, Oakland, California
Stephen Korsman, Cape Town, South Africa
Wendy Kramer, Donor Sibling Registry, Nederland, Colorado
Bernadette Ku, Brooklyn, New York
Emily Kunkle, Delanson, New York
Madalyn LeBlanc, Shreveport, Louisiana
Trudo Lemmens, University of Toronto, Toronto, Canada
Donald Light, Harvard University - Center for Ethics, Cambridge, Massachusetts
Darla Lindenmayer, Moms Who Have Mito Kids, Charlestown, Indiana
Abby Lippman, McGill University, Montreal, Canada
Douglas Long, Indianapolis, Indiana
Brenda Lowe, Brooksville, Florida
Mark Lulgjuraj, Shelby Twp., Michigan
Calum MacKellar, Scottish Council on Human Bioethics, Edinburgh, United Kingdom
Marlene Mantey, Dryden, Michigan
Gina Maranto, University of Miami, Miami, Florida
Laura Martin, Houston, Texas
Elvia MartinDelCampo, El Paso, Texas
Barbaar Massey, Newport News, Virginia
Denise Maxwell, Saint Marie, Montana
Steve May, Fund for Genetic Equity, Cohasset, Massachusetts
Cynthia Mazelin, Westfield, Indiana
Bess McAneny, DE Pro Life Coalition/DE Nurses for Life, Newark, Delaware
Melissa McCall, Emmett, Idaho
Noelle McCusker, Evington, Virginia
David A. McElhannon, McAllen, Texas
Sherri Mcgrath, Manassas, Virginia
Robert McIntyre, Trenton, Michigan
Philip McManus, Santa Cruz, California
Sam Mellon, Albuquerque, New Mexico
Jared Mercier, Hollywood, Florida
Aimee Metzinger, Sacramento, California
Animas-Rafael Mijangos, Eljelavida, Sanford, North Carolina
Aaron Mowery, Garden City, Georgia
Catherine Myers, Falls Church, Virginia
Alice Narey, University of Manchester, Manchester, United Kingdom
Gail Nebenzahl, San Francisco, California
Stuart Newman, New York Medical College, Valhalla, New York
Barbara Nicholson, Nashville, Tennessee
Angela Nielsen, Spokane, Washington
Judy Norsigian, Our Bodies Ourselves, Cambridge, Massachusetts

David Nunes, Shawnee, Oklahoma
Osagie Obasogie, University of California, Hastings College of Law, San Francisco, California
Karina Olivares, La Puente, California
Peggy O'Mara, peggyomara.com, Santa Fe, New Mexico
Seamus O'Neill, Manchester, United Kingdom
Charissa Orban, Streator, Illinois
Mariann-Bassey Orovwuje, Environmental Rights Action/Friends of the Earth Nigeria, Abuja, Nigeria
Louis Orrison, Olathe, Kansas
Maria Pantano, Hartford, Connecticut
Christina Pasterz, Glendale, Arizona
Megan Pena, Phoenix, Arizona
Laura Pesqueda, Springtown, Texas
Douglas Pet, East Bay Innovations, Berkeley, California
Julia Petuhova, Riga, Latvia
Cheryl Phyllaier, Strasburg, Pennsylvania
Michelle Pineault, Fall River, Massachusetts
Joseph Pippet, North Cape May, New Jersey
Jean Piziak, Wilmington, Delaware
Loretta Pleasant-Jones, Olney, Maryland
Catherine Powell, Alliance for Humane Biotechnology, San Francisco, California
Brian Powell, Lynchburg, Virginia
Linda Pride, Chicago, Illinois
David Radcliff, New Community Project, Peoria, Arizona
Alice Rainville, Livonia, Michigan
Melissa Ramey, Bowling Green, Ohio
Amber Reid, Orange Park, Florida
Christopher Reilly, Stafford, Virginia
Jesse Reynolds, Amsterdam, The Netherlands
Milton Reynolds, Facing History and Ourselves, San Leandro, California
Heather Ricco, Hamilton, Ohio
Tennille Richard, Milestone, Canada
Dorothy Roberts, University of Pennsylvania, Philadelphia, Pennsylvania
Shawn Roche, Ball Ground, Georgia
Tim Rochte, Trinity United Methodist Church and Society Commission, Los Osos, California
Dennis Rodano, Verona, New Jersey
Beth'Keila Rosario, Pompano, Florida
James Rusthoven, McMaster University, Hamilton, Canada
John Ryng, Bristol, Connecticut
Bethany Salad, Wailuku, Hawaii
Blair Sandler, San Francisco, California
Madeline Sapienza, Washington, District of Columbia
Jennifer Sappington, Worcester, Massachusetts
Jamie Sarver, Wright City, Missouri
Christiane Schmilinsky, Walnut Creek, California
Michal Schonbrun, Natural Fertility, Jerusalem, Israel
Yael Schwartz, Poughkeepsie, New York
Carmel Shalev, Haifa University, Haifa, Israel
Pete Shanks, Santa Cruz, California

Stephen Shmanske, California State University, East Bay, Berkeley, California
Erica Shorter, Lewes, United Kingdom
Evelyn Shuster, University of Pennsylvania/ VA Medical Center, Philadelphia, Pennsylvania
Margaret Smith, Philadelphia, Pennsylvania
Robert Spino, Denville, New Jersey
Robert Sr., Wasilla, Alaska
Nathan Stanton, Vancouver, Washington
Emily Stehr, Law offices of Lawless & Lawless, San Francisco, California
James E. Stevens, Alliance For Humane Biotechnology, San Francisco, California
Tina Stevens, San Francisco State University, San Francisco, California
Karen Stewart, Meridian, Idaho
Patty Stewart, Greenville, South Carolina
Mary Stroster, Clarkston, Michigan
Veit Stumpfenhausen, Limeira, Brazil
Rebecca Taylor, Spokane, Washington
Charis Thompson, London School of Economics; University of California, Berkeley, Berkeley, California
Anne Tindal, Coventry, Connecticut
Jodi Tristano, Cleveland, Ohio
Shauna Tucker, Waterbury, Connecticut
Diane Turner, Hamden, Connecticut
Chris Turner, Keller, Texas
Ryan Vander Heide, Camarillo, California
Rosa Velasquez, Pomona, California
Veronica Virtue, Hopkins, Minnesota
Uta Wagenmann, Gen-ethical Network, Berlin, Germany
Debbie Wallace, HOPE Clinic, Benton, Kentucky
John Walsh, West Melbourne, Florida
Pat Watkins, Caretakers of God's Creation, New York, New York
Karen Watts, Massasas, Virginia
Lisa Wheeler, Richmond, Maine
Sally Whelan, Our Bodies Ourselves, Cambridge, Massachusetts
Harry Wilkinson, Yuba City, California
Libby Wilson, Fairfax, Virginia
David Winickoff, University of California, Berkeley, Berkeley, California
Michelle Wonacott, Boise, Idaho
Jan Woodruff, Sanford, Michigan
Walt Woodruff, Sanford, Michigan
Susan Wright, University of California, Santa Cruz, Santa Cruz, California
Jane Yett, Women Donors Network, Santa Cruz, California