

Professional Ethics Report



ADVANCING SCIENCE, SERVING SOCIETY

Publication of the American Association for the
Advancement of Science (AAAS),
Scientific Freedom, Responsibility & Law Program,
in collaboration with the AAAS Committee on Scientific
Freedom & Responsibility

VOLUME XXIII

NUMBER 2

SPRING 2010

THE COMING REVOLUTION IN PRENATAL GENETIC TESTING

Henry T. Greely and Jaime S. King

Greely is the Deane F. and Kate Edelman Johnson Professor of Law and a Professor, by courtesy, of Genetics at Stanford University. King is an Associate Professor at the Hastings College of Law. Correspondence should be addressed to Greely at hgreely@stanford.edu.

At least since the 1932 publication of *Brave New World*, our society has worried about the possibility of *someone* selecting the next generation based on its genes. Prospective parents have had the opportunity to do prenatal genetic testing for over forty years, and yet the *Brave New World* has not appeared.

Of the roughly 5.2 million American women who were pregnant in 2009, only about 60,000 – just over 1 percent – obtained some form of prenatal genetic diagnosis. The mystery of why so few women get this testing is not hard to solve – the testing is expensive, uncomfortable, and carries risks. That may soon change. If it changes as we expect, millions of women will receive this kind of testing every year, a quantitative change that will force our societies to face questions that we have been able until now to ignore.

Prenatal Testing, Today and Tomorrow

Current reproductive genetic testing methods can be divided into two categories – prenatal and preimplantation. Prenatal genetic diagnosis requires DNA from the fetus, but the fetus is carefully insulated from the outside world, floating aloof and apart in its amniotic sac, its only connection through the placenta it

shares with the woman carrying it. Obtaining DNA from this protected source has required invasive methods. Amniocentesis, the most common method, pokes a needle through the pregnant woman's abdomen at 16 to 20 weeks of pregnancy to withdraw amniotic fluid containing fetal cells. Another method, chorionic villus sampling (CVS), is performed at 10 to 12 weeks, usually by snaking a catheter through the vagina and the cervix to retrieve a bit of placenta. Both methods are expensive and uncomfortable; both increase the risks of miscarriage for the fetus by about one-half to one percentage point. Improvements in non-invasive ways to screen for Down syndrome and neural tube defects have led to the decline in the number of women seeking invasive prenatal genetic testing.

Another way to get a potential child's DNA is through preimplantation genetic diagnosis (PGD), which allows prospective parents to select embryos for transfer to the uterus based on genetic characteristics. This method can be done only with *in vitro* fertilization, where the embryo is easily accessible rather than hidden somewhere in the Fallopian tubes or uterus. A few thousand babies are born in the United States each year after PGD. But, of course, *in vitro* fertilization with PGD is even more expensive, uncomfortable, and risky to the mother than amniocentesis or CVS – and its chances of producing a baby are limited.

So we *can* test the genetic make-up of the next generation, but, for reasons of cost, discomfort, and risk, we rarely do it. This is about to change – and with it may change the future of human reproduction. Change is coming because of a technological advance that permits access

to a previously untapped source of fetal DNA.

Scientists have known for many years that fetal DNA leaks into the maternal blood stream through the placenta, usually in the form of whole fetal cells. Detecting such cells is difficult, but possible. Testing them for fetal DNA, however, is complicated by the fact that many women still have some cells in their blood derived from earlier pregnancies. Finding the fetal cell needles in the haystack of a pregnant woman's blood will not be helpful if they are not from the current pregnancy.

But blood also contains a great deal of cell-free DNA ("cfDNA"), DNA that has been released by the death of cells and then chopped up by blood-borne enzymes into fragments about 100 base pairs long. We all have large quantities of cfDNA circulating in our own blood. Pregnant women, though, have cfDNA not only from their own cells but from fetal cells. Within the first few weeks of a pregnancy, five to ten percent of the cfDNA in a pregnant woman's blood serum is from the current fetus. After delivery or termination, cfDNA from the fetus disappears from the woman's system within 24 hours, eliminating any question regarding the origin of any non-maternal DNA.

Several academic researchers (and several companies) are trying to develop useful genetic tests from fetal cfDNA. Professor Steve Quake at Stanford is exploiting the sharply reduced cost of DNA sequencing to examine by shotgun sequencing all the cfDNA in 7 to 15 milliliters of pregnant woman's blood serum. Roughly 90 percent of the DNA will be from the woman, but the other 10 percent or so will be from the fetus. By counting matching sequences, he expects

to be able to determine reliably which bits of sequence are from the pregnant woman alone and which are from the fetus. In a 2008 study, Quake demonstrated the effectiveness of his approach in ascertaining aneuploid fetuses (those not bearing the usual 46 chromosomes), by accurately distinguishing between nine fetuses with trisomy 21 (Down syndrome), two with trisomy 18 (Edward syndrome), one with trisomy 13 (Patau syndrome), and six with the normal number of chromosomes [1].

The Conference

On May 7, 2010, the Stanford Center for Law and the Biosciences and the Stanford Center for Integrating Research in Genetics and Ethics sponsored a day-long conference at Stanford Law School to discuss this technology [2].

Fundamentally, we were interested in two questions. First, does this seem likely to work (and, if so, how well)? Second, what would be the social and ethical implications if it did?

As to the first question, the conference did not bring to light any reasons to believe some version of this method would not work. The reduced cost of DNA sequencing makes it possible to sequence as many tags as necessary to illuminate the relevant sections of the fetus's genome. Aneuploidies are clearly discoverable, including not only the three

trisomies already demonstrated, but variations in the sex chromosomes. Determining fetal sex is almost trivially easy.

Whether and how well the method can work beyond counting chromosomes remains to be seen. Quake believes that he can detect several megabases of genomic sequence, picking out those that may be of particular interest to potential parents, such as the common pathogenic alleles in Mendelian diseases – or, perhaps, the whole sequence for the exons and other sensitive regions of the genes involved in those diseases. No obvious barrier exists, but the accuracy of such a method (and, perhaps, its accuracy when repeated a second time for critical regions) is likely to determine whether the technique is useful as a diagnostic test or as just another screening procedure.

The answer will make a huge difference in the technique's use. Another blood-based screen for aneuploidies will spark only limited interest; a non-invasive diagnostic test for aneuploidies would ignite more. For Mendelian diseases and traits, a non-invasive screening would likely find substantial interest, but a non-invasive diagnostic test would probably be revolutionary.

The bulk of the conference considered this last possibility. We assumed that non-invasive cfDNA testing could provide diagnostic information about aneuploidies and roughly 100 Mendelian diseases or traits without needing follow-up by amniocentesis or CVS needed. This hypothetical test would require 10 milliliters of blood from the pregnant woman, could be performed as early as the fifth week after the last menstrual period, and would cost about \$1,000. If so, we asked, "What happens?"

The Implications

A few writers have discussed some social and ethical issues raised by non-invasive prenatal diagnosed [3-5]. We examined this particular technology and asked six specific questions raised by the limited literature on its likely social and ethical implications:

- How widely would the technique be used?
- Who is going to talk to patients about it and how?
- Who will pay for it?
- What will the effects be?
- What will, and can, the law do?
- What *should* we, as a society, do?

In general, the social and ethical challenges raised by fetal cfDNA testing differ in degree rather than in kind from those raised by current reproductive genetic testing techniques.

The first three areas were all linked to each other and to the effectiveness and cost of the testing. Uptake of testing would likely vary by socioeconomic, religious, education, cultural, and other characteristics of pregnant women, in ways that might be socially important. Variations in who uses genetic testing for reproductive selection can further stratify socioeconomic groups across not just wealth lines, but also in their predisposition to disease and undesirable genetic traits. Less obviously, but equally importantly, uptake would also vary by the nature of the communication and consent process. If women just receive one more form to sign, authorizing more tests on yet another blood draw, many may be shocked later to find that they had authorized genetic testing of the fetus. The conference reached a consensus around the need to educate both pregnant women and the general population about the implications of all forms of genetic testing. Providing good counseling for millions of women a year will be extremely challenging.

Who will pay will also be important. At the stipulated \$1,000 per test, some people might choose to pay for it themselves, but far more, no doubt, would opt for the test if it were covered by their health plans. Whether health plans would cover this kind of testing is unclear. They might find it in their financial self-interest, both as less expensive than other testing methods and as a result of the termination of pregnancies – and eventual children – involving expensive diseases or conditions. More broadly, it is unclear whether a health plan not motivated by profit would or should find the benefits of widespread testing worth the costs.

(Greely & King continued on page 3)

Editor: Mark S. Frankel

Deputy Editor: Nicole Carlozo

Contributing Authors: Nicole Carlozo, Rebecca Carlson, Erin Heath, Anna Ing, Jordan Johnson, Emil Kiner, Lindsay Pascal

The *Professional Ethics Report* is published quarterly by the Scientific Freedom, Responsibility and Law Program in collaboration with the Committee on Scientific Freedom and Responsibility.

American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005 (202) 326-6217; Fax(202)289-4950; Email nearlozo@aaas.org <http://www.aaas.org/spp/sfr/l/per/newper>

Back issues of *Professional Ethics Report* are on-line at <http://www.aaas.org/spp/sfr/l/per/archives1.shtml>

This newsletter may be reproduced without permission as long as proper acknowledgement is given. ISSN: 1045-8808

Letters to the Editor: The editors welcome comments from our readers. We reserve the right to edit and abridge the letter as space permits. Please address all correspondence to the deputy editor.

(Greely & King continued from page 2)

One fascinating question is the position of Medicaid. Medicaid pays for about 40 percent of the births in the United States. It is a joint federal/state program. States might well differ in whether they wanted to pay for testing that could lead to more abortions. For all health plans, coverage might also be affected by whether the technique had been reviewed and approved by the Food and Drug Administration.

The social effects, of course, depend on how many women choose to be tested, what genetic conditions will be tested, the test's accuracy, and how the test affects abortion decisions. Because it might be available as early as five weeks gestation, cfDNA testing could change the calculus for many women in deciding whether to have an abortion. At five weeks, the woman has only known she was pregnant for a short time, she has not experienced fetal movement, she is not showing, and a chemical, rather than surgical abortion, remains an option. By eliminating many of the inherent personal, physical, financial and moral barriers associated with current reproductive genetic testing, cfDNA testing has the potential to increase dramatically the number of people engaging in reproductive selection and thereby its social ramifications. For instance, the number of children born with certain genetic diseases (or other genetic traits) could decline significantly. This could have negative implications for people already living with those conditions or those who would continue to be born with them. They could see less research into their conditions, less understanding of their conditions, and diminished political power to fight for their rights and interests.

If the technology becomes common, the law is likely to become involved, but how? Obstetricians could be affected by potential liability in "wrongful birth" suits brought by parents complaining about a failure to offer the test, which would probably increase use of the test. Whether the FDA will regulate the safety and efficacy of such tests is not at all clear. Neither is the possible role of the state or federal governments in restricting or promoting the availability or use of a test so closely tied to parental decisions about their children. The sheer volume

of tests is likely to force us finally to face challenging questions we have been avoiding - whether a woman should be able to abort a fetus for any reason, no matter how trivial, or whether there are some genetic characteristics (sex, cosmetic traits, predispositions to certain conditions, etc.) for which no embryo should be terminated. A handful of states have already prohibited abortions performed on the basis of the fetus's sex; others might attempt to restrict access to tests they consider inappropriate. The federal Constitution may limit such interventions - or it may not. And, of course, in a world of easy travel and "reproductive tourism," we would need to think about what the law should or can do across national borders?

Finally, what *should* we do . . . we scientists, physicians, lawyers, ethicists, citizens, prospective parents, and moral beings? What if the parents choose to terminate a fetus based on its sex, on its cosmetic characteristics, on its having - or *not* having - a particular disability? We might ignore testing that affects one percent of pregnancies; should we - can we - ignore it if affects two-thirds of pregnancies?

The conference shed a great deal of light on some of these questions, but produced very few clear answers. What is clear, though, is that within the next two or three years, ready or not, our society will have to start answering these and other questions. Some new world, brave or otherwise, seems likely to be born. We must begin preparing for it.

References

[1] H.C. Fan, Y.J. Yair, U. Chitkara, L. Hudgins, S. R. Quake, *Noninvasive Diagnosis of Fetal Aneuploidy by Shotgun Sequencing DNA from Maternal Blood*, Proc. Nat'l Acad. Sci. 105:16,266-16,271 (Oct. 21, 2008).

[2] *The Coming Revolution in Prenatal Genetic Testing? Scientific, Ethical, Social, and Policy Responses to Maternal Serum Cell-Free Fetal DNA Testing*. Speakers included Wade Aubry, Audrey Chapman, Alan Fleischman, Jeremy Goldhaber-Fiebert, Henry T. Greely, Louanne Hudgins, Jaime King, Jessica Lehman, Mary Norton, Kelly Ormond, Steven R. Quake, John Robertson, Michael Snyder, and Sharon Terry. http://www.law.stanford.edu/calendar/details/3908/#related_media

[3] Carolyn Jacobs Chachkin, *What Potent Blood: Non-Invasive Prenatal Genetic Diagnosis and the Transformation of Modern Prenatal Care*, Am. J. Law Med. 33:9- (2007).

[4] Peter A. Benn and Audrey R. Chapman, *Practical and Ethical Considerations of*

Noninvasive Prenatal Diagnosis, J. Am. Med. Ass'n, 301:2154-56 (2009)

[5] Peter A. Benn and Audrey R. Chapman, *Ethical Challenges in Providing Noninvasive Prenatal Diagnosis*, Curr. Opin. Ob. & Gyn. 22:128-134 (2010)

This work was supported in part by a grant from the National Human Genome Research Institute to the Stanford University Center for Integration of Research in Genetics and Ethics (#2P50HG003389).

In the News

AT THE BLEEDING EDGE OF SYNTHETIC GENOMICS

In an article in *Science* published online on May 20, 2010, researchers reported "the synthesis, assembly, cloning, and successful transplantation of the 1.08Mbp [million base pair] . . . genome, to create a new cell controlled by this synthetic genome" [1].

"I actually thought it was going to be a whole lot faster. We feel bad it's taken us so long," replied J. Craig Venter to the House Committee on Energy and Commerce, upon being asked how long he thought it would take when he and his team at the J. Craig Venter Institute (JCVI) first undertook the endeavor [2].

The process involved designing the genome on a computer, chemically synthesizing it in 1,000bp segments, and a series of steps to progressively "stitch" the segments together into the final product. Since the synthetic genome was mostly a copy of a naturally occurring genome, the JCVI team added four "watermarks" into inactive portions of the genome to differentiate it from the naturally occurring variety. A secret code within the watermark contains the names of the 46 JCVI team members, quotations from famed scientists and philosophers, as well as a web site to which successful code-breakers can report.

To be sure, the synthetic genome does not contain anything that does not currently exist in nature. Venter, calling DNA the software of life, says that the already living recipient cell was "booted-up" with new software. According to Venter, the new approach, itself a proof of concept, "should be applicable to the synthesis and transplantation of more novel genomes as genome design

(News continued on page 4)

(News continued from page 3)

progresses.”

Asked about the implications of his achievement, Venter explained the only limit is one’s imagination. Synthetic Genomics, a for-profit company founded by Venter, funded the current study and retained ownership of the intellectual property rights. The company has a \$600mm contract with ExxonMobil to develop algae that will consume carbon dioxide and secrete fuel [2]. Venter testified before Congress that within the next year, and possibly for the next flu season, he expects this technology to eliminate the 3-month turnaround time for flu vaccine development. Instead, a vaccine candidate can be ready for testing within 24 hours of its design [2].

A week after the JCVI study, *Nature* published an article giving the opinions and impressions of leading biologists, bioethicists, and philosophers [3]. The scientists were congratulatory, expressing hope for the future implications of the technology, but also urged caution and put a realistic spin on the media’s initial claims that scientists have created life. Arthur Caplan, professor of bioethics at the University of Pennsylvania, said the achievement “is likely to prove as momentous to our view of ourselves and our place in the Universe as the discoveries of Galileo, Copernicus, Darwin and Einstein.” Mark Bedau, professor of philosophy and humanities at Reed College, unsure about the consequences of making new forms of life, called for “fundamental innovations in precautionary thinking and risk analysis.” Meanwhile, George Church, geneticist at Harvard Medical School, reminded us that, “[p]rinting out a copy of an ancient text isn’t the same as understanding the language.”

Outside of the academic community, reactions toward the scientific achievement have mostly ranged from reservedly inquisitive to outright supportive. The day the study was published, President Obama asked the Presidential Commission for the Study of Bioethical Issues to consider the potential medical, environmental, and security benefits as well as the possible risks associated with this “scientific milestone” [4]. The Vatican expressed optimism for the medicinal implications but urged

caution lest the discovery “turn against the dignity of and respect for human life” [5]. At the congressional hearing, concerns were expressed about the implications for security and bioterrorism, but the committee members’ fears were assuaged when the invited panel assured them that this development didn’t add any new capabilities to a nefarious actor’s tool kit. The committee also seemed satisfied with the statement by the Director of the National Institute of Allergy and Infectious Disease, Dr. Anthony Fauci, that the current regulatory framework in place at the NIH is equipped to deal with this new development. Congressman Burton (R-TX) jokingly expressed hope for the development of a synthetic gene that would predispose people to vote republican [2].

[1] Gibson, D.G. *et al.*, Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome. *Science*. (May 20, 2010).

<http://www.sciencemag.org/cgi/rapidpdf/science.1190719v1.pdf>

[2] Hearing on Developments in Synthetic Genomics and Implications for Health and Energy. 05/27/2010.

http://energycommerce.house.gov/index.php?option=com_content&view=article&id=2012:hearing-on-developments-in-synthetic-genomics-and-implications-for-health-and-energy&catid=128:full-committee&Itemid=84

[3] Life after the synthetic cell. *Nature*. 465, 422-424 (05/27/2010).

<http://www.nature.com/nature/journal/v465/n7297/full/465422a.html>

[4] President’s letter to Dr. Amy Gutmann. (05/20/2010).

<http://www.whitehouse.gov/sites/default/files/microsites/ostp/Gutmann-Letter.pdf>

[5] Rizzo, A. (May 21, 2010). Church warns cell scientists not to play God. *The Associated Press*. <http://www.google.com/hostednews/ap/article/ALeqM5ha2hlikQvHx347p3JzHAAAdXUIIjAD9FRB9480>

*EK

NIH PROPOSES INCREASED OVERSIGHT FOR FINANCIAL CONFLICTS OF INTEREST

On May 21, 2010 the National Institutes of Health (NIH) released its proposal for amending current regulations of financial conflicts of interest (FCOI) in behavioral and biomedical research at institutions that receive Public Health Service (PHS) funding. The PHS receives funding applications from approximately 5,000 research institutions annually. Over the past fifteen years, however, there has

been a significant increase in research financing by the industrial sector [1].

In a press release on May 20, NIH Director Francis S. Collins stressed the importance of the relationships between researchers and industry, noting, however, the often complex financial arrangements between the two [2]. The new proposal raises the standards of financial accountability for both participating institutions and investigators. It explicitly defines financial conflict as “a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research” [3]. The basic intent of the policy is the reduction of or removal of bias, especially that which may be tied to external funding, from scientific research.

The current policies, which were instated in 1995, entrust research institutions with the primary responsibility for identifying and regulating financial conflicts. They require that research institutions maintain and enforce policy aimed at the lessening of financial conflicts of interest. All conflicts must be reported to the PHS Awarding Component, and direct action must be taken to remove or to reduce the problem. Additionally, investigators must disclose any Significant Financial Interests (SFIs), those that are greater than \$10,000.

In response to the increasing visibility of biomedical and behavioral research, and in conjunction with the growing demand for alternative funding from non-governmental sources, NIH sought policy recommendations to ensure research integrity and monitoring of FCOIs. The proposal reads, “Investigator collaborations have become more complex and public scrutiny has increased significantly creating an environment that would benefit from a regulation with more effective means for management and oversight” [4]. The series of modifications proposed by NIH include, in summary:

Definitional clarifications

- Included is a revision of “Significant Financial Interests,” reducing the required reported value from \$10,000 to \$5,000 of any type of payment not constituting salary or

(News continued on page 5)

(News continued from page 4)

job related expense.

Revision of institutional responsibilities

- All institutional FCOI policies must be publicized on the web
- Required training of all participating investigators with respect to the institution's FCOI policy
- Increased guidelines for the participation of subrecipients in PHS-funded research
- Refined disclosure obligations for investigators

Regulations for the reporting of FCOIs

- New requirement for the implementation of a management plan when a financial conflict is identified
- Institutional review and assessment of whether an FCOI exists within sixty days of SFI disclosure by either a new or current investigator, after PHS funded research has begun
- Any incidents of investigator FCOI, or pre-existing SFIs, must be accessible to the public online. These must also be reported to the PHS Awarding Component before any funds are used.

The policy changes are intended to increase the visibility of the financial practices of research institutions, and the accountability of both investigators and institutions. The disclosure regulations will ensure that the PHS is informed of any conflicts. Although under the NIH proposal, much of the financial regulatory responsibility will remain in the hands of the institutions, increased monitoring of research practices will be more directly accessible to both the public and the government. The NIH proposal will be open for comment until July 20, 2010.

To view the NIH proposal, go to:
<http://www.gpo.gov/fdsys/pkg/FR-2010-05-21/pdf/2010-11885.pdf>

To learn more about FCOIs, go to:
<http://grants.nih.gov/grants/policy/coi/tutorial/coi.htm>

[1] <http://www.gpo.gov/fdsys/pkg/FR-2010-05-21/pdf/2010-11885.pdf>

[2] <http://www.nih.gov/news/health/may2010/od-19.htm>

[3] <http://www.gpo.gov/fdsys/pkg/FR-2010-05-21/pdf/2010-11885.pdf> p. 28690

[4] <http://www.gpo.gov/fdsys/pkg/FR-2010-05-21/pdf/2010-11885.pdf> p. 28702

*RC

FDA AIMS FOR TRANSPARENCY IN ADVISORY COMMITTEES

On April 21, the Food and Drug Administration issued draft guidelines for enhancing transparency in its 49 advisory committees, panels that advise the agency on a variety of scientific, technical and policy matters. These matters can include product approvals as well as regulations and guidance.

Members of FDA advisory committees can seek waivers to participate in meetings if they have financial conflicts of interest. The waiver system allows the agency to maintain flexibility and to seek out broad expertise. In deciding on a waiver, the FDA must consider the nature of the conflict, the function of the advisory committee, and the justification for including an expert with a conflict. There is an annual cap on how many waivers the agency may grant.

Said FDA Commissioner Margaret Hamburg: "FDA staff should search far and wide for experts who have the requisite knowledge without conflicts of interest. At the same time, however, I recognize the fact that many of the top authorities in specific areas may have conflicts of interest."

Current advisory panel members must disclose to the agency if they work with a sponsor or competitor of a drug or device under FDA review. Under the new guidelines, they would have to go further, revealing publicly the names of the relevant companies along with the range of how much money is involved. FDA plans to post the information on its web site.

Public comment on the draft guidelines is open until June 21.

The agency subsequently announced changes to the way its expert panels review and discuss data during hearings on medical devices under review for pre-market approval, effective on May 1. Instead of voting on the approvability of applications, panels will now vote on device safety and effectiveness and its risks versus benefits. Panel members will vote by ballot instead of a show of hands; although the results of the vote will still be public, the change is intended to allow

votes that are not at risk of being influenced by other votes. In addition, device reviewers will no longer present a unified consensus analysis of supporting data but rather the range of scientific opinions in the group.

The draft guidelines are posted at:
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM209201.pdf>

For more on changes in the work of expert panels on medical device matters, see:
<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm209791.htm>

*EH

REFORM LEGISLATION SEEKS TO INCREASE TRANSPARENCY IN HEALTH CARE SECTOR

In a widely supported initiative, the health care reform bill includes a provision that will require drug/medical device companies to publicize their payments to physicians and hospitals. Commonly-known as the Physician Payments Sunshine Act of 2009, the legislation states that manufacturers will soon be required to submit annual reports to the Secretary of Health and Human Services (HHS).

The Physician Payments Sunshine Act (H.R. 3590, Section 6002) was signed into law by President Barack Obama on March 23, 2010 as part of the Patient Protection and Affordable Care Act of 2009. The Act requires that annual reports must include all "payments or other transfers of value" between the company and the covered recipients (i.e., physicians and teaching hospitals). Information excluded from annual reports include: educational materials, drug/medical device samples, and transfers valued less than \$10 (unless the yearly aggregate exceeds \$100). Manufacturers need only publicize payments related to a new drug or medical technology after approval from the Food and Drug Administration or four calendar years after the initial payment, whichever occurs earlier. In addition to requiring the submission of transparency reports, the law requires manufacturers and group purchasing organizations to disclose information regarding physicians who have ownership or investment interests.

The law also grants HHS the regulatory power to penalize manufacturers or group

(News continued on page 6)

(News continued from page 5)

purchasing organizations that do not comply with its provisions. Failure to submit yearly reports before the 90th day of each year is subject to civil money penalties up to \$10,000 for each violation of the Act, and may not exceed \$150,000 annually. In a more severe scenario, group purchasing organizations and manufactures that knowingly fail to report may be fined at least \$10,000, but may not exceed \$100,000. Annually, these fines may not total more than \$1,000,000. The funds collected from these enforcement actions will be used to fund continued surveillance and regulation.

Ultimately, the yearly reports submitted to HHS are to be made available on an Internet website so that consumers can easily access and search for information. The Secretary is also responsible for presenting an annual report to Congress that summarizes the aggregate information of each manufacturer/group purchasing organization as well as the enforcement actions taken during the previous year. In addition, the Secretary must submit a report to each state. The reports only contain the summaries that pertain to covered recipients in a particular state.

These provisions of the Act are scheduled to go in effect on January 1, 2012, which is the date that manufacturers must begin recording all payments and transfers of value. On March 31, 2013, each manufacturer must file its first transparency report with the Secretary of Health and Human Services.

To view H.R. 3590, Section 6002, visit: http://www.prescriptionproject.org/tools/sunshine_docs/files/Sunshine_Leg_Language.pdf

*JJ

BRITISH CHIROPRACTIC ASSOCIATION HALTS LIBEL CASE AGAINST SCIENCE WRITER

On April 1, 2010, England's Court of Appeal ruled in favor of UK author and journalist Simon Singh in a libel case between Singh and the British Chiropractic Association (BCA). The BCA sued Singh in 2008 following publication of an opinion piece in *The Guardian*, in which he questioned the effectiveness of the BCA's chiropractic treatments for children.

Singh spent two years fighting against the libel suit. In May of 2009, High Court judge Justice Eady ruled in favor of the BCA by labeling Singh's comments as "fact" and requiring him to procure evidence to prove his claims against the association. April's Court of Appeal ruling, however, overturned that decision. The judges determined that Singh's comments were "honest opinion" and allowed his appeal, as well as his use of the "fair comment" defense. In response to this decision, the BCA dropped its libel case against Singh on April 15, just two weeks after the appeal was granted.

This ruling follows a libel reform campaign from charitable trust Sense About Science and free speech groups English PEN and Index on Censorship. Supporters of the campaign include groups such as the British Science Association and the National Union of Journalists. The campaign stems from concerns about the restriction of academic debate and open discussion among scientists, journalists, and publishers due to England's libel laws.

The Royal Courts of Justice addressed concerns over England's libel laws in the April 1 judgment, stating that scientific controversies should not be settled in the courtroom, but by other means. The judgment also noted the "chilling effect" that current libel laws have had on public debate. While Singh's case has come to a close, other libel cases remain in limbo. For example, consultant cardiologist Dr. Peter Wilmschurst is currently being sued by NMT Medical for questioning a heart implant device. Further debate might assist patients when deciding whether or not to follow suit or seek other treatment options, but the current legal situation has limited such discussions.

The Singh ruling is viewed as a triumph by the scientific community, as well as for journalists and publishers alike. In a statement on the Libel Reform Campaign website, Singh argues "fear of libel means that good research is not always published because those with vested interests might sue, and bad research that should be withdrawn is not pulled because the authors might sue the journal." If the appeal had been rejected, then scientists, journalists and other professionals would have faced greater risks of libel action [1].

The Court of Appeal ruling adds to present political concerns over England's libel laws. Justice Secretary Jack Straw's libel working group released a *Libel Working Group Report* in March of 2010. The report was to determine if "the law of libel, including the law relating to 'libel tourism', in England and Wales was in need of reform and, if so, to make recommendations as to solutions," and addressed concerns such as libel tourism; the role of public interest considerations in establishing defense to libel action; rules about multiple publications; and procedural and case management issues relating to the conduct of libel litigation. The working group's proposals and conclusions will serve, along with other considerations, as a basis for libel law reform, which will be considered in the next Parliament session [2].

For further background on this issue, see [PER Volume 23\(1\), Winter 2010](#)

To view the Court of appeal judgment, visit: <http://www.senseaboutscience.org.uk/PDF/Judgment.pdf>

To view the Libel Working Group Report, visit: <http://www.justice.gov.uk/publications/docs/libel-working-group-report.pdf>

[1] "Science writer Simon Singh wins libel appeal," BBC News: http://news.bbc.co.uk/2/hi/uk_news/8598472.stm

[2] "Reform of libel laws will protect freedom of expression," Ministry of Justice News Release: <http://www.justice.gov.uk/news/newsrelease230310b.htm>

*NC

EU NANOTECHNOLOGY CODE OF CONDUCT TO BE REVISED

On March 24, 2010, the European Commission released results from a public consultation of its *Code of Conduct for Responsible Nanosciences and Nanotechnologies*. The Commission has been involved with the responsible use of nanotechnology in Europe since 2004, when it began targeting policy makers, industry members, and media and civil society organizations involved or interested in nanosciences and nanotechnologies (N&N) research. Subsequent dialogues led to a 2007 report on the implementation of Europe's Nanotechnologies Action Plan and the eventual adoption of the February 2008 Code of Conduct.

The Code of Conduct was intended to

(News continued on page 7)

(News continued from page 6)

“promote integrated, safe and responsible nanosciences and nanotechnologies research in Europe for the benefit of society as a whole,” by providing Member States, employers, funders, researchers and other organizations with “guidelines favoring a responsible and open approach to N&N research in the Community.” The Commission based its guidelines on the general principles of sustainability, precaution, inclusiveness, excellence, innovation and accountability. The Commission also supported comprehensive research activities performed in the best interest of the public.

On September 26, 2008, the European Commission released the *Council Conclusions on Responsible Nanosciences and Nanotechnologies*. The Council acknowledged the pivotal role of nanotechnology in Europe’s economy and society at large and recognized the need for “safe and responsible development of nanotechnologies,” especially with respect to researchers, workers, health care professionals, and patients exposed to nanoparticles. Ultimately, the Commission agreed to monitor EU and international N&N developments while advancing efforts to support N&N research and continuing dialogues with Member States, stakeholders, and the general public. The Commission planned to revise the Code of Conduct regularly, beginning in February 2010. Accordingly, public comments were accepted for consultation from October 20, 2009 to January 3, 2010.

Respondents to the Commission’s public consultation included researchers, members of industry, and policy makers. Overall, 88% of respondents believe that Code of Conduct revisions are necessary, and about 75% agree that the code should not be limited to research. All policy makers who commented fall into these categories. While a majority of the researchers who commented want revisions to the Code, few elaborated on what those revisions might entail. Over 60% of all respondents suggested alterations to the Code’s principles, and about 53% want more appropriate research regulations.

Industry members made conflicting contributions to the N&N consultation. Companies such as EuCheMs and CEFIC submitted positive comments on the code and its effectiveness in promoting a global dialogue, but many national organizations voiced negative opinions, labeling it “unnecessary” due to the national guidelines and regulations already in place. All comments from the public consultation will be considered in the revision process.

To view the 2008 Commission Recommendation on a Code of Conduct for Responsible Nanosciences and Nanotechnologies Research, visit: http://ec.europa.eu/research/science-society/document_library/pdf_06/nanocode-recommendation-pe0894c08424_en.pdf

To view the 2008 Council Conclusions on Responsible Nanosciences and Nanotechnologies, visit: <http://register.consilium.europa.eu/pdf/en/08/st13/st13672.en08.pdf>

To view the 2009-2010 public consultation analysis, visit: http://ec.europa.eu/research/consultations/nanocode/results_en.pdf

*NC

VATICAN SUPPORTS STEM CELL PARTNERSHIP

On April 23, 2010, the Vatican and the Istituto Superiore di Sanita, the Italian equivalent to the U.S. National Institutes of Health, announced a stem cell research partnership with the University of Maryland School of Medicine. This International Intestinal Stem Cell Consortium will lead a research coalition to study adult intestinal stem cells in hopes of discovering treatments for diseases without the use of controversial embryonic stem cells.

Though the exact amount of the grant is being negotiated, the Vatican has agreed to provide around \$2.7 million for the research efforts. The funding will go directly to the University of Salerno’s Medical School Foundation in Italy, and will then be distributed to the project partners.

Intestinal stem cells are highly active cells that support the shedding and replacing of all the cells lining the intestine once every four to seven days. The cells are multipotent and can be programmed to generate a variety of cell types. Importantly, adult intestinal stem cell research does not require the destruction of an embryo, a practice the

Roman Catholic Church has long opposed.

Adult stem cells are thought to be less versatile than embryonic cells and scientists have had more trouble growing adult stem cells than embryonic cells. Yet, adult stem cells may be easier to use because they could be harvested from the patients themselves and may therefore have less risk of rejection or reaction to a transplant.

However, little is known about adult intestinal stem cells, and clinical research is not currently feasible. The consortium will work initially to answer two essential questions about intestinal stem cells. The researchers must first determine how to coax the intestinal cells to survive and replicate in the laboratory, and once flourishing, the researchers must then determine how to induce the cells to transform into different types of cells.

In 2006, Pope Benedict XVI said the Roman Catholic Church approves and encourages the use of adult stem cells because this research respects human life at every stage of existence [1]. The church has funded non-embryonic stem cell research in the past, providing grant money for adult stem cell research in South Korea and Australia.

To read the University of Maryland press release, visit: http://www.umm.edu/news/releases/stem_cell_vatican.htm

[1] Pope Benedict XVI. Address of His Holiness Benedict XVI to the Participants in the Symposium on the Theme: “Stem Cells: What Future for Therapy?” http://www.vatican.va/holy_father/benedict_xvi/speeches/2006/september/documents/hf_ben-xvi_spe_20060916_pav_en.html

*LP

CHILDREN’S STEM CELL BOOK RECEIVES MIXED RESPONSE

On April 8, 2010, Jef Akst of *The Scientist* posted a review of a children’s book called *Super Stemmys: Doris and the Super Cells*, authored by David Granovsky, with illustrations by Greg Boone. Granovsky is the director of communications for the Repair Stem Cell Institute (RSCI), which provides patients with the contact information of stem cell treatment centers located around the world. The story follows a bone marrow stem cell, named Doris, through her journey to repair a damaged heart.

(News continued on page 8)

(News continued from page 7)

The book was published by RSCI in July 2009 in an effort to increase awareness of stem cell treatments. Granovsky wrote the book at a sixth-grade level, although there are some who consider its use of rhyming and illustrations more juvenile. There is also controversy on the subject matter, itself. Some scientists are concerned that children will be misguided about the true nature and function of stem cells because of the book's narrow focus. The author does not explain that there are different types of stem cells, nor does he define scientific terms so that readers could understand the scientific procedure underlying the storyline. However, Xiangru Xu, a molecular biologist at Yale University, called the story a "scientific-based fairytale" that provides readers with an introduction to stem cells in an exciting way.

To read the Jef Akst's article, visit: <http://www.the-scientist.com/blog/display/57276/>

To learn more about *Super Stemmys: Doris and the Super Cells*, visit: <https://www.createspace.com/3391680>

*AI

GERMAN FUNDER LIMITS PUBLICATION CITATIONS IN RESEARCH PROPOSALS

On February 23, 2010, the Deutsche Forschungsgemeinschaft (DFG), Germany's leading research foundation, announced new regulations to counter the flood of publications in scientific research. Beginning July 1, 2010, the new policy will limit the number of publications that researchers can list in their funding proposals and final reports.

The ruling aims to reduce the importance of publication lists and numerical indices in proposal reviews and seeks to place more emphasis on the description of the research project. By restricting the number of publication citations, the main content of a proposal—an applicant's research objectives and preliminary work—is highlighted. Until now, researchers could list an unlimited number of publications.

The regulations apply to two key sections within all proposals and final reports: the publication lists cited on an applicant's curriculum vitae, and the references to

publications directly relating to the research project.

Under the new regulations, researchers are allowed to cite a maximum of five publications on their curriculum vitae. Reports of proposed or finished projects are restricted to two publications per year of funding. An individual researcher applying for three years of grant funding may, therefore, list up to six publications. Proposals involving multiple applicants may include up to three publications per year. In addition, citations are limited to published work only.

The president of DFG, Matthias Kleiner, claims that conventional mechanisms to evaluate proposal quality rely heavily on numerical indicators like the Hirsch index and impact factor—this approach deemphasizes proposal content and puts pressure on researchers to publish as much as possible. Limiting citations may also prevent cases of scientific misconduct, in which false statements concerning the status of a publication are provided. For instance, to bolster their curriculum vitae, some past applicants have fallaciously claimed that certain articles had been submitted for publication even when they had not [1].

Similar publication restrictions exist in other countries. For example, in the U.S., research proposals submitted to the National Science Foundation are permitted to cite five publications related to the proposal project and up to five additional publications, while the National Institutes of Health allow a total of 15 publications.

To read the press release, visit: www.dfg.de/en/service/press/press_releases/2010/pressemitteilung_nr_07/index.html

[1] Kleiner, M. (2010). Quality Over Quantity. *German Research*, 32(1), 2-3. http://www.dfg.de/download/pdf/dfg_magazin/wissenschaft_oeffentlichkeit/forschung_magazin/german_research_1_10_en.pdf

*LP

Announcements

Award – The Health Improvement Institute invites applications for the 2010 Award for Excellence in Human Research Protection. Individuals and institutions conducting research involving human beings or contributing to human research protection are eligible. Applications may be submitted for one or more of the award categories: best practice, innovation, life-time achievement. Contact: hii@hii.org. Visit: <http://www.hii.org/>

Professional Ethics Report

Call for Applications – The OpenSeminar in Research Ethics will hold a two-day workshop on teaching ethics on July 12-13, 2010 at North Carolina State University. Visit: <http://openseminar.org/ethics/>.

Call for Case Studies – The Center for the Study of Ethics at Utah Valley University invites submissions of case studies on environmental ethics for its archive. Accepted studies will be used as classroom discussion and research resources. For more information, see: <http://environmentalethics.info>. Send submissions to: david.keller@uvu.edu and david@keller.cc

Call for Papers – The Center for Applied Ethics and Philosophy at Hokkaido University invites papers for the Fifth International Conference on Applied Ethics from November 5-7, 2010 in Sapporo, Japan. Paper topics may include bio/medical ethics, engineering ethics, ethics of science and technology, information ethics, environmental ethics, and business ethics, among others. Abstract submissions of 300-500 words are due by August 7. Visit: <http://ethics.let.hokudai.ac.jp>.

Call for Papers – The American Journal of Bioethics-Neuroscience is accepting articles on neuroethics-related topics such as imaging, mental illness, neuromarketing, lie detection, human enhancement and animal models, among others. To submit articles for peer review, visit: <http://mc.manuscriptcentral.com/neuroscience>

Call for Papers – Articles, case studies, commentaries, and other submissions are invited for the *Cambridge Quarterly of Healthcare Ethics*' new Professionalism Department. Topics of interest include conscience-based refusals to provide health related services; strikes; prescribing medications for physical and/or cognitive enhancement; professional obligations during pandemics, bioterrorist attacks, and natural disasters; and cosmetic surgery, among others. Send manuscripts and abstracts to co-editors Mark Wicclair, wicclair@pitt.edu; and David Barnard, barnard@pitt.edu. For submission guidelines, visit: http://assets.cambridge.org/CQH/CQH_ifc.pdf.

Centers – The Regional Documentation and Information Centre for Bioethics and Ethics of Science and Technology was opened on March 29, 2010 at the Academy of Scientific Research and Technology with support from the UN Educational, Scientific and Cultural Organization (UNESCO). This regional center, based in Cairo, Egypt, will organize seminars and workshops on ethics issues, develop teaching curricula, establish ethics committees and databases, and disseminate information on bioethics and ethics education. UNESCO Contacts: Ms Orio Ikebe; o.ikebe@unesco.org; Ms Rania Anis, rha@asrt.sci.eg.

Conference – The University of Pennsylvania Center for Neuroscience and Society is hosting the Penn Conference on Clinical Neuroscience and Society from July 23-25, 2010. This Conference will review the latest developments in brain imagery, psychopharmacology, and medicolegal practices while exploring ethical, legal, and social issues for healthcare practitioners. For more information, see: <http://neuroethics.upenn.edu/index.php/events/clinical-conference>. Contact: conference@neuroethics.upenn.edu