IN THE UNITED STATES COURT OF APPEALS
FOR THE D.C. CIRCUIT

JAMES L. SHERLEY, *et al.*,

Appellees,

v.

KATHLEEN SEBELIUS, in her official capacity as Secretary of the Department of Health and Human Services, *et al.*,

Appellants.

No. 10-5287
[Civil Action No. 1:09-cv-, 1575 (RCL) (D.D.C.)]

DEFENDANTS' EMERGENCY MOTION TO STAY PRELIMINARY INJUNCTION PENDING APPEAL AND REQUEST FOR IMMEDIATE ADMINISTRATIVE STAY

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INTRODUCTION AND SUMMARY

Defendants, the Secretary of Health and Human Services, et al., respectfully ask the Court to stay pending appeal the district court's preliminary injunction of August 23, 2010. The order enjoins the National Institutes of Health ("NIH") "from implementing, applying, or taking any action whatsoever pursuant to the National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009), or otherwise funding research involving human embryonic stem cells as contemplated in the Guidelines." Add. 1 (Order 1). The order is at odds with the express intent of Congress in enacting the funding restriction at issue, and with the longstanding interpretation of that restriction by NIH, of which Congress was fully aware. To avoid immediate loss of ongoing medical research aimed at curing the most devastating illnesses afflicting Americans, we also ask that the Court issue an administrative stay pending its consideration of this motion. The district court denied the government's motion for a stay pending appeal on September 7, 2010.

The preliminary injunction rests on the district court's erroneous legal conclusion that NIH Guidelines violate an appropriations restriction known as the Dickey-Wicker Amendment. Congress first enacted the Dickey-Wicker Amendment in 1996 and has included the same language in subsequent appropriations bills without substantive change. In its current form, it prohibits the use of federal funds for "(1) the creation of a human embryo or embryos for research purposes; or (2) research in

which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death * * * ." Pub. L. No. 111-117, Div. D, § 509(a), 123 Stat. 3034, 3280-81.

NIH has consistently interpreted this provision throughout the past decade to distinguish between funding for research that involves the creation or destruction of embryos (which is prohibited) and funding for research that involves the use of stem cell lines derived from embryos. *See* Add. 95 (65 Fed. Reg. 51,975 (Aug. 25, 2000)); Add. 89 (74 Fed. Reg. 32,170, 32,173 (July 7, 2009)); *see also* Add. 12-13 (discussing NIH's interpretation). In repeatedly reenacting the same statutory language, Congress has been well aware of the agency's interpretation of the funding restriction. Indeed, the relevant Committee Report for the 2010 appropriations bill, which was enacted after issuance of the current NIH Guidelines, noted that the bill "should not be construed to limit Federal support for research involving human embryonic stem cells carried out in accordance with policy outlined by the President." H.R. Rep. No. 111-220, at 273 (July 22, 2009); *see also* S. Rep. No. 111-66, at 121-22 (Aug. 4, 2009) (welcoming the Guidelines and noting the "congressional intent to expedite this important area of research"); H.R. Rep. No. 111-366, at 982 (Dec. 8, 2009) ("In implementing this conference agreement, the Departments and agencies should be guided by the language and instructions set forth in House Report 111-220 and Senate Report 111-66 accompanying the bill, H.R. 3293.").

The district court set aside this longstanding agency interpretation that had been repeatedly ratified by Congress, and erased the distinction between, on the one hand, funding the derivation of stem cell lines and, on the other hand, funding research using stem cell lines already derived from human embryos. In the court's view, because embryonic stem cells "must be derived from an embryo," embryonic stem cell research "is clearly research in which an embryo is destroyed." Add. 13 (Aug. 23 Op.). That view necessarily precludes federal funding for any and all embryonic stem cell research.

The order stops NIH funding for embryonic stem cell research in its tracks, and precludes NIH from acting on embryonic stem cell grant applications that have already been fully reviewed and from considering dozens of other applications in various stages of the review process. Absent a stay, it will likely take as long as 6 to 8 months to re-initiate the peer review process for grant applications. Add. 54, ¶ 18 (Decl. of Francis S. Collins, Director of NIH). Disruption of ongoing research will result in irreparable setbacks and, in many cases, may destroy a project altogether.

The two plaintiff scientists, by contrast, identify no imminent irreparable harm to themselves that would result from a stay. Indeed, they identify no irreparable harm that has occurred in the 10 months since their suit was originally dismissed for lack of standing. In a prior opinion, this Court concluded that the two scientists, who engage in research using adult stem cells, have standing to challenge the allocation of funds to

other stem cell research based on possible competitive injury. *See* Add. 74 (D.C. Cir., June 25, 2010). A stay pending appeal will not impair that asserted interest. Dr. Deisher has never applied for research funding from NIH and states only that she is "in the process of applying" for funding. Add. 56, ¶ 24; 59, ¶ 4 (Decl. of Dr. Deisher). And Dr. Sherley has received $425,500 in NIH grant funds since implementation of the Guidelines. Add. 55-56, ¶ 23 (Decl. of Dr. Sherley). The speculative interest of competitive injury by those who have not sought to compete previously or have successfully competed cannot outweigh the disruption or ruin of research into promising treatments for the most debilitating illnesses and injuries.

In sum, because the injunction rests on legal error and will result in significant, irreparable injury, we ask that the Court stay the ruling pending appeal and issue an administrative stay pending consideration of this motion.

STATEMENT

I. Stem Cell Research.

Three kinds of stem cells are available for research – human embryonic stem cells, adult stem cells, and induced pluripotent stem cells. *See* National Academies, *Understanding Stem Cells: An Overview of the Science and the Issues from the National Academies* 2, *available at* http://dels.nas.edu/bls/stemcells/basics.shtml. Most embryonic stem cells - and all those eligible for use in federally funded projects - are produced from stem cell lines derived from embryos that were created in an *in vitro* fertilization clinic

for reproductive purposes. In many cases, more embryos are created than are necessary to meet an individual or couple's reproductive goals or some embryos may be unsuitable for transfer. Those individuals or couples may choose to donate their remaining embryos for stem cell research.

Embryonic stem cells are pluripotent, meaning that they are able to transform into any of the approximately 200 types of cells in the human body. Adult stem cells are not pluripotent and can only differentiate into a restricted set of specialized cells. Induced pluripotent stem cells, a recent innovation, are adult cells that are reprogrammed to assume a state similar to embryonic stem cells.

Each of these types of cells has its own capabilities and limitations and presents its own research possibilities and challenges, and NIH is committed to funding research on each type of stem cell line. *See* Add. 48-49, ¶ 7; 55, ¶ 22. For FY 2010, NIH has provided approximately $380 million in funding to non-embryonic (adult and pluripotent) stem cell research; for FY 2010 to date, NIH has provided $131 million to funding human embryonic stem cell research. Add. 55, ¶ 22.

II. Regulatory Background.

A. Beginning in 1996, Congress has restricted appropriations in language known as the Dickey-Wicker Amendment. The language, which has not been substantively altered since its first enactment, prohibits NIH from funding "research

in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death." *See* Pub. L. No. 111-117, Div. D, § 509(a).

This language has always been understood to bar funding for extracting stem cells from embryos to create embryonic stem cell lines, but not for research using stem cell lines. As noted, embryonic stem cell lines eligible for use in federally funded projects are created using cells extracted from embryos that were created in an *in vitro* fertilization clinic and donated for research purposes by individuals or couples when there was no longer a need for them for reproductive purposes.

A stem cell line is typically created by growing the cells extracted from a four- or five-day-old embryo in a laboratory culture dish where, with appropriate care, the cells begin to divide. Embryonic stem cells that have continued to divide for a prolonged period without differentiating, and are genetically identical to the original cells, are referred to as an embryonic stem cell line. With appropriate care, embryonic stem cell lines continue to divide and produce additional identical embryonic stem cells indefinitely. NIH does not fund the creation of stem cell lines.

NIH has consistently recognized, however, that research using stem cells is not "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death." *See* Add. 97 (65 Fed. Reg. at 51,976 (Aug. 25, 2000)). As the current Guidelines explain, funding "of the derivation of stem cells from human embryos is prohibited" but NIH has "consistently interpreted

[the Amendment] as not applicable to research using [embryonic stem cell lines], because [embryonic stem cells] are not embryos as defined by" the Amendment. Add. 93 (Fed. Reg. at 32,173 (July 7, 2009)). The researchers using stem cell lines are rarely those who derived the stem cells in the first instance.

B. On March 9, 2009, President Obama issued Executive Order No. 13,505. *See* Add. 86. The order provided that NIH "may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law." Add. 87, § 2. The President directed NIH to review existing guidelines on human stem cell research, and to "issue new NIH guidance on such research that is consistent with this order." *Id.* § 3.

The executive order also withdrew two directives that had been issued in the prior administration: (1) a presidential statement of August 9, 2001, and (2) Executive Order No. 13,435, 72 Fed. Reg. 34,591 (June 20, 2007). Add. 88, § 5. In these directives, President Bush had announced his policy of permitting federal funding of some research using embryonic stem cells, but limiting funding to research involving stem cells produced by lines that were created by private or foreign researchers from "embryos that have already been destroyed." *See* Address to the Nation on Stem Cell Research From Crawford, Texas, 37 Weekly Comp. Pres. Doc. 1149 (Aug. 9, 2001); *see also* Executive Order No. 13,435, 72 Fed. Reg. 34,591.

NIH issued the final Guidelines on July 7, 2009, through notice-and-comment rulemaking. Add. 89. The Guidelines require that research involve only embryonic stem cells produced by lines that "have been derived from human embryos" that "were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose" and "were donated by individuals * * * who gave voluntary written consent for the human embryos to be used for research purposes." Add. 93.

III. Prior Proceedings.

A. Plaintiffs Dr. James L. Sherley and Dr. Theresa Deisher are scientists who perform research using adult stem cells. The suit originally included several other plaintiffs, including an agency facilitating the adoption of frozen embryos, three of its clients, the Christian Medical Association, and embryos created using *in vitro* fertilization and no longer needed for reproduction. The district court dismissed claims by all plaintiffs for lack of standing. The ruling was appealed only with respect to the two scientists. This Court held that the two scientists fell within the "competitor standing" doctrine, under which "'plaintiffs may establish their constitutional standing by showing that the challenged action authorizes allegedly illegal transactions that have the clear and immediate potential to compete with [their] own sales.'" Add. 80 (citation omitted). The Court reasoned that the increase in grant applications for embryonic cell research resulting from the Guidelines would

"intensif[y] the competition for a share in a fixed amount of money." Add. 83.[1] The Court declined plaintiffs' invitation to reach the merits of their claims and remanded to the district court. *Ibid.*

B. On August 23, without receiving any additional filings from the parties to address developments that had taken place during the 10 months during which there had been no stay in place, the district court issued a preliminary injunction. The order enjoins defendants from "implementing, applying, or taking any action whatsoever pursuant to the National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009), or otherwise funding research involving human embryonic stem cells as contemplated in the Guidelines." Add. 1 (Aug. 23 Order).

The district court denied the government's motion for a stay pending appeal on September 7. Add. 19.

ARGUMENT

In considering whether to grant a stay pending appeal, the Court is guided by the four factors set out in *Washington Metro. Area Transit Comm'n* v. *Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977). The government's likelihood of success on the merits as well as the balance of harms strongly militate in favor of a stay in this case.

[1] The government respectfully disagrees with the panel's holding. We recognize, however, that the ruling is binding on other panels.

I. The Government Has A Strong Likelihood Of Success On The Merits.

A. Congress has included the Dickey-Wicker Amendment in NIH's annual appropriations bill without substantive change since 1996, despite policy shifts in federal funding for stem cell research. As enacted in the FY 2010 appropriations bill, the amendment restricts funds for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death."

At no point in the 14 years since the Amendment was first enacted has NIH interpreted this language to bar embryonic stem cell research. Instead, it has consistently interpreted the Amendment to prohibit federal funding of the derivation of a stem cell line. *See* Add. 97 (65 Fed. Reg. at 51,976 (Aug. 25, 2000)) (research using embryonic stem cells is not "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death").

Although President Bush limited federal funding to projects that used stem cells produced by lines created prior to the announcement of his policy, that policy rested on the premise that research using embryonic stem cells is not "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death." Congress explicitly recognized in reenacting the Dickey-Wicker language for FY 2002 that the Bush policy was consistent with the Amendment, which does not categorically prohibit funding of all research using embryonic stem cells. *See*

H.R. Rep. No. 107-229, at 180 (Oct. 9, 2001); *see also* S. Rep. No. 107-84, at 18 (Oct. 11, 2001).

After President Obama revoked the orders issued by President Bush, NIH issued the Guidelines challenged here. Like their predecessors, these Guidelines do not authorize funding for the extraction of embryonic stem cells or the creation of embryonic stem cell lines. They provide, moreover, that research using embryonic stem cells will be eligible for federal funding only if the stem cells were produced by stem cell lines that "have been derived from human embryos" that "were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose" and "were donated by individuals * * * who gave voluntary written consent for the human embryos to be used for research purposes." Add. 94.

When Congress included the Dickey-Wicker Amendment in the FY 2010 appropriations bill, it was fully aware of the NIH Guidelines. The relevant Committee Report, like Committee Reports issued during the Bush administration, declared that the Amendment's "language should not be construed to limit Federal support for research involving human embryonic stem cells carried out in accordance with policy outlined by the President." H.R. Rep. No. 111-220, at 223 (July 22, 2009); *see also* S. Rep. No. 111-66, at 121 (Aug. 4, 2009) ("The Committee is pleased that stem cell research was included as a special emphasis area in the NIH Challenge Grant program * * * . The Committee also welcomes the recent release of guidelines for the use of

human embryonic stem cells [hESC] with NIH funds * * * ."); H.R. Rep. No. 111-366, at 982 (Dec. 8, 2009) ("In implementing this conference agreement, the Departments and agencies should be guided by the language and instructions set forth in House Report 111-220 and Senate Report 111-66 accompanying the bill, H.R. 3293.").

Even absent such clear statements of legislative intent, the reenactment of legislative language with knowledge of the existing Executive Branch interpretation would counsel hesitation in setting that interpretation aside. This Court has noted that "Congress is presumed to preserve, not abrogate, the background understandings against which it legislates." *United States* v. *Wilson*, 290 F.3d 347, 356 (D.C. Cir. 2002); *see also Lorillard* v. *Pons*, 434 U.S. 575, 580-58 (1978) ("Congress is presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it re-enacts a statute without change."); *N.L.R.B.* v. *Bell Aerospace Co.*, 416 U.S. 267, 274-75 (1974) ("[A] court may accord great weight to the longstanding interpretation placed on a statute by an agency charged with its administration. This is especially so where Congress has re-enacted the statute without pertinent change.").

B. In invalidating the NIH Guidelines, the district court concluded that it would not "defer[] to the NIH's interpretation" of the Dickey-Wicker Amendment because, in the court's view, that interpretation was not "'based on a permissible construction of the statute.'" Add. 10-11 (quoting *Chevron U.S.A., Inc.,* v. *Natural*

Resources Defense Counsel, Inc., 467 U.S. 837, 843 (1984)). As noted, the Amendment restricts funds for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death." This plain language, on its face, does not apply to research that uses embryonic stem cells from previously derived stem cell lines, which is not research in which embryos are destroyed.

The district court nonetheless concluded that "'Congress had directly spoken to the precise question at issue.'" Add. 10-12 (quoting *Chevron*, 467 U.S. at 842). The court declared that "the term 'research' as used in the Dickey-Wicker Amendment has only one meaning, *i.e.*, 'a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.'" Add. 11 (quoting 45 C.F.R. § 46.102(d)).[2] In the court's view, this definition compels the conclusion that "[d]espite defendants' attempt to separate the derivation of [embryonic stem cells] from research on the [embryonic stem cells], the two cannot be separated." Add. 13.

To say that research is a "systematic investigation" does not mean that each research project includes the projects and actions that preceded it– including projects performed by different scientists. At a minimum, the court's interpretation does not

[2] The definition cited by the district court is contained in the Human Subject Protection Regulations, referenced in the Dickey-Wicker Amendment, which govern research involving human subjects.

constitute a declaration of the statute's "plain language." The court opined that if Congress had meant to enact the distinctions reflected in NIH interpretations, "Congress could have written the statute that way." Add. 12. It is sufficient, however, that the legislative language is fully consistent with the longstanding NIH interpretation cited by Congress in reenacting the Dickey-Wicker Amendment. Indeed, if Congress had meant to ban all federal funding for "research involving human embryonic stem cells," as the district court held, it could certainly "have written the statute that way" when it first enacted the Amendment or on later occasions, rather than use the markedly different language "research in which a human embryo or embryos are destroyed." Thus, the district court's conclusion that a stay pending appeal "would flout the will of Congress," Add. 20 (Sept. 7 Stay Order), is not well founded.

II. The Balance Of Harms And The Public Interest Strongly Favor A Stay.

Even if the government's case on the merits were far less compelling, the balance of harms would warrant issuance of a stay.

The district court's assessment of the injuries resulting from its order is altogether asymmetric. On the one hand, the court accepted uncritically plaintiffs' assertion "'that obtaining NIH funding is necessary for their continued research.'" Add. 14 (citing plaintiffs' opposition at 44.). To demonstrate irreparable harm, the

court found it sufficient that the plaintiffs might suffer some competitive injury if research funds were awarded to other scientists whose research involves embryonic stem cell lines. It was irrelevant to the court's analysis that Dr. Deisher has never applied for research funding from NIH and states only that she is "in the process of applying" for funding. Add. 56, ¶ 24; 59, ¶ 4. Dr. Sherley's declaration states only that he has in the past received NIH grants and now has two grants pending. Add. 72-73 (Decl. of Dr. Sherley). It fails to note that he has received $425,500 in NIH grant funds *since* implementation of the current Guidelines. Add. 55-56, ¶ 23. Indeed, NIH funding for adult and induced pluripotent stem cell research far exceeds funding for embryonic stem cell research. For FY 2010, NIH has provided approximately $380 million in funding to non-embryonic stem cell research and $131 million in funding human embryonic stem cell research. The $380 million provided during FY 2010 is also far greater than the $297 million for non-embryonic stem cell research provided in 2008. Add. 135-36, ¶ 18 (Decl. of Sarah Jean Rockey); Add. 55, ¶ 22. There is, moreover, no reason to conclude that an immediate halt of funding of embryonic stem cell research would result in a reallocation of funds in a way that would have any short-term impact whatsoever on Dr. Sherley's pending applications.

The harm to the current, ongoing NIH funded research using embryonic stem cellls, on the other hand, is direct and immediate, and potentially blocks lifesaving medical advances. Under the injunction, NIH is barred outright from funding such

research. The district court nevertheless declared that its injunction "would not seriously harm [embryonic stem cell] researchers" because it "would not interfere with their ability to obtain private funding for their research." Add. 15. But it is unclear why the federal funding that the court deemed *"necessary* for [plaintiffs'] continuing research," Add. 14 (quoting plaintiffs' opposition at 44), is not similarly necessary to the research of those scientists who are now cut off altogether. *See also* Add. 59, ¶ 4 (Decl. of Dr. Deisher) (stressing that "private funding is scarce").

The declaration of the Director of NIH, Dr. Collins, explains that the injunction bars funding for an additional 20 human embryonic stem cell research projects, which have successfully completed NIH's rigorous peer review process. Add. 53, ¶ 15. NIH planned to award $24 million in funding to these projects by September 30. *Ibid;* Add. 49-50, ¶ 9. The injunction also halts NIH consideration of all pending applications for projects using embryonic stem cells. NIH has ceased peer review activities of all human embryonic stem cell research applications and estimates that if the injunction is not stayed pending appeal, it will take as long as 6 to 8 months for the process to begin again. Add. 54, ¶ 18. As a result of the injunction, NIH has also ceased reviewing stem cell lines to determine whether they are eligible for placement on the NIH Human Embryonic Stem Cell Registry and has put on hold work on a revision of the NIH guidelines that has been under development for over 7 months. Add. 54, ¶¶ 19, 20.

In denying the government's motion for a stay, the district court stated that plaintiffs, in their opposition to the government's district court stay motion, "question whether this Court's order prevents NIH from doing peer review of applications." Add. 20. The injunction enjoins NIH "from *implementing, applying, or taking any action whatsoever* pursuant to the" challenged Guidelines "or otherwise funding research involving human embryonic stem cells as contemplated in the Guidelines." Add. 1 (emphasis added). The court did not explain how its order could be construed to continue the application review process. Indeed, plaintiffs did *not* question whether the injunction applies to the peer review process, arguing instead that "the processing of additional Registry and grant applications contributes directly to the competitive injuries to Plaintiffs (and other scientists) that the preliminary injunction was designed to prevent, and was properly enjoined." Add. 28. The district court disregarded that argument, however, and instead stated that "one would have expected these issues to have been briefed and decided with the preliminary injunction motion." Add. 20. As noted, the Court issued its injunction without any supplemental briefing to address developments that had taken place over the course of the intervening 10 months during which there had been no stay in place.

The court also stated that "Plaintiffs question whether this Court's order exempts so-called 'intramural' NIH projects—that is, research carried out onsite by NIH researchers." Add. 20. Plaintiffs did not, in fact, question the injunction's

applicability to NIH researchers. Add. 28. The court suggested that additional briefing on plaintiffs' standing to challenge intramural research might be appropriate, Add. 20, but did not narrow the scope of its injunction to make it inapplicable to these activities.

It is extraordinary that the district court would enjoin ongoing federal intramural research without first considering whether plaintiffs have standing to challenge such research. Dr. Collins' declaration explains that the injunction cripples NIH's internal research program. NIH conducts eight intramural human embryonic stem cell research projects staffed by approximately 45 scientists and other personnel, with a combined budget of approximately $9.5 million for 2009. Add. 53-54, ¶ 17. The longer that NIH is prevented from carrying out intramural research, the more likely it is that unique biological materials that have taken years to develop and that require ongoing maintenance and attention will be lost. Add. 52, ¶ 12.

The district court injunction does not apply to funds already received by third parties. *See* Add. 27 (plaintiffs' opposition) (noting that the injunction "on its face * * * applies only to Defendants and their agents, not to third parties" and therefore does not affect funds provided prior to August 23); Add. 19 (citing pl. op. at 5). Dr. Collins explains in his affidavit, however, that 24 multi-year human embryonic stem cell projects were expecting to receive continuation funds on September 30 for their continued existence. Add. 50-51, ¶ 10. It is not clear whether the order applies to

these projects, but if those annual continuation funds are not forthcoming, even during the period of appellate review, many of these research projects will be terminated before the fruits of their research can be realized. *Ibid.* Valuable and unique research resources are likely to be lost, and, with them, the potential for life-saving therapies. Add. 47-52, ¶¶ 6, 12. The premature termination of these 24 federal research projects will also waste much of the approximately $64 million in funds that NIH had already invested in this research. Add. ¶ 10.

The district court dismissed the significance of its ruling to the public interest, stating that "the harm to individuals who suffer from diseases that one day may be treatable as a result of" research using embryonic stem cell lines "is speculative." Add. 15. "It is not certain," the court declared, whether such "research will result in new and successful treatments for diseases such as Alzheimer's and Parkinson's disease." Add. 15. It is quite true that the path to a cure for any disease is fraught with uncertainties. It is quite another thing to describe as "speculative" the importance of one of the most vital areas of research into the origins and treatments of human disease. *See* Add. 46-49, ¶¶ 5-7. The progress made by scientists using human embryonic stem cell lines is real, and is particularly important because embryonic stem cells, unlike adult stem cells, are pluripotent. The district court's discounting of the significance of this research does not reflect the public interest at stake.

CONCLUSION

For the foregoing reasons, the Court should grant a stay pending appeal of the preliminary injunction entered on August 23, 2010, and an immediate administrative stay pending its consideration of this motion.

Respectfully submitted,

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SEPTEMBER 2010

CERTIFICATE OF SERVICE

I hereby certify that on this 8th day of September, 2010, I electronically filed the foregoing motion with the Clerk of the Court for the United States Court of Appeals for the D.C. Circuit by using the appellate CM/ECF system and by hand-delivering four paper copies.

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to D.C. Circuit Rule 28(a)(1), the undersigned counsel certifies as follows:

A. Parties And Amici. Plaintiffs in the district court, and appellees in this appeal, are Dr. James L. Sherley, Dr. Theresa Deisher, Nightlight Christian Adoptions, Shayne Nelson, Tina Nelson, William Flynn, Patricia Flynn, Christian Medical Association, and Embryos.

Defendants in the district court, and appellants in this appeal, are Kathleen Sebelius, in her official capacity of Secretary of the Department of Health and Human Services, Department of Health and Human Services, Francis S. Collins, in his official capacity as Director of National Institutes of Health, and National Institutes of Health.

Coalition for the Advancement of Medical Research moved to appear as amicus in the district court, but the district court denied that motion.

B. Rulings Under Review. The rulings under review are the August 23, 2010, order and memorandum opinion of the district court, issuing a preliminary injunction. *Sherley v. Sebelius*, No. 1:09-cv-1575-RCL (D.D.C. Aug. 23, 2010) (Chief Judge Royce C. Lamberth). The order and opinion appear at page 1 of the Addendum. The district court's opinion is also available at 2010 WL 3296974.

Also under review is the district court's September 7 order denying the government's motion for stay. Add. 19.

C. Related Cases. This matter has previously come before this Court in *Sherley v. Sebelius,* No. 09-5374 (June 25, 2010). The opinion is available at 610 F.3d 69 and at page 74 of the Addendum. Counsel is aware of no other related cases within the meaning of D.C. Circuit Rule 28(a)(1)(C).

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ADDENDUM

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, *et al.*, Plaintiffs,	)	
v.	)	Civ. No. 1:09-cv-1575 (RCL)
KATHLEEN SEBELIUS, *et al.*, Defendants.	)	

ORDER

Upon consideration of plaintiffs' Motion [3] for a Preliminary Injunction, the opposition and reply thereto, the applicable law, and the entire record herein, it is, for the reasons set forth in the accompanying Memorandum Opinion, hereby

ORDERED that plaintiffs' motion is GRANTED; it is further

ORDERED that defendants and their officers, employees, and agents are enjoined from implementing, applying, or taking any action whatsoever pursuant to the National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009), or otherwise funding research involving human embryonic stem cells as contemplated in the Guidelines.

SO ORDERED.

Signed by Royce C. Lamberth, Chief Judge, on August 23, 2010.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, *et al.*, Plaintiffs,	)	
v.	)	Civ. No. 1:09-cv-1575 (RCL)
KATHLEEN SEBELIUS, *et al.*, Defendants.	)	

MEMORANDUM OPINION

I. INTRODUCTION

This matter comes before the Court on plaintiffs' Motion [3] for a Preliminary Injunction. Previously, this Court dismissed this case for lack of standing and denied plaintiffs' motion for a preliminary injunction as moot. Plaintiffs appealed. On appeal, plaintiffs argued that plaintiffs Drs. Sherely and Diesher had competitor standing and conceded that other plaintiffs lacked standing. The Court of Appeals reversed, holding that plaintiffs Sherley and Diesher have standing, and remanded the matter to this Court for consideration of plaintiffs' motion for a preliminary injunction. The mandate from the Court of Appeals was filed in this Court this date.

For the reasons set forth below, the Court will GRANT plaintiffs' motion and issue a preliminary injunction.

II. BACKGROUND

A. Procedural History

Plaintiffs Drs. James L. Sherley and Theresa Deisher, Nightlight Christian Adoptions ("Nightlight"), Embryos, Shayne and Tina Nelson, William and Patricia Flynn, and Christian

Medical Association ("CMA") brought this suit for declaratory and injunctive relief to prevent defendants' Guidelines for Human Stem Cell Research ("Guidelines") from taking effect. (Compl.¶¶ 4, 6-12.) Specifically, plaintiffs sought "an order (a) declaring that the Guidelines are contrary to law, were promulgated without observing the procedures required by law, and constitute arbitrary and capricious agency action; and (b) enjoining [d]efendants from applying the Guidelines or otherwise funding research involving the destruction of human embryonic stem cells." (*Id.* ¶ 4.) On October 27, 2009, this Court dismissed plaintiffs' suit, finding that plaintiffs lacked standing, and denied plaintiffs' motion for a preliminary injunction as moot. *Sherley v. Sebelius*, 686 F. Supp. 2d 1, 5-7 (D.D.C. 2009). Plaintiffs appealed.

The Court of Appeals reversed, concluding that Drs. Sherley and Deisher had standing under the competitor standing doctrine. *Sherely v. Sebelius*, – F.3d –, 2010 WL 2540358, *5 (D.C. Cir. 2010). Because the Nightlight, the Embryos, the Nelsons, the Flynns, and CMA did not contest this Court's finding that they lacked standing, the Court of Appeals treated "their lack of standing as conceded." *Id.* at *2. The Court of Appeals then remanded this matter back to this Court for consideration of plaintiffs' motion for a preliminary injunction. *Id.* at *6.

B. Stem Cell Research

Stem cell research has the potential to produce medical breakthroughs in the treatment of many life-threatening diseases and conditions that have resisted traditional methods of treatment. (Pls.' Mot. [3] for Prelim. Inj. at 2; Defs.' Opp'n [22] at 2.) There are three types of stem cells available for research: adult stem cells ("ASCs"), induced pluripotent stem cells ("IPSCs"), and human embryonic stem cells ("ESCs"). (Pls.' Mot. [3] for Prelim. Inj. at 2.) Each type of stem cell possesses unique capabilities and limitations. (Def.'s Opp'n [22] at 3.) As a result, many

scientists believe that research should be conducted on each type of stem cell. (*Id.* (citing Nat'l Insts. of Health, *Stem Cell Information: Frequently Asked Questions*, http://stemcells.nih.gov/info/faqs.asp).) Other scientists, however, believe that research should be conducted only on ASCs and IPSCs because ESC research has not produced positive results and is morally objectionable. (Pls.' Mot. [3] for Prelim. Inj. at 2-3.)

ESCs have been available for research since 1998, when Dr. James Thomson of the University of Wisconsin discovered a process for deriving stem cells from an embryo. (*Id.* at 3.) ESCs are pluripotent, *i.e*, they have "the capability to give rise to any of the approximately 200 types of cells in the human body." (Def.'s Opp'n [22] at 3.) Once they are derived from an embryo, ESCs may be maintained indefinitely. *See* Nat'l Insts. of Health, *Stem Cell Information: Frequently Asked Questions*, http://stemcells.nih.gov/info/faqs.asp.

ESCs may be used to treat diseases in two ways. First, researchers can transplant ESCs into patients. (*See* Defs.' Opp'n [22] at 3.) To transplant ESCs, researchers must guide the differentiation of ECSs into certain kinds of cells. (*Id.*) Differentiation of ESCs reduces the risk of benign tumor forming after the ESCs are transplanted. (*Id.* (citing Nat'l Acads., *Understanding Stem Cells: An Overview of the Science and the Issues from the National Academies* at 5 (2009)).) Second, ESCs may be used to "study disease mechanisms that cannot be studied in the human body, and to develop other, non-stem-cell based therapies for these conditions." (Defs.' Opp'n [22] at 4.) Recent studies employing both methods of treatment suggest that ESCs will contribute to the development of medical knowledge in the future. (*See id.*)

ASC research, in which Drs. Sherley and Deisher specialize, is approximately fifty years

old and began with the discovery of hematopoietic stem cells. (*Id.*) ASCs are found in tissues that are normally discarded after birth, such as the umbilical cord, and in the body. (Pls.' Mot. [3] for Prelim. Inj. at 3.) Because researchers have been able to study ASCs for decades, they have been able to develop treatments for numerous diseases with ASCs. (*Id.*; Defs.' Opp'n [22] at 5.) ASCs, however, are limited because, unlike ESCs, they are multipotent, not pluripotent. (Defs.' Opp'n [22] at 5 (citing Nat'l Insts. of Health, *Hematopoietic Stem Cells*, http://stemcells.nih.gov/info/scireport/chapter5.asp).) As a result, ASCs cannot differentiate into the 200 types of cells in the human body. (*Id.*) Nevertheless, ASC research remains of great importance in the treatment of disease. (*Id.* at 6.)

IPSC research is the newest form of stem cell research. Discovered in 2007, IPSCs "are adult stem cells that have been genetically reprogrammed such that they are virtually identical to embryonic stem cells." (Pls.' Mot. [3] for Prelim. Inj. at 4.) Because research involving IPSCs is at such an early stage, its full potential is unknown. (Defs.' Opp'n [22] at 5.) Some researchers, however, believe that IPSCs offers the most promise for advancements in medical research and treatment. (Pls.' Mot. [3] for Prelim. Inj. at 4-5.)

C. Regulatory Background

In 1996, Congress enacted the Balanced Budget Downpayment Act, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996). The Balanced Budget Downpayment Act contained a rider, known as the Dickey-Wicker Amendment, which prohibited the use of federal funds for "(1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses *in utero* under" applicable federal regulations.

Id. Congress has included the Dickey-Wicker Amendment in every appropriations bill for Health and Human Services ("HHS") since 1996 without substantive alteration. *See* Omnibus Appropriations Act 2009, Pub. L. No. 111-8, § 509(a)(2), 123 Stat. 524, 803 (2009).

In 1999, defendants determined that the Dickey-Wicker Amendment was not applicable to ESC research because ESCs are not embryos as defined by statute. (*See* Lingo Decl. Ex. D.) Specifically, defendants recognized a distinction between deriving ESCs from an embryo, which is prohibited by the Dickey-Wicker Amendment because it results in the destruction of the embryo, and research on ESCs, which does not result in the destruction of an embryo. *See* Nat'l Insts. of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32170, 32173 (July 7, 2009). Defendants have maintained this interpretation of the Dickey-Wicker Amendment since 1999. (*Id.*) Congress, however, has not altered the Dickey-Wicker Amendment in response. (Defs.' Opp'n [22] at 9-10.)

On August 9, 2001, President Bush announced a policy statement on stem cell research that limited federal funding for research on ESCs. *See* Address to Nation on Stem Cell Research From Crawford Texas, 37 Weekly Compl. Pres. Doc. 1149 (Aug. 9, 2001). Specifically, the President prohibited federal funding for research on ESCs that were created after the date of the policy statement. (*Id.*) Federal funding remained available, however, for research on ESCs that were created by private researchers prior to his policy statement. (*Id.*) The President formalized this policy statement in Executive Order No. 13,435, which provided federal funding for IPSC research and left the limitations on ESC research unchanged. *See* Exec. Order No. 13,435, 72 Fed. Reg. 34,591 (June 20, 2007).

On March 9, 2009, President Obama, by executive order, removed President Bush's

limitations on ESC research in order "to expand NIH support" for human stem cell research and "to enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind." Executive Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009) As a result, the National Institutes of Health ("NIH") "may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem research, to the extend permitted by law." *Id.* To achieve that end, the President directed NIH to review the existing stem cell research guidelines and "issue new NIH guidance on such research that is consistent with this order." *Id.*

In response to President Obama's executive order, NIH published draft guidelines entitled "National Institutes of Health Guidelines for Human Stem Cell Research." 74 Fed. Reg. 18,578 (Apr. 23, 2009). The draft guidelines allowed "funding for research using human embryonic stem cells that were derived from human embryos created by *in vitro* fertilization (IVF) for reproductive purposes and were no longer needed for that purpose." *Id.* NIH received approximately 49,000 comments, including plaintiffs' submission, on the draft guidelines during the comment period. 74 Fed. Reg. at 32,170. After reviewing the comments, NIH published its final Guidelines on human stem cell research on July, 7 2009.

The Guidelines set forth eligibility requirements to determine which ESC lines "could be used in research funded by NIH." (Defs.' Opp'n [22] at 8.) If a research applicant proposes research on ESCs derived after the effective date of the Guidelines, the applicant must use either ESCs that are posted on the NIH registry, or submit an assurance of compliance with requirements contained within Section II(A) of the Guidelines. 74 Fed. Reg. at 32,174. Section II(A) requires that research involves only ESCs that were derived from human embryos that

"were created using *in vitro* fertilization for reproductive purposes and were no longer needed for this purpose" and "were donated by the individuals who sought reproductive treatment . . . and who gave voluntary written consent for the human embryos to be used for research purposes." *Id.* Section II(A) further requires documentation of the following: (a) that "[a]ll options available in the health care facility where treatment was sought pertaining to the embryos no longer needed for reproductive purposes were explained to the individual(s) who sought reproductive treatment"; (b) that no payments were offered for the embryos; (c) that the health care facility has procedures in place to ensure that the quality of care provided to potential donors would not be affected by their consent or refusal to donate embryos; (d) that there was a "clear separation" between the donor's decision to create the embryos for reproductive purposes and the donor's decision to donate the embryos for research; and (e) that donors were provided with certain information during the consent process. *Id.*

If a research applicant proposes research on ESCs derived before the effective date of the Guidelines, the applicant must use either ESCs that are posted on the NIH registry, or establish funding eligibility in one of two ways: the applicant may either comply with Section II(A), or submit materials to a Working Group of the Advisory Committee to the Director of NIH, which will make recommendations regarding funding eligibility. *Id.* at 32,175. If an applicant submits materials to the Working Group, the applicant must demonstrate that the ESCs were derived from embryos that were created using *in vitro* fertilization, that the embryos were no longer needed for reproductive purposes, and that the donors gave voluntary written consent that their embryos could be used for research. *Id.* In addition, the Working Group will consider the factors contained in Section II(A). *Id.*

Finally, the Guidelines provide that "NIH funding of the derivation of stem cells from human embryos is prohibited by" the Dickey-Wicker Amendment. *Id.* Thus, according to defendants, the Guidelines "recognize the distinction . . . between the derivation of stem cells from an embryo that results in the embryo's destruction, for which Federal funding is prohibited, and research involving hESCs that does not involve an embryo nor result in an embryo's destruction, for which Federal funding is permitted." *Id.* at 32,173.

III. LEGAL STANDARD

A preliminary injunction is "an extraordinary remedy that should be granted only when the party seeking the relief, by a clear showing, carries the burden of persuasion. *Cobell v. Norton*, 391 F.3d (251, 258 (D.C. Cir. 2004). A party carries this burden of persuasion by establishing: (1) that there is a substantial likelihood of success on the merits; (2) that the plaintiff would suffer irreparable injury absent an injunction; (3) that an injunction would not substantially injure other interested parties; and (4) that an injunction would further public interest. *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998) (quoting *CityFed Fin. Corp. v. Office of Thrift Supervision*, 58 F.3d 738, 746 (D.C. Cir. 1995)).

The Court evaluates these factors on a "sliding scale." *Davis v. Pension Benefit Guar. Corp.*, 571 F.3d 1288, 1291 (D.C. Cir. 2009). Under this approach, the Court balances the factors against each other to determine whether the plaintiff has shown that "all four factors, taken together, weigh in favor of the injunction." *Id.* at 1292. Thus, a particularly strong showing on one factor may offset a weaker showing on another factor. *See id.* at 1291-92 ("If the movant makes an unusually strong showing on one of the factors, then it does not necessarily have to make as strong a showing on another factor."). The plaintiff, however, must show at

least some injury to warrant the preliminary injunction because "the basis for injunctive relief in the federal courts has always been irreparable harm." *CityFed Fin. Corp.*, 58 F.3d at 747.

IV. ANALYSIS

The Court finds that the likelihood of success on the merits, irreparable harm to plaintiffs, the balance of hardships, and public interest considerations each weigh in favor of a preliminary injunction. *See Winter v. Natural Res. Def. Counsel, Inc.*, 129 S. Ct. 365, 374 (2008). Accordingly, the Court will GRANT plaintiffs' motion and issue the preliminary injunction.

A. Likelihood of Success

Plaintiffs assert two independent arguments as to why they are likely to succeed on the merits. First, they argue that the Guidelines violate the plain language of the Dickey-Wicker Amendment. Second, they contend that, in promulgating the Guidelines, defendants violated the Administrative Procedure Act ("APA"). Because the Court concludes that plaintiffs have demonstrated a strong likelihood of success that the Guidelines violate the Dickey-Wicker Amendment, the Court need not address whether defendants violated the APA.

1. The Dickey-Wicker Amendment Is Unambiguous

Defendants argue that the Dickey-Wicker Amendment is ambiguous. Specifically, they argue that the term "research" is ambiguous, and that, as a result, their interpretation of research should be entitled to *Chevron* deference. *See Chevron U.S.A., Inc., v. Natural Resources Defense Counsel, Inc.*, 467 U.S. 837, 843 (1984). Defendants' argument fails.

Under *Chevron*, the Court must first ask whether Congress has "directly spoken to the precise question at issue." *Id.* at 842. If it has, the Court must "give effect to the unambiguously expressed intent of Congress." *Id.* at 843. If, however, the "the statute is silent or ambiguous

with respect to the specific issue," then the Court defers to the NIH's interpretation provided it is "based on a permissible construction of the statute." *Id.*

Congress has spoken to the precise question at issue—whether federal funds may be used for research in which an embryo is destroyed. The Dickey-Wicker Amendment provides that *no* federal funds shall be used for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses *in utero* under 45 C.F.R. § 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b))." Pub. L. No. 111-8, § 509(a)(2). Thus, as demonstrated by the plain language of the statute, the unambiguous intent of Congress is to prohibit the expenditure of federal funds on "research in which a human embryo or embryos are destroyed." *Id.*

Contrary to defendants' argument, the term "research" as used in the Dickey-Wicker Amendment has only one meaning, *i.e.*, "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." 45 C.F.R. § 46.102(d); *see also* Random House Dict. (listing the first definition of research as "diligent and systematic inquiry or investigation into a subject in order to discover or revise facts, theories, applications, etc."). This is the most common definition of research, and no other definition of research is supported by the language of the statute.

The language of the statute does not support defendants' alternative definition of research as "a piece of research." (Def.'s Opp'n [22] at 31 (citing RANDOM HOUSE DICT. (2009).) Indeed, the Dickey-Wicker Amendment does not contain any language to support such a limited definition of research. Rather, the language of the statute reflects the unambiguous intent of Congress to enact a broad prohibition of funding research in which a human embryo is destroyed.

This prohibition encompasses *all* "research in which" an embryo is destroyed, not just the "piece of research" in which the embryo is destroyed. Had Congress intended to limit the Dickey-Wicker to only those discrete acts that result in the destruction of an embryo, like the derivation of ESCs, or to research on the embryo itself, Congress could have written the statute that way. Congress, however, has not written the statute that way, and this Court is bound to apply the law as it is written. Accordingly, this Court must "give effect to the unambiguously expressed intent of Congress" to prohibit federal funding of research in which a human embryo is destroyed. *Chevron*, 467 U.S. at 843.

2. The Guidelines Violate the Dickey-Wicker Amendment

Having concluded that the Dickey-Wicker Amendment is unambiguous, the question before the Court is whether ESC research is research in which a human embryo is destroyed. The Court concludes that it is.

Defendants argue that the ESC research is not research in which a human embryo is destroyed because ESC research does not involve embryos nor result in their destruction. This argument rests on defendants' interpretation of "research," as used in the Dickey-Wicker Amendment, to mean "a piece of research." (Defs.' Opp'n [22] at 31 (citing RANDOM HOUSE DICT. (2009).) This interpretation allows defendants to define ESC research and the derivation of ESCs from embryos as separate and distinct "pieces of research." Thus, the Guidelines, according to defendants, are consistent with Dickey-Wicker Amendment because the Guidelines only allow funding of ESC research, and not the derivation of ESCs, which results in the destruction of an embryo.

Defendants' argument is unavailing. Their entire argument assumes that the Dickey-

Wicker Amendment is ambiguous and that, as a result, they are entitled to *Chevron* deference. As discussed above, defendants' assumption is incorrect. The Dickey-Wicker Amendment unambiguously prohibits the use of federal funds for all research in which a human embryo is destroyed. It is not limited to prohibit federal funding of only the "piece of research" in which an embryo is destroyed. Thus, if ESC research is research in which an embryo is destroyed, the Guidelines, by funding ESC research, violate the Dickey-Wicker Amendment.

ESC research is clearly research in which an embryo is destroyed. To conduct ESC research, ESCs must be derived from an embryo. The process of deriving ESCs from an embryo results in the destruction of the embryo. Thus, ESC research necessarily depends upon the destruction of a human embryo.

Despite defendants' attempt to separate the derivation of ESCs from research on the ESCs, the two cannot be separated. Derivation of ESCs from an embryo is an integral step in conducting ESC research. Indeed, it is just one of many steps in the "systematic investigation" of stem cell research. 45 C.F.R. § 46.102(d). Simply because ESC research involves multiple steps does not mean that each step is a separate "piece of research" that may be federally funded, provided the step does not result in the destruction of an embryo. If one step or "piece of research" of an ESC research project results in the destruction of an embryo, the entire project is precluded from receiving federal funding by the Dickey-Wicker Amendment. Because ESC research requires the derivation of ESCs, ESC research is research in which an embryo is destroyed. Accordingly, the Court concludes that, by allowing federal funding of ESC research, the Guidelines are in violation of the Dickey-Wicker Amendment.

* * *

In sum, plaintiffs have demonstrated a strong likelihood of success on the merits. The Dickey-Wicker Amendment is unambiguous. It prohibits research in which a human embryo is destroyed, discarded, or knowingly subject to risk of injury or death greater than that allowed under applicable regulations. The Guidelines violate that prohibition by allowing federal funding of ESC research because ESC research depends up on the destruction of a human embryo.

B. Irreparable Injury

This Circuit has established a high standard for irreparable injury . *Chapliancy of Full Gospel Churches v. England*, 454 F.3d 290, 297 (D.C. Cir. 2006). First, a plaintiff must allege an injury that is "both certain and great; it must be actual and not theoretical." *Id.* (quoting *Wisc. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985). The alleged injury must be "of such *imminence* that there is a 'clear and present' need for equitable relief to prevent irreparable harm." *Id.* (citation omitted). Second, the plaintiff's alleged injury "must be beyond remediation." *Id.* Plaintiffs Sherley and Deisher have met this high burden.

Plaintiffs are researchers who work exclusively with ASCs. They seek funds for their research projects from defendants and allege "that obtaining NIH funding is *necessary* for their continued research." (Pls.' Mot. [3] at 44.) The Guidelines, by allowing federal funding of ESC research, increases competition for NIH's limited resources. This increased competition for limited funds is an actual, imminent injury. *See Sherely*, 2010 WL 2540358 at *5 (explaining that the increased competition that plaintiffs face is "substantial enough to deem the injury to them imminent"). There is no after-the-fact remedy for this injury because the Court cannot compensate plaintiffs for their lost opportunity to receive funds. *See Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997) (quoting *Hoffman-Laroche Inc. v. Califano*, 453 F.

Supp. 900, 903 (D.D.C. 1978) (stating that even if an injury is economic in nature, the injury may be irreparable if "there is 'no adequate compensatory or other corrective relief' that can be provided at a later date"). Accordingly, plaintiffs would suffer irreparable injury in the absence of the injunction.

C. Balance of Hardships

The balance of hardships weighs in favor of an injunction. Defendants argue that two interested parties would be injured if the Court issues an injunction: ESC researchers and individuals who suffer from diseases that may be treatable in the future as a result of ESC research. The Guidelines give ESC researchers, like plaintiffs, the opportunity to compete for NIH funding. The injunction, however, would not seriously harm ESC researchers because the injunction would simply preserve the *status quo* and would not interfere with their ability to obtain private funding for their research. In addition, the harm to individuals who suffer from diseases that one day may be treatable as a result of ESC research is speculative. It is not certain whether ESC research will result in new and successful treatments for diseases such as Alzheimer's and Parkinson's disease.

Plaintiffs' injury of increased competition, however, is not speculative. It is actual and imminent. Indeed, the Guidelines threaten the very livelihood of plaintiffs Sherley and Deisher. Accordingly, the irreparable harm that plaintiffs would suffer absent the injunction outweighs the harms to interested parties.

D. Public Interest

Finally, the public interest weighs in favor of a preliminary injunction. "It is in the public interest for courts to carry out the will of Congress and for an agency to implement properly the

statute it administers." *Mylan Pharms. Inc. v. Shalala*, 81 F. Supp. 2d 30, 45 (D.D.C. 2000). Here, the will of Congress, as expressed in the Dickey-Wicker Amendment, is to prohibit federal funding of research in which human embryos are destroyed. Accordingly, it is in the public interest to enjoin defendants from implementing the Guidelines because the Guidelines allow federal funding of ESC research, which involves the destruction of embryos.

V. CONCLUSION

Plaintiffs have established that the preliminary injunction factors—the likelihood of success on the merits, irreparable injury, the balance of hardships, and the public interest—weigh in favor of a preliminary injunction. Accordingly, the Court will GRANT plaintiffs' motion [3] for a preliminary injunction. A separate order shall issue this date.

Signed by Royce C. Lamberth, Chief Judge, on August 23, 2010.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

JAMES L. SHERLEY, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	Case No. 1:09-cv-01575-RCL
	)	
KATHLEEN SEBELIUS, in her official capacity as Secretary of the Department of Health and Human Services, *et al.*,	)	
	)	
Defendants.	)	

NOTICE OF APPEAL

PLEASE TAKE NOTICE that defendants Kathleen Sebelius, in her official capacity as Secretary of the Department of Health and Human Services; the Department of Health And Human Services; Dr. Francis S. Collins, in his official capacity as Director of the National Institutes of Health; and the National Institutes of Health appeal to the United States Court of Appeals for the District of Columbia Circuit from the Opinion and Order granting Plaintiffs' Motion for Preliminary Injunction (Dkt Nos. 44 and 45), entered August 23, 2010.

Dated: August 31, 2010

Respectfully submitted,

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

JAMES L. SHERLEY, *et al.*,	
Plaintiffs,	
v.	**Civil Action No. 09-1575 (RCL)**
KATHLEEN SEBELIUS, in her official capacity as Secretary of the Department of Health and Human Services, *et al.*,	
Defendants.	

ORDER

Upon consideration of defendants' Emergency Motion to Stay Preliminary Injunction Pending Appeal (ECF No. 48), the opposition thereto (ECF No. 51), and the record herein, it is hereby

ORDERED that defendants' motion for a stay is DENIED.

Defendants are incorrect about much of their "parade of horribles" that will supposedly result from this Court's preliminary injunction.

Plaintiffs agree that this Court's order does not even address the Bush administration guidelines, or whether NIH could return to those guidelines. (Defs.' Opp'n 5.) The prior guidelines, of course, allowed research only on existing stem cell lines, foreclosing additional destruction of embryos.

Plaintiffs also agree that projects previously awarded and funded are not affected by this Court's order. (*Id.*)

Plaintiffs question whether this Court's order exempts so-called "intramural" NIH projects—that is, research carried out onsite by NIH researchers—since the record is unclear whether those funds could be re-programmed for the grant programs. (*Id.* at 6.) Obvious standing questions are presented for the Court if such funds are not available for persons such as plaintiffs, and a motion to clarify this issue can be expeditiously briefed and decided.

Plaintiffs also question whether this Court's order prevents NIH from doing peer review of applications or from maintaining the Human Embryonic Stem Cell Registry. (*Id.*) Again, one would have expected these issues to have been briefed and decided with the preliminary injunction motion. Plaintiffs do not contest NIH document or website preservation activities, or other activities related solely to adult or induced pluripotent stem cell research. Whether and how these can be separated out is not clear from the record today.

Additionally, since plaintiffs anticipate filing their motion for summary judgment by September 10, (*id.* at 13 n.4,) the length of time this preliminary injunction will be in place should be limited.

In this Court's view, a stay would flout the will of Congress, as this Court understands what Congress has enacted in the Dickey-Wicker Amendment. Congress remains perfectly free to amend or revise the statute. This Court is not free to do so.

Congress has mandated that the public interest is served by preventing taxpayer funding of research that entails the destruction of human embryos. It is well-established that "[i]t is in the public interest for courts to carry out the will of Congress and for an agency to implement properly the statute it administers." *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 45 (D.D.C. 2000).

SO ORDERED.

Signed by Royce C. Lamberth, Chief Judge, on September 7, 2010.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al., Plaintiffs,	)	
v.	)	Civil Action No. 09-CV-01575-RCL
KATHLEEN SEBELIUS, et al., Defendants.	)	

MEMORANDUM OF LAW IN OPPOSITION TO DEFENDANTS' MOTION TO STAY PRELIMINARY INJUNCTION PENDING APPEAL

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INTRODUCTION

Defendants' motion to stay pending appeal effectively asks this Court to reconsider its August 23, 2010, decision granting Plaintiffs' motion for a preliminary injunction. Because that ruling was correct, and because nothing material has changed in the week since it was issued, Defendants' motion for a stay should be denied.

Defendants' claims of irreparable harm absent a stay rest on speculation, misinformation, and hyperbole. At every turn, Defendants present this case as a choice between spending federal dollars on human embryonic stem cell research—funding that this Court previously determined has only speculative benefits and likely violates federal law—or nothing at all. To the contrary, the preliminary injunction frees up millions in limited grant dollars that the National Institutes of Health ("NIH") can now award to projects that promise more tangible medical benefits, raise fewer ethical issues, and comport with the law, including adult and induced pluripotent stem cell research.

The administrative record before the NIH when it promulgated the Guidelines demonstrated the overwhelming scientific and ethical advantages of adult and induced pluripotent stem cell research over embryonic stem cell research. Even NIH Director Dr. Francis S. Collins, however, effectively admits in his declaration that adult stem cells have proven to date to have more practical medical applications, such as "FDA-approved treatments that reconstitute the immune system after leukemia, lymphoma, and various blood or autoimmune disorders have been treated with chemotherapy." Declaration of Francis S. Collins ¶ 7 (Aug. 31, 2010) (hereinafter "Collins Decl."). The most Dr. Collins can muster in claiming irreparable injury is that embryonic stem cell research "offer[s] hope" to patients suffering from diseases and that beneficial treatments are "possible" in the future. *Id.* ¶ 5. Likewise, with respect to proposed or ongoing experiments that

may be temporarily delayed due to this Court's preliminary injunction, Dr. Collins again resorts to conjecture that the experiments "may" take a long time to restart and that researchers "may" move to other countries in the meantime. *Id.* ¶ 12.[1] This falls far short of the *imminent* and *irreparable* injury that the law requires; mere speculation or hope cannot support a finding of irreparable harm. *Sherley v. Sebelius*, Civ. No. 1:09-cv-1575 (RCL), 2010 U.S. Dist. LEXIS 86441, at *20-22 (D.D.C. Aug. 23, 2010).

By contrast, both this Court and the D.C. Circuit have acknowledged the importance of the competitive injuries that scientists like Plaintiffs suffer immediately when they have to compete with illegal research proposals for a limited pool of federal dollars. Moreover, this Court's August 23 order left no room for serious doubt that Plaintiffs will prevail on the merits of their claim—*i.e.*, that the Guidelines violate the Dickey-Wicker Amendment, which "unambiguously" prohibits federal funding of the destruction of human embryos. *See id.* at *18; *see also id.* at *19 ("[B]y allowing federal funding of ESC research, the Guidelines are in violation of the Dickey-Wicker Amendment."). Due to this holding, the Court did not even reach Plaintiffs' argument that the Guidelines violate the Administrative Procedure Act ("APA"), which is an independent basis why Plaintiffs prevail on the merits, and is not even addressed in Defendants' brief. There is nothing to be gained by staying this Court's order for a temporary period pending appeal of the preliminary injunction order, when there is every reason to expect that Plaintiffs will soon obtain permanent injunctive or declaratory relief invalidating the Guidelines. A stay will only result in

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[1] In addition, the Collins declaration is replete with exaggerations and factual mischaracterizations. *See generally* Exhibit A, Declaration of Dr. Theresa Deisher (Sept. 3, 2010). In particular, the declaration repeatedly overstates the promise of embryonic stem cell research, while downplaying the discoveries made through adult stem cell research. *See id.* ¶¶ 9, 12.

further injury to Plaintiffs and additional waste of taxpayer dollars being poured into an illegal, unethical, and scientifically speculative enterprise.

For these reasons, Defendants' request for a stay pending appeal should be denied.

ARGUMENT

To obtain a stay pending appeal of a decision on a motion for a preliminary injunction, the moving party must show "(1) a substantial likelihood of success on the merits, (2) that it would suffer irreparable injury if the injunction is not granted, (3) that an injunction would not substantially injure other interested parties, and (4) that the public interest would be furthered by the injunction." *Mylan Labs., Inc. v. Leavitt*, 495 F. Supp. 2d 43, 46 (D.D.C. 2007) (quoting *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998) (internal citations omitted)). For the reasons set forth in this Court's August 23 opinion and in Plaintiffs' motion for a preliminary injunction, and as further explained below, Defendants cannot meet any of the factors of this test.

I. This Court Has Already Decided The Issues Presented In Defendants' Motion In Plaintiffs' Favor.

As an initial matter, this Court's August 23, 2010 order granting Plaintiffs' motion for a preliminary injunction has already resolved all of the issues raised by Defendants' motion to stay. The motion should be denied for that reason alone.

As the D.C. Circuit and this Court have frequently observed, the standards governing a motion for a preliminary injunction and a motion for a stay pending appeal are the same. *See, e.g.*, *Wash. Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 844 (D.C. Cir. 1977); *Mylan Labs.*, 495 F. Supp. 2d at 46 ("The court analyzes motions for a stay pending appeal under the same factors that it considers for motions for a preliminary injunction."). Indeed, the two forms of relief serve the same purpose—to prevent irreparable harm pending the out-

come of litigation. Defendants provide no compelling reason why this Court should revisit its recent decision, made after full briefing and oral argument, which held that a preliminary injunction is necessary to prevent Plaintiffs from suffering further illegal competitive injury by virtue of NIH's consideration of illegal embryonic stem cell research grant applications. "Most of [Defendants'] arguments—if not all of them—are simply repetitions of points made before. They were not considered persuasive then, and they are not persuasive now." *Brown v. Artery Org., Inc.*, 691 F. Supp. 1459, 1461 (D.D.C. 1987) (denying motion for a stay pending appeal of order granting preliminary injunction); *cf. Abdulla Thani Faris Al-Anazi v. Bush*, 370 F. Supp. 2d 188, 199 n.11 (D.D.C. 2005) ("[I]f the petitioners cannot meet the prerequisites of a motion for preliminary injunction (as the Court concludes), it is unlikely that they should receive that same relief through the backdoor of a stay [pending appeal].").

Moreover, "because [the Court] has previously considered the precise legal issue on appeal, the movant's showing of likelihood of success must be impressive." *Mylan Labs.*, 495 F. Supp. 2d at 47 (ruling on a motion to stay following ruling on motion for preliminary injunction). "The law-of-the-case doctrine, which prevents a court from revisiting an issue it has already decided, reinforces this conclusion." *Id.* (citing *LaShawn v. Barry*, 87 F.3d 1389, 1393 (D.C. Cir. 1996)). Under the law-of-the-case doctrine, "the *same* issue presented a second time in the *same case* in the *same court* should lead to the *same result*." *Barry*, 87 F.3d at 1393 (emphases in original).

Defendants cannot clear the high hurdle necessary for this Court to reconsider its recent decision and lift the preliminary injunction pending appeal. Among other reasons, this Court has correctly concluded that Plaintiffs have "a strong likelihood of success" on the merits of their claims, because the NIH Guidelines violate an "unambiguous" statutory provision expressly pre-

cluding any funding for research in which embryos are injured or destroyed. *Sherley*, 2010 U.S. Dist. LEXIS 86441, at *14, *18-19. There is no reason for this Court to allow illegal federal funding for embryonic stem cell research to continue, even for a brief period pending appeal, when those projects are likely to be terminated if and when this Court grants Plaintiffs permanent relief. Conversely, there is no reason to impede for another day meritorious grant proposals from adult stem cell researchers (and other NIH applicants) who have illegally been forced to compete with embryonic stem cell researchers for scarce federal funding.

II. This Court's Preliminary Injunction Order Is Not Overly Broad.

Nor is it necessary for this Court to narrow or otherwise amend its August 23 preliminary injunction order. Defendants devote the lion's share of their motion to challenging the scope of that order, reciting a parade of horribles that will supposedly follow should the order remain in place without modification.

Defendants' concerns are misplaced. A reasonable reading of the Court's order reveals that it either does not apply to the activities that Defendants describe or that Defendants mischaracterize the harm that will allegedly result from the order:

- **Funds Already Awarded to Third Parties for "Extramural" Projects**. Defendants express concern about possible application of the preliminary injunction to third-party grantees that received funds from NIH prior to this Court's August 23 order, but on its face, the Court's order applies only to Defendants and their agents, not to third parties.

- **Research on Stem Cell Lines Approved By Bush Administration.** Defendants also claim that this Court's order prohibits federal funding of research involving stem cell lines in existence prior to August 9, 2001, although such funding was allowed under the prior Administration's policies. The Court's order that Defendants not "tak[e] any action whatsoever pursuant to the . . . Guidelines . . . or otherwise," however, is limited by the phrase, "funding research involving human embryonic stem cells *as contemplated in the Guidelines*." (Emphases added). The order itself thus does not address the prior and much narrower (and since rescinded) NIH policy, or whether NIH could return to that pre-Guidelines policy pursuant to appropriate procedures and federal law.

- **Administrative and Regulatory Activities**. Defendants seek clarification as to whether this Court's order prevents NIH from doing peer review of applications for human embryonic stem cell research or from maintaining or processing applications for the Human Embryonic Stem Cell Registry. The Registry and the peer review processes, of course, are integral parts of the mechanism whereby embryonic stem cell research proposals are submitted and approved for NIH funding in violation of federal law. Therefore, the processing of additional Registry and grant applications contributes directly to the competitive injuries to Plaintiffs (and other scientists) that the preliminary injunction was designed to prevent, and was properly enjoined. But to the extent that the NIH seeks merely to conduct document or website preservation, or activities that are related solely to adult or induced pluripotent stem cell research, the Court's order plainly does not apply.

- **"Intramural" NIH Research**. Finally, Defendants argue that this Court's order should exempt so-called "intramural" NIH projects—that is, research carried out onsite by NIH employees—because Plaintiffs supposedly do not compete with NIH researchers for federal dollars. The only evidence that Defendants submit to support this proposition, however, is Dr. Collins's carefully qualified statement that "[f]unds for intramural and extramural research are specifically budgeted each fiscal year and are not *readily* interchangeable." Collins Decl. ¶ 4 (emphasis added). Congress imposes no such limitation, instead allocating funds to each NIH institute as a whole, so any funds freed up by the prohibition on illegal intramural research could be used to fund additional legal extramural research. *See* Consolidated Appropriations Act, 2010, Pub. L. No. 111-117, div. D, tit. II, 123 Stat. 3034, 3243 (2009); Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, div. F, tit. II, 123 Stat. 524, 767 (2009).

For these reasons, Defendants' requests for clarification or modification of the Court's preliminary injunction order are without merit. And for the reasons explained below, Defendants should also remain enjoined from funding new or existing "extramural" proposals for embryonic stem cell research.

III. This Court's Prior Decision Was Correct On The Merits.

A. Defendants Are Unlikely To Prevail on the Merits of Their Claims

Although the Court need not retread this well-known territory, its August 23 order and decision were also correct on the merits.

1. The Guidelines Violate The Plain Language Of The Dickey-Wicker Amendment.

As this Court explained, Plaintiffs are likely to succeed on their claims for declaratory and permanent injunctive relief because the NIH Guidelines violate the plain language of the

Dickey-Wicker Amendment, which strictly prohibits the funding of "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death." *See Sherley*, 2010 U.S. Dist. LEXIS 86441, at *15. The Court left little doubt that Plaintiffs would ultimately prevail; it "conclude[d] that, by allowing federal funding of ESC research, the Guidelines are in violation of the . . . Amendment." *Id.* at *19.

For all of the reasons set forth in Plaintiffs' motion for a preliminary injunction, *see* D.E. 3, Pls.' Mot. for a Prelim. Inj., at pp. 7-16, this conclusion is undoubtedly correct. Defendants ask this Court to reconsider its ruling for three principal reasons, but none is persuasive.

First, Defendants acknowledge that, under applicable regulations, the term "research" under the Amendment is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Basic HHS Policy for Protection of Human Research Subjects, 45 C.F.R. § 46.102(d) (2010). Defendants argue, however, that the derivation of embryonic stem cells from embryos for the very purpose of experimenting on them is somehow not part of the same "systematic investigation" as the actual use of those cells. According to Defendants, the word "systematic" means "having, showing, or involving a system, method, or plan," and therefore a research project does not need to "include within its scope all steps . . . that made the research possible." Defs.' Mot. to Stay, at 10.

Defendants are incorrect. Under Defendants' own definition, the test is not whether the term "research" includes all "steps that made the research possible," but whether the derivation process is part of the researcher's "system, method or plan." Under that test, the derivation of a stem cell from an embryo is undoubtedly part of the "system, method, or plan" of a researcher who is experimenting on embryonic stem cells. Defendants' interpretation of the statute also ig-

nores its prohibition of funding "research" in which human embryos "are . . . *discarded*." (Emphasis added.) Defendants' view leads to the absurd conclusion that merely "discard[ing]" an embryo would constitute its own, standalone "research" project. To the contrary, the Amendment plainly prohibits funding for any "systematic investigation" that entails, as one part of the overall "system, method, or plan" of research, the discarding or destruction of an embryo.

Second, Defendants claim that the words "in which" and "are destroyed" limit Dickey-Wicker's scope to that part of the research process that involves deriving an embryonic stem cell from an embryo, resulting in its destruction. Defendants' counsel are correct, of course, when they assert that the words "in which" are necessarily limiting. Without a subordinate clause the statute would prohibit *all* NIH funding. This tells us nothing, however, about *what* the statute prohibits.

Defendants' entire argument, therefore, rests on the slender reed of Congress's use of the present tense in describing embryos that "*are*" destroyed or discarded, which Defendants view as restricting the statute to the specific act a researcher is performing at a given moment in time. Defendants' argument, however, divorces the verb "are" from the subject "research." The statute bans the destruction of embryos as part of a "research" project, which is a *continuing* or *systematic* process. Because the destruction of embryos is an essential aspect of the embryonic stem cell research process, it is only logical to speak of the destruction as an event that is concurrent with the "research." Moreover, the implications of Defendants' arguments are absurd. If the Dickey-Wicker Amendment prohibited only the funding of present destruction of human embryos, as Defendants now argue, then NIH could fund even the already-completed—and hence past tense—act of destroying human embryos that was necessary to produce stem cell lines for which researchers "are" now seeking NIH approval. Not even Defendants take that position, in-

stead conceding that they cannot fund such destruction (even though it has by definition already occurred with respect to any NIH-approved stem cell lines). *See* NIH Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170, 32,175 (Jul. 7, 2009) ("NIH funding of the derivation of stem cells from human embryos is prohibited by the annual appropriations ban on funding of human embryo research."). In short, Defendants' argument based on verb tense must be rejected as inconsistent with the NIH's own interpretation of the statute.

Third, Defendants rely on snippets of legislative history to argue that Congress somehow accepted or acquiesced in the validity of the Guidelines under the Dickey-Wicker Amendment. *See* Defs.' Mot. to Stay, at 11-12. Reference to legislative history is inappropriate, however, when as here the text of a statute is unambiguous. *Dep't of Hous. & Urban Dev. v. Rucker*, 535 U.S. 125, 132 (2002). Moreover, the legislative history in this case also contains statements by the Amendment's co-author, Congressman Jay Dickey, and others that support Plaintiffs' reading of the statute.[2] The history is therefore even less helpful than usual, because it "supports conflicting inferences and provides scant illumination." *Carter v. United States*, 530 U.S. 255, 271 n.9 (2000). This only "further confirms the wisdom of relying on the *legislative text* to de-

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[2] Dickey explained that federal funding of embryonic stem cell experiments that incentivizes the destruction of human embryos "undermines the spirit and letter of the law." *Special Hearing on Stem Cell Research: Hearing before the Subcomm. on Labor, Health, and Education of the S. Comm. on Appropriations*, 106th Cong. 9-10 (Nov. 4, 1999); *see also* Statement of Senator Brownback, 147 Cong. Rec. S6393, 6394 (June 19, 2001) (placing in the record a letter from twenty Senators to NIH urging the agency to withdraw the "Clinton-era guidelines which call for the destruction of human embryos for the purpose of subsequent federal funding for the cells that have been derived through the process of embryo destruction" because they were "contrary to the law and Congressional intent," and stating that "[c]learly, the destruction of human embryos is an integral part of the contemplated research, in violation of the law").

termine the purpose of [the statute]." *Nat'l Ass'n of Mfrs. v. Taylor*, 582 F.3d 1, 13 (D.C. Cir. 2009) (emphasis added).

Even if Defendants' warped reading of the term "research" were correct, moreover, the funding they propose would still be illegal, because Dickey-Wicker's prohibition also encompasses research in which embryos are "knowingly subjected to risk of injury or death." Pub. L. No. 111-8, § 509(a)(2), 123 Stat. 803. In order to give any meaning to the phrase "knowingly subjected to risk of injury or death," Defendants must be prohibited from funding research that they know will place additional human embryos at substantial risk of destruction. The NIH, of course, is well aware that the stem cell derivation process necessarily destroys an embryo. By creating a financial incentive for embryonic stem cell research—an incentive that by NIH's own admission involves investments of "hundreds of millions of dollars"—and by specifying the precise means by which embryos must be destroyed in order to qualify for federal funding, the NIH necessarily and knowingly subjects embryos to a substantial risk of injury or death.

2. The Guidelines Are Arbitrary And Capricious And Therefore Invalid Under The Administrative Procedure Act.

Although this Court did not reach the issue, Defendants are also unlikely to succeed on appeal because the NIH Guidelines are arbitrary and capricious under the APA. In their motion for a stay pending appeal, Defendants do not even address Plaintiffs' APA arguments, but they cannot establish likelihood of success on appeal unless they show they will likely prevail on *both* sets of issues. Because Defendants have made no such showing, their motion should be denied.

As Plaintiffs have demonstrated at length elsewhere (*see* D.E. 3, Pls.' Mot. for Prelim. Inj., at pp. 16-33), they are highly likely to succeed on their APA challenge to the Guidelines.

NIH issued the Guidelines pursuant to President Obama's Executive Order 13,505, which provided that the agency "may support and conduct responsible, scientifically worthy human

stem cell research, including human embryonic stem cell research, to the extent permitted by law." Exec. Order No. 13,505, 74 Fed. Reg. 10,667, 10,667 (Mar. 9, 2009). In promulgating the Guidelines, however, the NIH refused to consider or address the thousands of comments it received (roughly 60 percent of 49,015 public comments) that opposed federal funding of embryonic stem cell research. Those comments demonstrated, among other things, that embryonic stem cell research is ethically problematic and shows no signs of leading to effective medical treatments, whereas adult and induced pluripotent stem cell research deliver far greater scientific and medical benefits, are ethically responsible, and comport with the law. *See* D.E. 3, Pls.' Mot. for Prelim. Inj., Declaration of Bradley J. Lingo, Exs. B, C (hereinafter "Lingo Decl."). Inexplicably, however, the agency failed to make *any* attempt to explain its *sub silentio* rejection of those highly relevant categorical objections to funding embryonic stem cell research. NIH thus failed to "examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *U.S. Telecom Ass'n v. FCC*, 227 F.3d 450, 461 (D.C. Cir. 2000) (internal quotation marks omitted). In addition, NIH's stated criteria in the Guidelines established that it could fund only "ethically responsible" and "scientifically worthy" research. NIH Guidelines, 74 Fed. Reg. at 32,170. The administrative record establishes that adult and induced pluripotent stem cell research are categorically superior to embryonic stem cell research under NIH's own stated criteria, because they offer greater scientific and medical promise than human embryonic stem cell research and are ethically superior alternatives. Defendants thus disregarded their own stated criteria and failed to justify their decision to fund embryonic stem cell research in light of those criteria. An agency's disregard of its own stated criteria is the essence of arbitrary and capricious decisionmaking. *See, e.g.*, *Am. Equity Inv. Life Ins. Co. v. SEC*, 572 F.3d 923, 934 (D.C. Cir. 2009) (an agency "must defend its

analysis before the court upon the basis it employed in adopting that analysis"—even if "the [agency] was not required" by statute to base its decision on those grounds).

Defendants' only proffered justification for their failure to consider the comments is that the President's Executive Order purportedly left the agency with no discretion not to fund embryonic stem cell research. That claim is patently incorrect. The language of the executive order itself—which uses the permissive language "*may* support and conduct"—defeats that argument. In any event, even if the Order did require the NIH to fund embryonic stem cell research, the President cannot direct an agency to disregard the requirements of the APA.

For these reasons, and those set forth more fully in Plaintiffs' motion for a preliminary injunction, Defendants are unlikely to prevail on appeal.

B. Defendants Will Not Be Irreparably Harmed By Denial Of A Stay.

Defendants next sound a jeremiad that this Court's preliminary injunction order, if kept in place for the brief period while an appeal is pending, will waste millions of dollars in federal grant money, terminate ongoing scientific experiments, and prevent discovery of potentially life-saving cures to debilitating illnesses. This analysis cannot withstand scrutiny.[3]

First, the harms that Defendants allege all flow from the approval and funding of research prohibited by federal law, as indicated by this Court's finding that Plaintiffs have "a strong likelihood of success." *Sherley*, 2010 U.S. Dist. LEXIS 86441, at *14. Because Defendants have violated the law, they cannot seek equitable relief on the basis that their actions were meritorious or could lead to beneficial results.

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[3] As an initial matter, Defendants' claims of urgency are belied by the fact that they did not file their "emergency" motion for a stay and for expedited briefing until August 31, over a week after this Court issued its order and decision.

Second, the preliminary injunction that the Court has issued will necessarily be of "short duration." *Hoffman-Laroche, Inc. v. Califano*, 453 F. Supp. 900, 903 (D.D.C. 1978). Because the core of this case is a legal rather than a factual dispute, this Court can proceed expeditiously to judgment on the merits of Plaintiffs' claims.[4] Defendants' pending appeal of the preliminary injunction order in the D.C. Circuit could also proceed on an expedited basis. In such circumstances, "[i]ssuance of a preliminary injunction—especially one of the short duration contemplated here—will not substantially harm defendants . . . ." *Id*.

Third, despite the claims made in Defendants' motion about the economic harm that would befall them from the preliminary injunction, Defendants provide little (if any) tangible evidence that any such harm is "certain and great," and "of such imminence that there is a clear and present need for equitable relief," as required by the governing standard. *Wis. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985) (emphasis and internal quotation marks omitted). Dr. Collins cites purely speculative injuries that may (or may not) occur at some point while the appeal is pending, such as the possible death of lab animals or the loss of researchers to opportunities in other countries. *See* Collins Decl. ¶ 12, 14.[5] On the issue of whether biological resources (such as cell cultures) would be lost if research were temporarily halted, Dr. Collins repeatedly hedges his conclusions, and states in general and cryptic terms that "it *may* take months or years

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[4] Plaintiffs intend to file a motion for summary judgment, seeking permanent injunctive and declaratory relief, by September 10, and would not object to expedited consideration of the motion.

[5] Contrary to what Dr. Collins's speculation may suggest, countries on the other side of the Atlantic lead the Americas in certain therapeutic uses of *adult* stem cell research. For example, nearly half (48%) of transplants performed using hematopoietic (blood-forming) adult stem cells in patients with blood disorders and malignancies were performed in Europe, as opposed to 36% in all of the Americas. Deisher Decl. ¶ 20.

to recreate" undefined "unique materials" and "reagents" used in current experiments. *Id.* (emphasis added).

Defendants make no showing that preservation of existing cell lines is impossible under this Court's order. To the contrary, when the NIH recently instructed researchers to halt "intramural" experiments on embryonic stem cells, it also directed that "[p]rocedures that will conserve and protect the research resources should be followed."[6] In short, there is no evidence that Defendants would be unable to resume their current research projects at a later date if the D.C. Circuit lifted the Court's preliminary injunction.

Fourth, Defendants' claim that a brief interruption in research could delay scientific discoveries that could benefit people with debilitating illnesses is, as this Court previously held, purely "speculative." *Sherley*, 2010 U.S. Dist. LEXIS 86441, at *22. Dr. Collins refers often to the promise of embryonic stem cell research, but concedes that the discovery of cures through such research is a mere possibility and has not yet been established. *See* Collins Decl. ¶¶ 5, 7.[7] If anything, the administrative record that the NIH had before it when it issued the Guidelines (including many critical comments that the agency never considered) showed that the promise of embryonic stem cell research is even more limited. That record establishes the serious risks associated with human embryonic stem cell treatments, as well as the inherent limitations on those

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6 Jocelyn Kaiser, *NIH Orders Immediate Shutdown of Intramural Human Embryonic Stem Cell Research*, Science Insider (Aug. 30, 2010), *available at* http://news.sciencemag.org/scienceinsider/2010/08/nih-orders-immediate-shutdown.html.

7 Dr. Collins' statement that a clinical trial involving human embryonic stem cells has been approved tells nothing about the likelihood that that trial will succeed or lead to tangible medical benefits. *See* Deisher Decl. ¶ 11. Similarly, his statement that "differentiated cells derived from hESC are already successfully being used to develop new therapeutic drugs" (Collins Decl. ¶ 6) is unsupported by any facts and does not define what "used to develop" means. *See id.* ¶ 9.

cells' therapeutic potential. *See* D.E. 3, Lingo Decl. Exs. B, C. It also details the substantial and verifiable medical results already delivered by adult stem cells, and other characteristics that render adult stem cells a superior scientific and ethical alternative. *Id.*; *see also* Deisher Decl. ¶ 12 (noting that, unlike embryonic stem cells, adult stem cells have "already produced published positive therapeutic benefits for spinal cord injury patients") (emphasis omitted). Thus, the loss of grant money for embryonic stem cell research that violates federal law will actually *further* scientific advances and future medical cures by freeing up additional funds for more promising grant proposals—such as adult stem cell research.

In short, Defendants' claims of irreparable harm assume (wrongly) that dollars not spent on embryonic stem cell research will simply disappear into the ether. To the contrary, the Court's order makes those dollars available for other, more promising and less ethically fraught medical research projects. In addition, given the fact that Plaintiffs are likely to obtain permanent injunctive and declaratory relief in the future, a stay is likely to cause Defendants *additional harm* in the long run. If federal funding resumed, NIH would spend additional federal dollars on embryonic stem cell research and initiate new projects. If this Court later issued a final judgment invalidating the Guidelines, all interested parties—the NIH, scientists, and taxpayers—would face additional purported losses of the type claimed by Defendants. Federal dollars should not be spent in so reckless a manner. Rather, the prudent course is to keep the preliminary injunction in place until this Court and the D.C. Circuit have had the opportunity to reach a final resolution of the important legal issues raised by this case.

C. A Stay Pending Appeal Would Cause Substantial Harm To Plaintiffs And Other Interested Parties.

In contrast to a temporary delay in illegal funding for research that raises grave ethical issues and has not proven to yield tangible medical benefits, Plaintiffs and other interested parties

(including adult stem cell researchers and other NIH grant applicants generally) would suffer irreparable competitive injuries from a stay of the preliminary injunction.

Defendants lampoon the harm suffered by Plaintiffs in this case as merely the need to invest more time in filling out research applications. *See* Defs.' Mot. to Stay, at 21. In reality, the NIH has a limited budget for funding scientific research that could lead to potentially life-saving medical breakthroughs, and Plaintiffs—as well as other adult stem cell researchers and the scientific community as a whole—must compete for those federal dollars. As the D.C. Circuit has recognized, Plaintiffs suffer immediate and legally cognizable injury from being forced to compete with illegal grant applications, and they and other applicants should not have to face such illegal competition for a single additional day. Defendants' claims of harm to third parties (embryonic stem cell researchers and persons seeking medical cures) rest on an utterly false dichotomy, namely the assumption that there is no alternative to funding embryonic stem cell research. As the administrative record makes clear, there are such alternatives, including both adult and induced pluripotent stem cell research, and those *alternatives* are *more* likely to result in cures for debilitating diseases, and thus *more* likely to benefit patients. *See supra* pp. 5-6, 10-11.

As this Court found in its August 23 decision, the Guidelines, "by allowing federal funding of ESC research, increase[] competition for NIH's limited resources." *Sherley*, 2010 U.S. Dist. LEXIS 86441, at *21. Therefore, adult stem cell researchers, such as Drs. Sherley and Deisher, would suffer "actual, imminent injury" if federal dollars continued to be diverted to embryonic stem cell research. *Id.*; *see also Sherley v. Sebelius*, 610 F.3d 69, 74 (D.C. Cir. 2010) (find-

ing that Plaintiffs suffer injury "whenever a project involving ESCs receives funding that, but for the broadened eligibility in the Guidelines, would have gone to fund a project of theirs").[8]

It is well-established that economic losses cause irreparable harm where there is "'no adequate compensatory or other corrective relief' that can be provided at a later date." *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997) (quoting *Hoffmann-Laroche, Inc. v. Califano*, 453 F. Supp. 900, 903 (D.D.C. 1978)).[9] That standard is met here because, as this Court found, "[t]here is no after-the-fact remedy for this injury because the Court cannot compensate plaintiffs for their lost opportunities to receive funds." *Sherley*, 2010 U.S. Dist. LEXIS 86441, at *21; *see also Sherley*, 610 F.3d at 74 (finding that Plaintiffs "are more likely to lose funding to projects involving ESCs than are researchers who do not work with stem cells because [adult stem cells] and ESCs are substitutes in some uses"). The Court's conclusion was amply supported by the record. *See* D.E. 3, Decl. of Dr. James L. Sherley in Support of Pls.' Mot. for Prelim. Inj., ¶¶ 3–4; D.E. 3, Decl. of Dr. Theresa Deisher in Support of Pls.' Mot. for Prelim. Inj., ¶¶ 3–4.

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[8] Defendants' allege that neither Plaintiff currently has any grant proposals pending that could be affected by funding for embryonic stem cell research. That is mistaken. Dr. Sherley currently has two proposals related to adult stem cell research pending before NIH. *See* Exhibit B, Declaration of Dr. James L. Sherley ¶ 4 (Sept. 2, 2010). Dr. Deisher in turn is in the process of applying for NIH grant money. *See* Deisher Decl. ¶ 4.

[9] Defendants' argument that they "will be forced to make payments that will be irrecoverable" in order to bring their (illegal) funding system into compliance with the Court's order is misplaced. Every dollar spent in violation of Dickey-Wicker is contrary to law and "will be irrecoverable," which is a significant reason why defendants' motion should be denied.

The harm that will result from a stay pending appeal is not merely pecuniary and is not limited to the Plaintiffs that appear before the Court.[10] To the contrary, adult stem cell researchers and other NIH grant applicants will lose the opportunity to pursue their own research interests, which could lead to potential cures and other medical and scientific breakthroughs. As Defendants repeat throughout their motion, this Court's decision will have an effect on patients with diseases and society as a whole. But that consideration weighs decisively *against* a stay, because (as shown in the administrative record) adult stem cell research has proven more likely to lead to effective treatments than embryonic stem cell research.

Moreover, a stay would itself cause irreparable harm to American taxpayers and flout the will of Congress. As noted above, the Court's order applies only to Defendants and their agents, not to third parties. As a result, NIH takes the position that awards granted on or before August 23, 2010, "are not affected by the preliminary injunction order, and award recipients may continue to expend the funds awarded to them prior to the date of the injunction."[11] If this Court were to grant a temporary stay, Defendants would have every incentive to disburse as much federal money as they could to third party grantees before the Court awarded Plaintiffs permanent relief. Once those millions of dollars are given to third parties and spent (in violation of Dickey-

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10 *See, e.g.*, *Mova Pharm. Corp.*, 140 F.3d at 1066 (standard permits consideration of harm to "other interested parties" in litigation); *Va. Petroleum Jobbers Ass'n v. Fed. Power Comm'n*, 259 F.2d 921, 925 (D.C. Cir. 1958) (court may consider harm to "other interested persons").

11 "Status of Applications and Awards Involving Human Embryonic Stem Cells, and Submissions of Stem Cell Lines for Eligibility Consideration," National Institutes of Health (Aug. 30, 2010), *available at* http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-126.html (last viewed Sept. 3, 2010).

Wicker), they are irreparably lost to taxpayers and other NIH researchers under the terms of the Court's order.

Finally, the harm to the embryos that would be destroyed if a preliminary injunction were lifted—precisely the harm that the Dickey-Wicker Amendment was enacted to prevent—would be irreversible. "Simply put, absent some form of preliminary relief [the embryos] run[] the real risk of dying and in such circumstances money damages would be wholly useless . . . ." *DiDomenico v. Employers Coop. Indus. Trust*, 676 F. Supp. 903, 907 (N.D. Ind. 1987).[12]

D. The Public Interest Favors Denial Of A Stay.

Finally, the public interest weighs strongly in favor of denying Defendants' request for a stay. In passing the Dickey-Wicker Amendment, Congress necessarily mandated that the public interest would be served by preventing taxpayer funding of research that entails the destruction of human embryos. It is well-established that "[i]t is in the public interest for courts to carry out the will of Congress and for an agency to implement properly the statute it administers." *Mylan Pharm., Inc., v. Shalala*, 81 F. Supp. 2d 30, 45 (D.D.C. 2000). By vindicating Congress's prohibition of research that entails the destruction of human embryos, keeping the preliminary injunction in place will serve the public interest. *See Sherley*, 2010 U.S. Dist. LEXIS 86441, at *22-23 (finding preliminary injunction is in public interest because "the will of Congress, as expressed

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[12] It makes no difference for purposes of irreparable injury analysis that the embryos in question are not yet mature human beings. On the contrary, courts have recognized that the threat of harm to a human being not yet born can constitute irreparable harm for purposes of determining the propriety of injunctive relief. *See, e.g.*, *Lewis v. Grinker*, 1987 WL 8412, at *6 (E.D.N.Y. Mar. 6, 1987) (finding that denial of Medicare may lead to irreparable harm of unborn child); *Woe v. Perales*, 1987 WL 108983 (W.D.N.Y. Oct. 29, 1987) (finding that denial of prenatal care constitutes irreparable harm "[g]iven the importance of this prenatal care to the health of the fetus and the future health of the yet unborn child").

in the Dickey-Wicker Amendment, is to prohibit federal funding of research in which human embryos are destroyed").

Moreover, denial of a stay will serve the public interest by preventing a wasteful diversion of public funds to needless and relatively unpromising research. Because the Guidelines divert funds away from more promising types of research and perpetuate popular misconceptions about the science of embryonic stem cells, a preliminary injunction will serve the interest of the public.

Finally, denial of a stay will also serve the public's interest by withholding taxpayer dollars from a type of research that many taxpayers and States recognize to be ethically and morally troubling. The laws of numerous States protect human life from the moment of conception or otherwise protect human embryos from being destroyed for the purpose of medical experimentation. *See* Lingo Decl. Ex. B, Appendix C (collecting authorities). The public interest is disserved by federal funding of an immoral and unnecessary research method.

CONCLUSION

In the face of this Court's holdings that Dickey-Wicker is "unambiguous" and that Plaintiffs therefore have "a strong likelihood of success on the merits," Defendants' arguments fall far short of demonstrating that *defendants* have a substantial likelihood of success on the merits. Moreover, for all the above reasons, Defendants are unlikely to succeed on appeal, and neither they nor the public will suffer irreparable harm from the denial of a stay pending appeal. To the contrary, this Court's preliminary injunction advances the public interest by ensuring that adult stem cell researchers and other meritorious NIH grant applicants can seek federal funding free from competition from illegal, ethically dubious, and scientifically problematic embryonic stem cell research. Defendants' motion for a stay pending appeal should be denied.

Dated: September 3, 2010

Respectfully Submitted,

/s/ Thomas G. Hungar

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Certificate of Service

I hereby certify that on September 3, 2010, I caused a true and correct copy of the foregoing Plaintiffs' Opposition to Defendants' Motion To Stay Preliminary Injunction Pending Appeal to be served on Defendants' counsel electronically by means of the Court's ECF system.

/s/ Thomas G. Hungar

Thomas G. Hungar

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al. Plaintiffs, v. KATHLEEN SEBELIUS, et al. Defendants.	Civil Action No. 1:09-cv-01575 (RCL)

DECLARATION OF FRANCIS S. COLLINS

I, Francis S. Collins, M.D., Ph.D., pursuant to 28 U.S.C. § 1746, declare under penalty of perjury as follows:

1. I am the Director of the National Institutes of Health ("NIH"). I am responsible for setting policy for NIH and for planning, managing, and coordinating the programs and activities of all the NIH components. I am informed about program priorities and accomplishments through Office of the Director staff, Institute and Center staff, as well as through the extramural scientific community, patient advocacy and voluntary health groups, and Congress. Prior to assuming the role of NIH Director in August 2009, I served as the Director of the National Human Genome Research Institute from 1993-2008. I have also worked part-time as a senior investigator of an NIH intramural research laboratory where I conduct experimental research and lead a team of biomedical research scientists.

2. In these positions, I am familiar with the process used by NIH to review applications for research grants as well as the day to day operations at NIH by intramural scientists, and I make this declaration based upon information within my personal knowledge or provided to me in my official capacity.

3. NIH funds grants, cooperative agreements, and contracts that support biomedical and behavioral research leading to the advancement of fundamental knowledge about the nature and behavior of living organisms and the application of that knowledge to the causes, diagnosis, prevention, treatment, and cure of human diseases, conditions, and injuries.

4. NIH supports research both within and outside the NIH community. Funds for research conducted by academic and other institutions not affiliated with NIH, referred to as extramural research, are provided through a competitive, peer review process operated by NIH. Extramural research accounts for approximately 84 percent of the NIH's budget. NIH also employs scientists who conduct research in government laboratories on the NIH campus and elsewhere. Research conducted directly by NIH through its scientist employees is referred to as intramural research, and accounts for approximately 10 percent of the NIH budget. Funds for intramural and extramural research are specifically budgeted each fiscal year and are not readily interchangeable. NIH supports all of its research through Institutes and Centers (ICs) that award grants and conduct intramural research, as well as the Office of the Director. See List of Institutes, Centers and Offices, at http://www.nih.gov/icd/. NIH supports both intramural and extramural human embryonic stem cell research.

The Importance of Human Embryonic Stem Cell Research

5. Human embryonic stem cells ("hESC") were first isolated in 1998 by Dr. James Thomson at the University of Wisconsin. On August 9, 2001, President George W. Bush determined that NIH funds could be used to support hESC research if the following criteria were met: (i) the derivation process (which begins with destruction of the embryo) was initiated prior to 9 pm EDT on August 9, 2001, (ii) the stem cells had to be derived from an embryo that was created for reproductive purposes and no longer needed, (iii) informed consent must have been obtained for the donation of the embryo, and (iv) there could be no financial inducements for the donation. NIH ultimately determined that 21 hESC satisfied President Bush's criteria and therefore were eligible for use in NIH funded research. Investigators have embraced this opportunity to realize the remarkable potential of hESC to pursue critical questions about how the different cells of the human body develop, how they are affected by disease, and how hESC can contribute to the development of therapeutics through cell replacement and/or drug screening.

One of the first awards for hESC research was made to Dr. George Daley at Children's Hospital in Boston in 2002 to dissect the molecular mechanisms responsible for turning hESC into blood cells and their precursors. He is currently funded to compare the ability of hESC and induced pluripotent stem cells (described in ¶ 7) to produce blood cells. Including that initial award and his present funding, NIH has provided more than $2.7 million dollars to his laboratory

alone, and as a result, Dr. Daley has produced a detailed procedure for the generation of blood cells from hESC. Based on his progress in directing hESCs to develop into blood cells, it is possible in the future that they could be used to address virtually all genetic and malignant blood diseases that are currently treated by gene therapy or bone marrow transplant. These include sickle cell anemia, Fanconi's and other congenital anemias, Hodgkin's lymphoma, chronic lymphocytic and myelogenous leukemias and myelomas, among others.

Since those first awards in 2002, NIH has a total aggregated investment of $546 million in intramural and extramural hESC research. As a result of these investments, NIH funded animal studies, often referred to as preclinical studies, are underway to test whether cells or tissues derived from embryonic stem cells, human and/or mouse, are of benefit for retinal degeneration, stroke, liver failure, muscular dystrophy, myelin deficiencies, motor neuron diseases, and Huntington's disease.

Stem cell research holds great promise for the development of treatments for a wide range of serious and life-threatening diseases and conditions. Some of those opportunities for basic and applied research are described in a document from the National Academies of Science, Understanding Stem Cells: An Overview of the Science and the Issues (2009). Research into the unique properties of stem cells may lead to major medical breakthroughs that would offer hope to people suffering from cancer, diabetes, cardiovascular disease, spinal-cord injuries, neurodegenerative conditions, and many other disorders. Both adult stem cell and hESC research show further promise to develop our understanding of and treatments for many diseases, conditions, and injuries, such as blood disorders, heart disease, autoimmune disorders like multiple sclerosis, lysosomal disorders, as well as joint and bone disease.

6. Indeed, remarkable progress has already been made in realizing the possible benefits of hESC research. Even though hESC were not even isolated until 1998, the first clinical trial of a hESC-derived therapy has received FDA approval to begin enrolling spinal cord injury patients. This trial will test the safety of using hESC-derived precursors for the cells that insulate nerves in the spinal cord to restore spinal cord function. This is a remarkable achievement and heralds what should be the beginning of a new era in cell-based therapy. Equally important, differentiated cells derived from hESC are already successfully being used to develop new therapeutic drugs for a number of diseases including amyotrophic lateral sclerosis ("Lou Gehrig's disease") and spinal muscular atrophy, to name just a few. Without dependable and consistent

support from NIH, hESC research and development of new therapies will be dealt a critical blow that will have dire ramifications for those suffering from the many diseases and disorders may be treatable with hESC-based therapies or drugs developed using hESC testing.

7. Opponents of hESC research posit that adult or non-embryonic stem cells have the same potential for therapeutic benefit as hESC. In considering the relative benefits of adult and embryonic stem cell research, it is critical to remember that adult stem cells were identified over a half century ago and have been the subject of robust research for decades. This research has produced FDA-approved treatments that reconstitute the immune system after leukemia, lymphoma, and various blood or autoimmune disorders have been treated with chemotherapy.

NIH believes that it is important to continue to support research using adult stem cells since there may be additional clinical applications for which they will be useful. However, adult stem cells also have serious limitations that fifty years of research have not been able to overcome. First, they are currently available in quantity only from blood forming tissues and cord blood and once collected, they do not divide indefinitely and therefore produce a finite number of cells. Second, despite many years of work, it has not been possible to differentiate adult stem cells into cell types that are very different from their tissue of origin. A bone marrow stem cell, for instance, cannot be differentiated into a neuron. In contrast, hESC can be expanded in cell culture to essentially limitless numbers. They are also "pluripotent": with appropriate protocols, it appears that they can be turned into any of the different cells of the human body. These expanded cell populations can be used to elucidate disease pathogenesis and screen new drugs, as well as to develop cell-based therapies. This is particularly important in the case of human brain cells, which are not readily available from other sources as brain biopsies are only justified for diagnostic purposes and brain autopsies do not yield viable nerve cells. Thus, hESC may offer significantly more scientific and clinical potential than do adult stem cells.

Very recently, scientists discovered that it is possible to instruct adult skin cells to return to a very early developmental stage. This can be accomplished using viruses carrying molecular signals that turn back the developmental clock so that they possess hESC-like properties: they continue to divide indefinitely and are pluripotent, with the potential to give rise to all the cells of the human body. These induced pluripotent stem cells ("iPSC") represent a new, third category of stem cells and were discovered as a direct result of the knowledge gained from studying hESC. They are of great interest to scientists. However, they are not well understood yet, and a

growing body of research suggests that there are significant biological differences between iPSC and hESC. In addition, there are significant safety issues because viruses and a cancer gene are used to induce pluripotency in most of the protocols used to generate iPSC. Most scientists believe that it is essential to continue research on hESC as we explore the potential of iPSC.

In FY 2009, NIH funded over 1,000 extramural projects and subprojects involving non-embryonic human stem cells (including adult stem cells and iPSC), totaling $397 million. During FY 2010, NIH has provided an estimated $380 million in non-embryonic human stem cell research funding.

The Impact of the Court's Order on hESC Research

8. The preliminary injunction issued in this case will have extraordinary adverse effects not only on the prospects of delivering new therapies to patients suffering from numerous diseases and disorders but also on scientific progress from the wider biomedical research community. It will result in immeasurable loss of valuable and one-of-a-kind research resources. Unique modifications and applications of hESC, underway in laboratories with federally-funded research as far back as 2002, could be lost irretrievably or could take years to recreate. Experiments that may have been months or years in development will be halted prematurely, before any promising results can be obtained. Investigators who have devoted their careers to this exciting area of research may have to close their laboratories or move to another country. Government resources already expended on hESC research to date, including over $546 million dollars of public funds, will have been wasted and the mission and operations of NIH will be severely hampered as a result of this Court's Order.

Disruption to Extramural Research

9. As a result of the Court's Order, NIH is prohibited from awarding funds to extramural research projects involving hESC, thereby jeopardizing grants for research projects that are in varying stages of funding. These grants include research projects that have the potential to advance the use of hESC in therapies for heart disease, sickle cell disease, liver failure, muscular dystrophy, and other critical diseases and conditions. Grants typically have 3-5 year project periods but receive funding only on an annual basis, consistent with NIH appropriations. At this time, three categories of grants are affected: (1) grants already awarded that are up for their next year of continuation funds by September 30, 2010, (2) applications for grants that have successfully completed the first level of peer review and are scheduled to

receive final approval by Institute Advisory Councils, after which NIH expected to provide the first year of funding by September 30, 2010, and (3) applications for grants that are currently in the peer review process.

10. With respect to research projects already under way, the Court's Order prevents NIH from providing $54 million in funds to 24 hESC research projects that were expecting to receive continuation funds by September 30, 2010. These 24 projects have already received a combined $64 million in funding from NIH over the previous years of their project periods. Taxpayer money already invested in these research projects will be irretrievably lost due to this Order. In addition, these institutions depend on NIH for continued financial support. Prior to this Court's Order, these projects would have been eligible to receive their next year of continued support, contingent upon the completion of an annual progress report. The grants include projects that study basic aspects of stem cell biology, advance stem cell technology, and work towards applying hESC to therapies for a variety of diseases and disorders. Examples of these projects include the following and all use lines that were eligible before the NIH Guidelines for Human Stem Cell Research ("Guidelines") were issued on July 7, 2009 (described in ¶ 5 above):

- Dr. Church and his research team from Children's Hospital in Boston, Massachusetts, and Harvard Medical School are conducting a comprehensive comparison of hESC and induced pluripotent stem cells ("iPSC"). It is absolutely essential that we learn whether or not there are significant functional differences between hESC and iPSC. A growing body of evidence suggests that the two classes of pluripotent cells are not identical and therefore iPSC cannot be universally substituted for hESC. This research is expected to provide invaluable information on the use of hESC as compared to iPSC for many applications, including development of life-saving therapeutic strategies.
- Dr. Fox at the University of Pittsburgh is exploring hESC as a potential replacement source of liver cells for transplantation. At present the only treatment for liver failure is liver transplantation. There are not enough donor livers available and the surgery is technically difficult and risky. One way to overcome these problems would be to use liver cells derived from hESC. Dr. Fox is making excellent progress and has shown that he can generate 100,000 to 200,000 pure liver cells and transplant them successfully into an animal model of liver failure. The next steps would be to develop methods to significantly increase the number of liver cells produced in preparation for exploring non-human primate models.

- Dr. Spence at the Children's Hospital Medical Center in Cincinnati, Ohio is working on methods to direct hESC more efficiently into therapeutically important tissues including the lung, liver, pancreas, and intestine. He has identified two chemical signals that determine whether the hESC will become liver or pancreas. This grant is a two-year fellowship to support his training before he looks for a position as an independent scientist. Absent a stay of this Court's Order, the funding for the second year would be suspended, likely terminating his training and quite possibly jeopardizing his future career.
- Dr. Parsons from the University of California Riverside is studying how to manipulate hESC differentiation into brain cells, both neurons and supporting cells. Death of nerve cells has devastating consequences since they do not regenerate and there is no source for replacement. As noted earlier, it is extremely difficult to obtain brain cells from children and adults for studies of possible therapeutic agents. The development of recipes for directing hESC reliably to form nerve cells would have extraordinary implications for cell replacement in neurodegenerative diseases like Parkinson's disease and amyotrophic lateral sclerosis ("Lou Gehrig's Disease"). Such derived nerve cells can also be extraordinarily useful for identifying new drugs that may protect the brain and prevent conditions like Alzheimer's disease. Dr. Parsons, who is early in his career as an independent scientist, is making remarkable strides toward this goal. If his funding lapses as a result of this Court's prohibition on funding hESC research, progress will cease and he may not be able to continue as an investigator.

11. The preliminary injunction affects not only NIH's ability to fund projects that have been initiated after Executive Order 13505 issued on March 9, 2009, and the Guidelines that the Plaintiffs challenge, but also its ability to fund projects that were already in progress during the previous Administration. Of the 24 hESC grants discussed above, almost all of them were in progress prior to July 7, 2009, when the Guidelines were issued. The preliminary injunction would therefore not return NIH and the research community to the position that they were in before the Guidelines issued, but would impede research that has been ongoing since 2002. Long-existing projects up for renewal in the period between now and final judgment will be shut down by lack of NIH funding and the scientific community and taxpaying public now stand to lose much of the benefits of many years of research in which NIH has thus far invested.

12. Even a temporary suspension of funds would jeopardize ongoing research projects. When a laboratory experiment is prematurely interrupted, it cannot be easily restarted. Such experiments involve biological materials such as cell lines growing in lab incubators that must be managed daily to encourage growth and prevent contamination. Valuable laboratory animals serving as models of spinal cord injury, Parkinson's disease, or diabetes that were being used to test new therapies under grants using hESC may be lost, many of them forced into euthanasia. Once critical research tools and reagents – including unique materials that have taken years to develop – have been lost due to the termination of research for lack of funding, it may take months or years to recreate them, if recreation is even possible. In addition, laboratory personnel whose jobs depend on grant funds may be let go and the best investigators, including promising young investigators, may abandon this line of research or move to other countries that support hESC studies. In fact, during the period when only 21 hESC lines were available for investigators to use with NIH funds, one prominent United States stem cell scientist moved to England to pursue hESC research.

13. Prior to this Court's Order, NIH had already provided funding to 199 grants for research on hESC in FY 2010 in the amount of $131 million. We do not interpret the intent of this Court's Order to require NIH to deobligate the funds already awarded to these projects. NIH payments on grant awards are managed through an electronic payment system. Each of the institutional grantees has its own account. These accounts hold funds for all the grants the institution has received from both NIH and other HHS operating divisions; thus, the funds in the grantees' accounts are from multiple grant awards addressing a variety of research topics. After the grant award, authorized grantee representatives access their accounts and draw down funds as needed at their discretion through the electronic payment system, with no involvement of agency officials.

14. Discontinuing support for all hESC grants in future Fiscal Years will have drastic economic and scientific consequences. Economically, it is estimated that each NIH grant directly supports six jobs at the local institution. See McGarvey, WE, Morris, P, Li, X, Li, J, Probus, M, Cissel, M, Haak, LL (2008) How Many Scientists Do the NIH Support? Improving Estimates of the Workforce. NIH Analysis Report 20081219, 1-23, http://report.nih.gov/FileLink.aspx?rid=530. Thus, discontinuing financial support for the 223 research projects (mentioned above as 199 grants given FY 2010 funds and 24 continuing grants

awaiting FY 2010 funds prior to this Order) would result in the loss of over 1,300 full or part-time jobs, as well as the potential loss of top U.S. scientific talent as lead scientists may be forced to move to other countries to pursue their cutting-edge hESC research. In addition, since these projects are being discontinued mid-stream, all the funds that have been put in accounts or already drawn down until this point ($270 million over the two to five year life of these grants, including what has been provided FY 2010) will have been wasted as investigators and labs can neither finish their current projects nor pursue what has been learned. The momentum that has finally been established in the hESC research field will be lost. Young scientists may turn away from this field due to the instability of stopping, then starting and now stopping again. More senior investigators may look to other countries such as Singapore, China, and the United Kingdom to pursue their work. The greatest loss, however, will be for the millions of Americans suffering from illnesses currently under study with hESC, including liver diseases, cardiovascular diseases, eye diseases, and neurodegenerative diseases like Alzheimer's and for those who might in the future have received transplants of cells and tissues created from hESC because donated organs are not available.

15. This Order also will prevent about 20 new hESC applications from being awarded for $24 million dollars. These 20 applications have not been previously supported by NIH, were approved in a rigorous peer review process as scientifically meritorious, and were expected to be approved by the Institute Advisory Councils in September 2010 to receive funding prior to this Order. As science is always changing, supporting new, cutting-edge science is critical to spur innovation and prevent stagnation of scientific progress.

16. In addition, this Order will prevent 211 grant applications, which have been submitted and are at varying stages of the peer review process, from completing the peer review process. It is not known how many of these applications would have been deemed sufficiently meritorious in peer review to be funded.

Disruption to Intramural Research

17. Implementation of this Order will have particularly harsh effects on the NIH intramural program. Currently there are 8 intramural hESC research projects staffed by approximately 45 scientists and other personnel, with a total combined budget of about $9.5 million (FY 2009 data). The scope of these projects is broad, covering research areas such as cancer, neurological diseases, cardiovascular disease, human development, and eye diseases.

NIH has already initiated research project termination activities in response to this Court's Order. In addition to the specific research projects, the intramural program also has a Human Stem Cell Unit which supports intramural hESC researchers. The members of the Unit characterize the properties of hESC lines, train intramural investigators to use hESC in experiments, and collaborate with them on specific projects. This unit has an annual operating budget of $800,000 and employs four people. NIH is also in the process of recruiting a new Director for the Center for Regenerative Medicine, one of my highest scientific priorities for the intramural program. The goals of this Center are to move pluripotent stem cells into clinical trials. The inability to use hESC for such comparison studies will likely affect this recruitment severely; recruiting a top notch scientist to take on this role under such circumstances is highly unlikely, and so the scope and value of the research planned for this regenerative medicine center will be lost.

Disruption to Agency Administration and Mission

18. Implementation of this Order has severely disrupted NIH from completely fulfilling its mission. For example, peer review, a cyclical rolling process involving approximately 15,000 reviewers reviewing approximately 80,000 applications on an annual basis, has been halted for hESC applications. If disruption to the cycle continues for a significant length of time and then the process is reinstated, it could take up to 6-8 months for the hESC applications that are currently in the system and being deferred to undergo consideration by peer review, causing significant delay to additional hESC research projects.

19. In addition, the process for determining eligibility of hESC lines for NIH funding and inclusion on the NIH Human Embryonic Stem Cell Registry will be halted, causing major disruption to the NIH and the biomedical community. Owners of cell lines who wish to receive a designation of eligibility for their lines from NIH must submit detailed documentation of the consent process and other factors related to compliance with the Guidelines. Review of this detailed documentation is performed by outside expert reviewers. NIH has already had to cancel a meeting of the reviewers overseeing these applications that had been scheduled for August 24, 2010, and the future of that group is in jeopardy.

20. Finally, the proposed change to the NIH Guidelines (per February 23, 2010 Federal Register notice) has been suspended. This change, as proposed, would have expanded the definition of "human embryonic stem cells" to include those derived from embryos that did not reach the blastocyst stage and allowed for additional lines to be considered by NIH.

21. Although difficult to quantify exactly, the financial loss to NIH and to the taxpaying public which has funded the research to date, including the hundreds of millions already spent on funding interrupted extramural research projects, the millions lost on intramural research, and the administrative costs of shutting down and restarting the NIH regulatory regime for hESC research, would be enormous. Though not all of the indirect consequences can be easily quantified, NIH has directly invested over $546 million of taxpayers' money in intramural and extramural hESC research since 2002.

Effect On Plaintiffs Sherley and Deisher

22. The plaintiffs argued that NIH support for hESC research harmed their ability to obtain funding for their own work on adult stem cells. But applications for research using adult stem cells, iPSC, and hESC are not in direct competition with each other for funds. As cited above, NIH estimates it will support $380 million in human non-embryonic stem cell research in FY 2010. That total is significantly more than the $131 million provided for all hESC research to-date in FY 2010. But it is highly unlikely that Plaintiffs would benefit from any additional available funds that would have gone to existing or approved hESC projects. Only a very small part, if any, of the money made available to the NIH's $26 billion extramural research program is likely to go to stem cell research because stem cell research proposals must compete with *all* other extramural research applications according to the ordinary NIH grant review process, which takes into account the research priorities of each NIH institute as well as the scientific merit of each proposal.

23. Plaintiff Dr. James Sherley has been a successful principal investigator ("PI") on prior research grants from NIH. In 2006, the Massachusetts Institute of Technology, with Dr. Sherley as PI, received the first year of a five year grant totaling $2.5 million in direct costs under the NIH Director's Pioneer Award (NDPA) Program that is expected to continue through 2011. In 2007, the NDPA was transferred to Dr. Sherley's current employer, the Boston Biomedical Research Institute. A grant supplement was also made on July 20, 2009, under the American Recovery and Reinvestment Act ("ARRA") of 2009. In 2010, despite the lifting of certain prior restrictions on hESC research funding and the allowance of a broader range of hESC research consistent with the Guidelines, Boston Biomedical Research Institute with Dr. Sherley as a PI received a $425,500 Shared Equipment Grant under the NIH ARRA program. Ongoing hESC research and applications for funding for new hESC projects have thus not posed

a barrier for Dr. Sherley. Prior to the promulgation of the Guidelines, between 2007 and 2009, Dr. Sherley has submitted five additional applications to NIH that were not awarded based on the results of peer review. The limited merits of the applications that Dr. Sherley submitted were the reasons for the declination of his applications, not competition from hESC applications. In addition Dr. Sherley's success rate equals or betters the NIH wide average of 20% since he received three grants out of eight applications.

24. While plaintiff Dr. Theresa Deisher received training support from NIH in the early 1990s, she has to my knowledge neither applied for nor received any NIH research grants either individually or as a PI for her organizations.

I declare under penalty of perjury that the foregoing is true and correct. Executed at Tecumseh, Michigan, this 31st of August, 2010.

Francis S. Collins

FRANCIS S. COLLINS, M.D., PH.D.
Director
National Institutes of Health

EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al., Plaintiffs, v. KATHLEEN SEBELIUS, et al., Defendants.	Civil Action No. 09-CV-01575-RCL

DECLARATION OF DR. THERESA DEISHER IN SUPPORT OF PLAINTIFFS' OPPOSITION TO A STAY OF THE PRELIMINARY INJUNCTION

I, Dr. Theresa Deisher, declare as follows:

1. I am a plaintiff in this action, and I am over the age of eighteen and competent to testify. I am knowledgeable about the facts set forth herein and make this declaration in opposition to Defendants' Motion for a Stay.

2. I received my B.A. in Human Biology and Ph.D. in Molecular and Cellular Physiology from Stanford University. I have nineteen years of experience in scientific and corporate leadership positions involving research, discovery, production, and commercialization of human therapeutics.

3. I am an adult stem cell researcher specializing in adult stem cell therapies and regenerative medicine. I work exclusively with adult stem cells, and I do not conduct research on human embryos or use human embryonic stem cells.

4. I am the founder, managing member, and research and development director of AVM Biotechnology. I personally founded AVM Biotechnology, with the help of private donors. These funds are limited, and additional private funding is scarce and difficult to obtain. In order to continue my research, and in order for AVM Biotechnology to achieve success, I must obtain funding from the National Institutes of Health ("NIH"). I am currently in the process of applying for NIH funding, and I will continue to seek funding for adult stem cell research in the future.

5. The National Institutes of Health Guidelines for Human Stem Cell Research will result in increased competition for the limited resources that are available to fund human stem cell research, threatening my ability to obtain federal funding for my adult stem cell research.

6. The Declaration of NIH Director Francis S. Collins ("Collins Decl.") submitted in support of the Government's Motion for Stay contains numerous factual assertions and characterizations regarding the nature of and prospects for adult stem research, human embryonic stem cell research, and induced pluripotent stem cell research that are directly contrary to the evidence in the administrative record, and that do not accurately reflect the published literature on those subjects. This declaration will address and correct some of Director Collins's more substantial errors and mischaracterizations.

History of Stem Cell Research

7. The Collins Declaration compares the history of embryonic stem cell research with adult stem cell research, but mischaracterizes the actual facts in that historical comparison,

by using the non-equivalent terms "isolated" and "identified." (See Collins Decl. ¶¶ 5, 7.) The declaration asserts that "[h]uman embryonic stem cells ("hESC") were first *isolated* in 1998" (*id.* ¶ 5 (emphasis added)), and then subsequently asserts that "adult stem cells were *identified* over a half century ago and have been the subject of robust research for decades" (*id*. ¶ 7 (emphasis added)). The comparison is not parallel, as "identified" simply indicates observation of the existence or potential existence of the stem cell, whereas "isolated" signifies verification of the existence of the stem cell by physically obtaining, manipulating, and growing the target stem cell in the laboratory. The accurate comparison from the published literature shows that mouse embryonic stem cells were first isolated and successfully grown in the laboratory in 1981,[1] while the first mouse adult stem cell was successfully isolated and purified in the laboratory in 1988.[2] Human embryonic stem cells, in contrast, were first isolated and grown briefly in the laboratory in 1994,[3] and first successfully maintained long-term in the laboratory in 1998.[4] The first human adult stem cell was first successfully isolated in the laboratory in 1992.[5] Director Collins's misleading references to "a half century" and "fifty years" of research with adult stem cells (*see id.* ¶ 7) relate to studies using whole bone marrow transplant, in which a stem cell was believed to be present as the effective entity, but, as noted, the actual stem cell had not been physically isolated and verified.

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1 Evans & Kaufman, *Nature* 292, 154 (July 1981); Martin, *Proc. Natl. Acad. Sci. USA* 78, 7634 (December 1981).

2 Spangrude, *et al.*, *Science* 241, 58 (1988).

3 Bongso, *et al.*, *Human Reproduction* 9, 2110 (1994).

4 Thomson, *et al.*, *Science* 282, 1145 (1998).

5 Baum, *et al.*, *Proc. Natl. Acad. Sci. USA* 89, 2804 (1992).

8. The Collins Declaration asserts that "NIH ultimately determined that 21 hESC [lines] satisfied President Bush's criteria and therefore were eligible for use in NIH funded research." (*Id.* ¶ 5.) In fact, NIH actually determined that 78 hESC lines satisfied President Bush's criteria and were eligible for funding,[6] although only 21 hESC lines were eventually grown in quantity for distribution to researchers.[7]

Embryonic Stem Cells

9. The Collins Declaration asserts that "remarkable progress has already been made in realizing the possible benefits of hESC research." (Collins Decl. ¶ 6.) Yet this assertion is not supported by any factual evidence (*e.g.*, published citations or textual examples), and ignores the significant failures and problems associated with hESC research that are identified in the administrative record, including that hESC research will not lead to safe therapeutics because hESC are not normal cells; they do not differentiate into desired adult phenotype cells, but to fetal, immature phenotype cells; they are not required for research using other pluripotent cells; they may form tumors when injected into a patient's body; they may be rejected by a patient's immune system; and they are biologically inadequate replacements for lost adult stem cells. (*See* Comments of Do No Harm, et al., at I-1–13, G-8.) As a result, embryonic stem cells have shown no success in therapeutic applications. (*Id.*, at G-1). The Collins Declaration further asserts that "differentiated cells derived from hESC are already successfully being used to develop new

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6 *See, e.g.*, "NIH Human Embryonic Stem Cell Registry Under Former President Bush," *available at* http://stemcells.nih.gov/research/registry/eligibilitycriteria.asp (last accessed Sept. 2, 2010).

7 *See* Previous NIH hESC Registry Listing, *available at* http://stemcells.nih.gov/research/registry/available.asp (last accessed Sept. 2, 2010).

therapeutic drugs" (Collins Decl. ¶ 6), but this assertion is likewise unsupported by any factual evidence.

10. The Collins Declaration further asserts (Collins Decl. ¶ 5) that Dr. George Daley "has produced a detailed procedure for the generation of blood cells from hESCs" and asserts that "it is possible in the future that they could be used to address virtually all genetic and malignant blood diseases that are currently treated by gene therapy or bone marrow transplant." However, this example simply highlights the failure of hESC research in developing effective therapies as well as the failure of NIH funding of hESC actually to make significant progress. Despite millions in funding since 2002, the use of blood cells from hESC still faces "major" challenges, as admitted by Dr. Daley himself in 2007 and 2010 publications,[8] with continuing pragmatic difficulties including tumor-forming cells and lack of production of useful adult blood-forming cells, as well as reliance on use of a potential cancer-causing virus for cell differentiation. And as the Collins Declaration admits, the diseases at issue are already being treated effectively by bone marrow transplants, *i.e.*, *adult* stem cell therapies. (*Id.* ¶ 7.)

11. The Collins Declaration further asserts that "the first clinical trial of a hESC-derived therapy has received FDA approval to begin enrolling spinal cord injury patients" and characterizes this as a "remarkable achievement." (*Id.* ¶ 6.) This mischaracterizes the actual facts, conflating any actual results from hESC research with an agency determination to proceed with a safety trial. In fact, no patients have been injected with human embryonic stem cells, and

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[8] McKinney-Freeman, S.L., and Daley, G.Q., *Curr. Opin. Hematol.* 14, 343 (July 2007); Lengerke, C. and Daley G.Q., *Blood Rev.* 24, 27-37 (January 2010).

even many human embryonic stem cell proponents are concerned that the trial is not safe to proceed.[9]

Adult Stem Cells

12. The Collins Declaration asserts that *adult* stem cell research "has produced FDA-approved treatments that reconstitute the immune system after leukemia, lymphoma, and various blood or autoimmune disorders have been treated with chemotherapy." (Collins Decl. ¶ 7.) This statement comports with the administrative record (*see* Do No Harm Comments at G-4–G-8), but dramatically understates the success of adult stem cell treatments in benefiting patients suffering from numerous diseases. The use of the term "FDA-approved treatments" implies that the treatment has passed all four required phases of clinical trial testing and received approval as a commercial product; it is not a medical standard to evaluate patient benefit, but an agency determination that benefits outweigh risks in a broad class of patients. The approved trial by Geron mentioned by the Collins Declaration (*id.* ¶ 6) has not yet passed even phase I results. By direct contrast, the administrative record and recent published literature make clear that adult stem cells have already produced published positive therapeutic benefits *for spinal cord injury patients* (see Do No Harm Comments at G-8), including patients who had chronic injury (up to 15 years).[10] When comparing approved clinical trials, the standard for comparison would be

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9 *See, e.g.*, R. Stein, "Human tests set for stem cells," *available at* http://www.washingtonpost.com/wp-dyn/content/article/2010/08/29/AR2010082903888.html (last accessed Sept. 2, 2010).

10 Press Release, Wayne State University, "Study shows adult stem cell grafts increased mobility in paralyzed patients," (Oct. 16, 2009), *available at* http://www.media.wayne.edu/2009/10/16/study-shows-adult-stem-cell-grafts-increased (last accessed Sept 3, 2010); Lima, C., *et al.*, "Olfactory Mucosal Autografts and Rehabilitation

[Footnote continued on next page]

whether a given trial is listed at ClinicalTrials.gov, a website developed and maintained by the NIH.[11] The listing of "interventional" trials[12] (eliminating simple "observational" trials) is particularly illuminating—1,973 adult stem cell interventional trials are currently listed at the site.[13] (*See* Do No Harm Comments at G-4–G-8.) The equivalent search for embryonic stem cells shows just *two* trials, both of which are actually *adult* stem cell trials that use the term "embryonic" within the background text.[14] The Geron trial is not yet listed at this website, so *zero* clinical trials with embryonic stem cells are currently listed on this NIH website.

13. The Collins Declaration asserts that adult stem cells are "available in quantity only from blood-forming tissues and cord blood" (Collins Decl. ¶ 7), but the administrative record contains examples of techniques to increase quantities of adult stem cells from various isolates (*see* Do No Harm Comments at G-2).

14. The Collins Declaration asserts that "it has not been possible to differentiate adult stem cells into cell types that are very different from their tissue of origin." (Collins Decl. ¶ 7.)

[Footnote continued from previous page]
for Chronic Traumatic Spinal Cord Injury," *Neurorehabil Neural Repair* 24, 10 (January 2010).

11 http://www.clinicaltrials.gov states that: "ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world The U.S. National Institutes of Health (NIH), through its National Library of Medicine (NLM), has developed this site in collaboration with the Food and Drug Administration (FDA), as a result of the FDA Modernization Act, which was passed into law in November 1997."

12 Interventional trials determine whether experimental treatments or new ways of using known therapies are safe and effective under controlled environments.

13 Using the search terms "adult stem cell transplant" within "Interventional Trials": http://www.clinicaltrials.gov/ct2/results?term=adult+stem+cell+transplant&type=Intr (last accessed Sept. 3, 2010).

14 Using the search terms "embryonic stem cell transplant" within "Interventional Trials": http://www.clinicaltrials.gov/ct2/results?term=embryonic+stem+cell+transplant&type=Intr (last accessed Sept. 3, 2010).

The administrative record refutes this assertion, making clear that some adult stem cells actually do show broad multipotent flexibility in generation of tissues, meaning that they can generate most or all of the different tissues of the body. (*See* Do No Harm Comments at G-1–G-2). Furthermore, the published literature contains additional examples of adult stem cells that can differentiate into cell types different from their tissue of origin, including recently-discovered very small embryonic-like ("VSEL") cells from adult bone marrow, and demonstrates that these bone marrow-derived cells can repair cardiac damage.[15]

15. In particular, the Collins Declaration asserts that a "bone marrow stem cell, for instance, cannot be differentiated into a neuron." (Collins Decl. ¶ 7.) The administrative record makes clear that this assertion is incorrect, and that there are documented, published examples for this precise differentiation of bone marrow to neuron. (*See* Do No Harm Comments at G-1–G-2). Indeed, the NIH itself has noted that bone marrow stem cells can form neurons:

> Some adult stem cells appear to have the capability to differentiate into tissues other than the ones from which they originated; this is referred to as plasticity. Reports of human or mouse adult stem cells that demonstrate plasticity and the cells they differentiate or specialize into include: 1) *blood and bone marrow (unpurified hematopoietic) stem cells differentiate into the 3 major types of brain cells (neurons, oligodendrocytes, and astrocytes)*, skeletal muscle cells, cardiac muscle cells, and liver cells; 2) bone marrow (stromal) cells differentiate into

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[15] *See, e.g.*, Kucia, M., *et al.*, Physiological and Pathological Consequences of Identification of Very Small Embryonic Like (VSEL) Stem Cells In Adult Bone Marrow, *J. Physiol. Pharmacol*. 57, Supp. 5, 5–18 (2006); Kucia, M., *et al.*, Bone Marrow-Derived Very Small Embryonic-Like Stem Cells: Their Developmental Origin and Biological Significance, *Developmental Dynamics* 236, 3309-3320 (2007); Ratajczak, M.Z., *et al.*, Very Small Embryonic-Like (VSEL) Stem Cells: Purification from Adult Organs, Characterization, and Biological Significance, *Stem Cell Rev*. 4, 89-99 (2008); Zuba-Surma, E.K. *et al.*, Transplantation of expanded bone marrow-derived very small embryonic-like stem cells (VSEL-SCs) improves left ventricular function and remodeling after myocardial infarction, *J. Cell. Mol. Med*. (Jul. 12, 2010).

> cardiac muscle cells, skeletal muscle cells, fat, bone, and cartilage; and 3) brain stem cells differentiate into blood cells and skeletal muscle cells.[16]

The statement is reiterated later in the same NIH report:

> Alternatively, adult stem cells may differentiate into a tissue that—during normal embryonic development—would arise from a different germ layer. For example, bone marrow-derived cells may differentiate into neural tissue, which is derived from embryonic ectoderm [15, 65].[17]

16. The Collins Declaration asserts that "brain autopsies do not yield viable nerve cells." (Collins Decl. ¶ 7.) To the contrary, the published literature shows that adult neural stem cells can indeed be obtained from the post-mortem human brain and yield nerve cells.[18]

Induced Pluripotent Stem Cells (iPSC)

17. The Collins Declaration asserts that induced pluripotent stem cells (iPSC) "were discovered as a direct result of the knowledge gained from studying hESC." (*Id.* ¶ 7.) The administrative record amply demonstrates that this assertion is false. (*See* Do No Harm Comments at H-1–H-7.) The technique used to generate iPSC was originally discovered by Yamanaka using knowledge from *mouse* ESC, and that same technique was used to create the

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16 *Stem Cells: Scientific Progress and Future Research Directions*, National Institutes of Health, at ES-7 (June 2001), *available at* http://stemcells.nih.gov/info/2001report/2001report.htm (emphasis added).

17 *Id.* at 26.

18 Palmer, T., *et al.*, Progenitor cells from human brain after death, *Nature* 411, 42 (May 3, 2001); Feldmann, R.E., Jr., and Mattern, R., The human brain and its neural stem cells postmortem: from dead brains to live therapy, *Int. J. Legal Med*. 120, 201 (July 2006).

first human iPSC. Yamanaka himself has explained that "[n]either eggs nor embryos are necessary. I've never worked with either."[19]

18. The Collins Declaration asserts that there are "significant biological differences between iPSC and hESC." (Collins Decl. ¶ 7.) The administrative record makes clear, however, that these cells "meet the defining criteria [that were] originally proposed for human [embryonic stem] cells, with the significant exception that the [induced pluripotent stem] cells are not derived from embryos."[20] (*See* Do No Harm Comments at H-2–H-4.) Recently published literature confirms the same.[21]

Standard Preservation of Cell Cultures

19. The Collins Declaration asserts that the injunction will result in "immeasurable loss of valuable and one-of-a-kind research resources," and that "[u]nique modifications and applications of hESC . . . could be lost irretrievably or could take years to recreate." (Collins Decl. ¶ 8.) These statements imply that currently-growing cell cultures will be discarded and lost forever. However, standard cell culture technique taught to even the most basic students for decades involves freezing (cryopreservation) of cell stocks from the very inception of a cell

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19 *See* "Scientists Make Stem Cells From Skin Of Mice Instead Of Embryos," Medical News Today, *available at* http://www.medicalnewstoday.com/articles/73381.php (last accessed Sept. 2, 2010).

20 Yu, J., *et al.*, Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells, 318 *Science* 1917 (2007).

21 "Human embryonic stem cells and reprogrammed cells virtually identical," *available at* http://www.physorg.com/news200224498.html (last accessed Sept. 2, 2010); Guenther, M.G., *et al.*, Chromatin Structure and Gene Expression Programs of Human Embryonic and Induced Pluripotent Stem Cells, *Cell Stem Cell* 7, 249 (Aug. 6, 2010); Newman, A.M., and Cooper, J.B., Lab-Specific Gene Expression Signatures in Pluripotent Stem Cells, *Cell Stem Cell* 7, 258 (Aug. 6, 2010).

culture and cell line. Cells are stored in liquid nitrogen at –196°C, at which temperature they can be maintained indefinitely;[22] methods have even been refined specifically for hESC.[23]

Global Perspective on Stem Cell Treatments

20. The Collins Declaration asserts that some hESC investigators "may have to close their laboratories or move to another country" (Collins Decl. ¶ 8), and "scientists may be forced to move to other countries" (*Id.* ¶ 14), and asserts that the "greatest loss, however, will be for the millions of Americans suffering from illnesses" (*Id.*). However, it is actually the myopic focus of NIH on hESC that endangers the future of treatments for Americans suffering from illness. A global perspective on current utilization of adult stem cell transplants clearly demonstrates that many other countries have focused on the reality of such treatments. The *Journal of the American Medical Association* has recently published data[24] showing that worldwide in 2006 a total of 50,417 transplants were performed using hematopoietic (blood-forming) adult stem cells alone. Almost half (48%) took place in Europe. Only 36% took place in all of the Americas in total. The study notes that adult stem cell transplants have become "the standard of care for many patients" with blood disorders and malignancies, though they are starting to be used for other conditions including autoimmune disorders and heart disease. The study also notes that

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22 Shannon, J.E., and Macy, M.L., Freezing, storage and recovery of cell stocks, in Tissue Culture. Methods and Applications 712-718 (Academic Press 1973); Perry, V.P., *et al.*,. Protected freezing of cell suspensions, *TCA Manual* 1, 119-120 (1976); Freshney, R., *Culture of Animal Cells: A Manual of Basic Technique* 220 (Alan R. Liss, Inc. 1987).

23 *See, e.g.*, Reubinoff, B.E., *et al.*, Effective cryopreservation of human embryonic stem cells by the open pulled straw vitrification method, *Human Reproduction* 16, 2187 (Oct. 2001).

24 Gratwohl, A., *et al.*, Hematopoietic Stem Cell Transplantation: A Global Perspective, 303 *JAMA* 1617, 1620 (April 2010).

this "demonstrates that it is an accepted therapy worldwide." Other countries have clearly noted the superiority of adult stem cells and emphasized their use.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed on September 3, 2010.

Dr. Theresa Deisher

EXHIBIT B

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al.,	Plaintiffs,	
v.		Civil Action No. 09-CV-01575-RCL
KATHLEEN SEBELIUS, et al.,	Defendants.	

DECLARATION OF DR. JAMES SHERLEY
IN SUPPORT OF PLAINTIFFS' OPPOSITION TO DEFENDANTS'
MOTION TO STAY PRELIMINARY INJUNCTION PENDING APPEAL

I, Dr. James L. Sherley, declare as follows:

1. I am a plaintiff in this action, and I am over the age of eighteen and competent to testify. I am knowledgeable about the facts set forth herein and make this declaration in support of Plaintiffs' Opposition to Defendants' Motion to Stay Preliminary Injunction Pending Appeal.

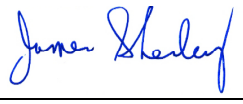
2. I am an adult stem cell researcher currently working at the Boston Biomedical Research Institute. My research focuses on improving methods for identifying adult stem cells and producing them in large numbers for therapeutic development. I work exclusively with adult stem cells, and I do not conduct research on embryos or use human embryonic stem cells.

3. Research grants are my sole source of research funding. The vast majority of grants I receive are from the National Institutes of Health ("NIH"). Since 1999, I have applied for NIH funding approximately 42 times. Fourteen of these proposals have received NIH funding, and two proposals are currently pending. Attached as Exhibit A is a list of my NIH grant submission activity from 1999-2010. During this time, I received only one significant private research award; and I have been a co-investigator on two other NIH grants providing minor funding for my adult stem cell studies.

4. Two recently submitted NIH grants are now undergoing review.

5. I will continue to seek NIH funding for adult stem cell research in the future. The National Institutes of Health Guidelines for Human Stem Cell Research will result in increased competition for the limited resources that are available to fund human stem cell research, threatening my ability to obtain federal funding for my adult stem cell research. Without NIH funding, I would likely be unable to continue my research.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed on September _2_, 2010.



Dr. James L. Sherley

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued April 12, 2010 Decided June 25, 2010

No. 09-5374

JAMES L. SHERLEY, ET AL.,
APPELLANTS

v.

KATHLEEN SEBELIUS, IN HER OFFICIAL CAPACITY AS SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, ET AL.,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 1:09-cv-01575-RCL)

Thomas G. Hungar argued the cause for appellants. With him on the briefs were *Bradley J. Lingo*, *Ryan J. Watson*, *Blaine H. Evanson*, *Samuel B. Casey*, and *Steven H. Aden*.

Stephanie R. Marcus, Attorney, U.S. Department of Justice, argued the cause for appellees. On the brief were *Mark B. Stern*, *Alisa B. Klein*, and *Abby C. Wright*, Attorneys. *R. Craig Lawrence*, Assistant U.S. Attorney, entered an appearance.

Before: GINSBURG, BROWN, and KAVANAUGH, *Circuit Judges*.

Opinion for the Court filed by *Circuit Judge* GINSBURG.

GINSBURG, *Circuit Judge*: An array of variously situated plaintiffs sued the Department and the Secretary of Health and Human Services and the National Institutes of Health and its Director, challenging newly promulgated guidelines that authorize the NIH to fund more research projects involving human embryonic stem cells than it had previously done. The district court dismissed the suit for want of a plaintiff with standing and dismissed as moot the plaintiffs' motion for a preliminary injunction. All the plaintiffs appeal those rulings, but they defend the standing of only two of their number, Drs. James Sherley and Theresa Deisher.

We conclude the two Doctors have standing. Therefore, we reverse the order of the district court insofar as it dismissed their claims and we reinstate the motion for a preliminary injunction.

I. Background

Because a stem cell can develop into any one of many specialized cells in the human body, it can be used in the treatment of a variety of diseases. There are two basic kinds of mammalian stem cells relevant to this case: embryonic stem cells (ESCs), which are found in human embryos, and adult stem cells (ASCs), which are found in the human body and in tissues discarded after birth.

Scientists, often with financial support from the NIH, have done research involving ASCs for about 50 years. They have done research involving ESCs only since 1998, and the

NIH did not fund such research until 2001, when President Bush authorized it to do so subject to the limitation that only ESCs derived from then-extant stem cell lines be used.

In 2009 President Obama removed that limitation, directing the "Secretary of Health and Human Services ... through the Director of NIH, [to] support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law" and to "issue new NIH guidance on such research that is consistent with this order." Exec. Order No. 13,505, 74 Fed. Reg. 10,667, 10,667 (Mar. 9, 2009). Pursuant to the resulting Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32170 (July 7, 2009), the NIH may now fund more projects involving ESCs than was previously possible.

The plaintiffs alleged the issuance of the Guidelines violated the Administrative Procedure Act because, among other reasons, the "promulgation and implementation of the Guidelines are not in accordance with law," Compl. ¶ 67; *see* 5 U.S.C. § 706(2)(A), to wit, the Dickey-Wicker Amendment, which the Congress has attached every year since 1996 to the Acts appropriating money for the DHHS and which prohibits federal funding of research in which a human embryo is to be harmed or destroyed, *e.g.*, Omnibus Appropriations Act of 2009, Pub. L. No. 111-8, div. F, Title V, § 509(a)(2), 123 Stat. 524. The defendants moved to dismiss the case on the ground that none of the plaintiffs had standing to challenge the issuance of the Guidelines. *Sherley v. Sebelius*, 686 F. Supp. 2d 1 (D.D.C. 2009).

The plaintiffs whose standing is at issue here are Drs. Sherley and Deisher, both of whom "specialize in adult stem cell research" and who, respectively, have received and plan to seek NIH grants for research involving ASCs. *Id.* at 3.

They claimed to have "competitor standing" because the Guidelines would "result in increased competition for limited federal funding and [would] thereby injure [their] ability to successfully compete for ... NIH stem cell research funds." *Id.* at 4. The district court rejected that contention. First, relying upon *Hardin v. Kentucky Utilities Co.*, 390 U.S. 1, 6 (1968), the court reasoned that a party may assert competitor standing only when the "particular statutory provision ... invoked" reflects a purpose "to protect a competitive interest" and that the Doctors had not shown they had a protected interest in receiving research funds from the NIH. *Sherley*, 686 F. Supp. 2d at 6. The court further concluded the cases upon which the Doctors relied established only that competitor standing applies to participants in "strictly regulated economic markets," whereas the Doctors were "applicants for research grants." *Id.* at 7. Finally, the court opined that even if the Doctors qualify as "competitors," they would still lack standing because the "application process to receive NIH funding is [already] extremely competitive," *id.*, *i.e.*, the additional competition made possible by the Guidelines would "not 'almost surely cause [them] to lose' funding," *id.* (quoting *El Paso Natural Gas Co. v. FERC*, 50 F.3d 23, 27 (D.C. Cir. 1995)).

The district court also held none of the other plaintiffs had standing. On appeal, those plaintiffs make no argument to the contrary, wherefore we take their lack of standing as conceded. *See, e.g.*, *Sitka Sound Seafoods, Inc. v. NLRB*, 206 F.3d 1175, 1181 (D.C. Cir. 2000) (argument not raised in opening brief on appeal is forfeited).

II. Analysis

In reviewing *de novo* the district court's decision to dismiss this suit on the ground that the Doctors lack standing

to sue, *Young Am.'s Found. v. Gates*, 573 F.3d 797, 799 (D.C. Cir. 2009), we "accept[] as true all of the factual allegations contained in the complaint and draw[] all inferences in favor of the nonmoving party," *City of Harper Woods Employees' Ret. Sys. v. Olver*, 589 F.3d 1292, 1298 (D.C. Cir. 2009). The Doctors' burden is to show they have standing not only under Article III of the Constitution of the United States but also under our doctrine of prudential standing. *See Shays v. FEC*, 414 F.3d 76, 83 (D.C. Cir. 2005).

A. Article III Standing

In order to establish their Article III standing, the Doctors must both identify an "injury in fact" that is "actual or imminent" and "fairly ... trace[able] to the challenged action of the defendant," and show it is "likely, as opposed to merely speculative, that [their] injury will be redressed by a favorable decision." *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992) (internal quotation marks omitted). The doctrine of competitor standing addresses the first requirement by recognizing that economic actors "suffer [an] injury in fact when agencies lift regulatory restrictions on their competitors or otherwise allow increased competition" against them. *La. Energy & Power Auth. v. FERC*, 141 F.3d 364, 367 (D.C. Cir. 1998); *accord New World Radio, Inc. v. FCC*, 294 F.3d 164, 172 (D.C. Cir. 2002) ("basic law of economics" that increased competition leads to actual injury); *see also Canadian Lumber Trade Alliance v. United States*, 517 F.3d 1319, 1332 (Fed. Cir. 2008) (doctrine of competitor standing "relies on economic logic to conclude that a plaintiff will likely suffer an injury-in-fact when the government acts in a way that increases competition or aids the plaintiff's competitors"). The form of that injury may vary; for example, a seller facing increased competition may lose sales to rivals, or be forced to lower its price or to expend more resources to achieve the

same sales, all to the detriment of its bottom line. Because increased competition almost surely injures a seller in one form or another, he need not wait until "allegedly illegal transactions ... hurt [him] competitively" before challenging the regulatory (or, for that matter, the deregulatory) governmental decision that increases competition. *La. Energy*, 141 F.3d at 367.

In considering whether the Doctors have Article III standing, we address only the question whether they allege a legally adequate injury-in-fact. That is the only element of constitutional standing upon which the parties focus, for it is clear the alleged injury is traceable to the Guidelines and redressable by the court.

We do not agree with the district court's suggestion that only a "participant[] in [a] strictly regulated economic market[]" may assert competitor standing. *Sherley*, 686 F. Supp. 2d at 7. We see no reason any one competing for a governmental benefit should not be able to assert competitor standing when the Government takes a step that benefits his rival and therefore injures him economically. In this vein, we have applied the doctrine of competitor standing to the political "market," holding incumbent congressmen had standing to challenge new campaign finance regulations that made it easier for rival candidates to compete against them for election. *Shays*, 414 F.3d at 87.

The district court also concluded the doctrine of competitor standing applies only where the "particular statutory provision ... invoked" reflects a purpose "to protect a competitive interest." *Sherley*, 686 F. Supp. 2d at 6 (quoting *Hardin*, 390 U.S. at 6). The requirement of a protected competitive interest, however, "goes to the merits" of a plaintiff's claim, not to his Article III standing. *See Ass'n of*

Data Processing Serv. Orgs., Inc. v. Camp, 397 U.S. 150, 153 (1970).

In order to bring themselves within the scope of the doctrine of competitor standing, the Doctors invoke our holding in *Associated Gas Distributors v. FERC*, 899 F.2d 1250 (1990), and similar holdings in other cases, that plaintiffs may "establish their constitutional standing by showing that the challenged action authorizes allegedly illegal transactions that have the clear and immediate potential to compete with [their] own sales," *id*. at 1259, and argue they are injured because "[a]s a result of the new Guidelines, [they] now face more competition for [NIH] research grants than they did before." For context, we note it is uncontested that, at least in the short run, the amount of money available from NIH for research grants is fixed notwithstanding the greater range of stem cell research projects made eligible for funding by the Guidelines.

The Government has two responses. First, it maintains the Doctors have not shown "an increase in funding for embryonic stem cell research ... require[s] a diminution in funding for adult stem cell research." To that we say: Nor need they do so. The Doctors need show only that they themselves will suffer some competitive injury, not that the NIH will spend less overall to fund projects involving ASCs.

Second, the Government argues the specific process by which the NIH awards grants makes it "entirely conjectural" whether the Doctors will face increased competition for funding. Each funding cycle proceeds in two stages. In the first, a peer-review committee assigns a preliminary score to each grant application. Each application with a score above the median then goes to one or more of the 24 Institutes and Centers (ICs) at the NIH. Each such component has its own

budget and awards grants to projects that address its particular mission; for instance, the National Cancer Institute funds research relating to cancer. In the second stage of the process, each IC decides which grant applications to fund.

The Government reasons that the Guidelines will not cause an increase in competition at the first stage because the NIH will always pass along to the ICs half the applications it receives. Therefore, each application, regardless how many there are, will still have a 50% chance of reaching the second stage of the process.

At the second stage, moreover, "it is ... entirely conjectural whether an application submitted by [one of the plaintiffs] would actually 'compete' with proposals involving [ESCs]" because the doctor's project would both have to "be ranked low enough to fall below the [IC's] funding capacity and be outranked by an [ESC] project." In other words, according to the Government, there is no certainty that an application for research involving ESCs will arrive at an IC in the same funding cycle as an application from one of the Doctors; even if the two applications do compete in the same funding cycle, there is no guarantee the one for research involving ESCs will get funding that would otherwise have gone to one of the Doctors. This mere possibility of injury does not establish competitor standing, argues the Government, which, as did the district court, reads our cases to require that a plaintiff asserting competitor standing show a challenged agency action will "almost surely cause [him] to lose business." *El Paso*, 50 F.3d at 27.

As the parties' arguments demonstrate, our cases addressing competitor standing have articulated various formulations of the standard for determining whether a plaintiff asserting competitor standing has been injured.

> Regardless how we have phrased the standard in any particular case, however, the basic requirement common to all our cases is that the complainant show an actual or imminent increase in competition, which increase we recognize will almost certainly cause an injury in fact.
>
> For instance, in *Louisiana Energy*, we held one seller of electric energy had standing to challenge a decision of the FERC that allowed a current competitor to sell energy at market-based rates. 141 F.3d at 366. We recognized the petitioner would "be injured by increased price competition" and that such injury was "imminent." *Id.* at 367 (explaining "parties suffer constitutional injury in fact when agencies lift regulatory restrictions on their competitors or otherwise allow increased competition"). In contrast, in *DEK Energy Co. v. FERC*, we held the plaintiff, a supplier of natural gas in Northern California, did not have competitor standing to challenge a decision of the FERC that would have allowed another company to ship a quantity of natural gas to Oregon and to sell it at a lower price than that at which DEK could sell its gas. 248 F.3d 1192, 1196 (2001). Although increased competition from lower-priced gas would likely cause DEK "to lose business or drop its prices," we concluded that increased competition was not imminent; there was only "some vague probability that any gas" sold by DEK's competitor would "actually reach [the] market" in which DEK sold its gas. *Id.* (noting decision of the FERC will not "almost surely" cause DEK "to lose business").
>
> The Doctors have met the basic requirement for competitor standing. This is not a situation like that in *El Paso*, in which it was uncertain whether a new seller would enter the market. 50 F.3d at 27. There can be no doubt the Guidelines will elicit an increase in the number of grant applications involving ESCs; indeed, the Government never

suggests otherwise. Because the Guidelines have intensified the competition for a share in a fixed amount of money, the plaintiffs will have to invest more time and resources to craft a successful grant application. That is an actual, here-and-now injury.

The Doctors will suffer an additional injury whenever a project involving ESCs receives funding that, but for the broadened eligibility in the Guidelines, would have gone to fund a project of theirs. They are more likely to lose funding to projects involving ESCs than are researchers who do not work with stem cells because ASCs and ESCs are substitutes in some uses. The Doctors illustrated this point in a post-argument letter in which they report Dr. Sherley recently submitted a grant for a project in which ASCs will be used to create a surrogate for a human liver and suggest his "chief competitor" will be a company that "engages in similar research using [ESCs]." Although no one can say exactly how likely the Doctors are to lose funding to projects involving ESCs, having been put into competition with those projects, the Doctors face a substantial enough probability to deem the injury to them imminent. *See, e.g., DEK Energy Co.*, 248 F.3d at 1195 ("substantial (if unquantifiable) probability of injury" shifts injury from "conjectural" to "imminent").

B. Prudential Standing

Parties "claiming standing under the APA must show ... their claims fall 'arguably within the zone of interests to be protected or regulated by the statute in question.'" *Shays*, 414 F.3d at 83 (quoting *Nat'l Credit Union Admin. v. First Nat'l Bank & Trust Co.*, 522 U.S. 479, 488 (1998)). This requirement "is not meant to be especially demanding" and there "need be no indication of congressional purpose to

benefit the would-be plaintiff"; it excludes "only those parties whose interests are not consistent with the purposes of the statute in question." *Amgen, Inc. v. Smith*, 357 F.3d 103, 108–09 (D.C. Cir. 2004) (internal quotation marks omitted).

Here the parties disagree about whether the injury the Doctors assert lies within the zone of interests protected by the Dickey-Wicker Amendment. The Doctors argue that pursuit of their interests furthers the purposes of that Amendment, which they say are "to fund permissible research, such as the adult stem cell research for which [they] seek funding, and ... [to] provide[] that federal funds could not be used for [ESC] research." The Government responds that the Amendment "was intended to protect [not] the financial interests of researchers engaging in adult stem cell research ... [but rather] society's interest in not funding 'research in which a human embryo ... [is] destroyed."

We conclude the Doctors have prudential standing. The Dickey-Wicker Amendment clearly limits the funding of research involving human embryos. Because the Act can plausibly be interpreted to limit research involving ESCs, the Doctors' interest in preventing the NIH from funding such research is not inconsistent with the purposes of the Amendment. Under the standard of *Amgen*, quoted above, that is all that matters.

III. Conclusion

We reverse the order of the district court dismissing the plaintiffs' claims for lack of standing insofar as it applies to the Doctors and affirm that order in all other respects. As a result, we also reverse the order dismissing as moot the plaintiffs' motion for a preliminary injunction.

The Doctors ask us to consider the merits of their motion, but it is not the usual practice of this court to grant a motion for a preliminary injunction that the district court denied without having considered its merits. "It falls to the district court in the first instance ... to balance the four factors [of the test for a preliminary injunction] in order to decide whether" the motion should be granted. *Belbacha v. Bush*, 520 F.3d 452, 459 (D.C. Cir. 2008).

This matter is remanded to the district court for further proceedings consistent with the foregoing opinion.

So ordered.

Federal Register

Wednesday,
March 11, 2009

Part IV

The President

Executive Order 13505—Removing Barriers to Responsible Scientific Research Involving Human Stem Cells

Memorandum of March 9, 2009—Presidential Signing Statements

Memorandum of March 9, 2009—Scientific Integrity

Federal Register
Vol. 74, No. 46
Wednesday, March 11, 2009

Presidential Documents

Title 3—

The President

Executive Order 13505 of March 9, 2009

Removing Barriers to Responsible Scientific Research Involving Human Stem Cells

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. *Policy.* Research involving human embryonic stem cells and human non-embryonic stem cells has the potential to lead to better understanding and treatment of many disabling diseases and conditions. Advances over the past decade in this promising scientific field have been encouraging, leading to broad agreement in the scientific community that the research should be supported by Federal funds.

For the past 8 years, the authority of the Department of Health and Human Services, including the National Institutes of Health (NIH), to fund and conduct human embryonic stem cell research has been limited by Presidential actions. The purpose of this order is to remove these limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research, and in so doing to enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind.

Sec. 2. *Research.* The Secretary of Health and Human Services (Secretary), through the Director of NIH, may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law.

Sec. 3. *Guidance.* Within 120 days from the date of this order, the Secretary, through the Director of NIH, shall review existing NIH guidance and other widely recognized guidelines on human stem cell research, including provisions establishing appropriate safeguards, and issue new NIH guidance on such research that is consistent with this order. The Secretary, through NIH, shall review and update such guidance periodically, as appropriate.

Sec. 4. *General Provisions.* (a) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(b) Nothing in this order shall be construed to impair or otherwise affect:

(i) authority granted by law to an executive department, agency, or the head thereof; or

(ii) functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity, by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

Sec. 5. *Revocations.* (a) The Presidential statement of August 9, 2001, limiting Federal funding for research involving human embryonic stem cells, shall have no further effect as a statement of governmental policy.

(b) Executive Order 13435 of June 20, 2007, which supplements the August 9, 2001, statement on human embryonic stem cell research, is revoked.

THE WHITE HOUSE,
March 9, 2009.

[FR Doc. E9–5441
Filed 3–10–09; 11:15 am]
Billing code 3195–W9–P

and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute on Alcohol Abuse and Alcoholism. Special Emphasis Panel Alcohol Pharmacotherapy and the Treatment and Prevention of HIV/AIDS. (RFA AA 09 007/008) and Other AIDS Related Research.

Date: August 6, 2009.

Time: 8 a.m. to 11 a.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, 5635 Fishers Lane, Bethesda, MD 20892. (Telephone Conference Call).

Contact Person: Katrina L Foster, PhD, Scientific Review Officer, National Inst on Alcohol Abuse & Alcoholism, National Institutes of Health, 5635 Fishers Lane, Rm. 2019, Rockville, MD 20852. 301–443–4032. *katrina@mail.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.271, Alcohol Research Career Development Awards for Scientists and Clinicians; 93.272, Alcohol National Research Service Awards for Research Training; 93.273, Alcohol Research Programs; 93.891, Alcohol Research Center Grants; 93.701, ARRA Related Biomedical Research and Research Support Awards, National Institutes of Health, HHS)

Dated: June 29, 2009.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. E9–15847 Filed 7–6–09; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of General Medical Sciences; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of General Medical Sciences. Special Emphasis Panel Minority Biomedical Research Support.

Date: July 19–20, 2009.

Time: 7 p.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Hyatt Regency Bethesda, One Bethesda Metro Center, Bethesda, MD 20814.

Contact Person: Margaret J. Weidman, PhD, Scientific Review Officer, Office of Scientific Review, National Institute of General Medical Sciences, National Institutes of Health, 45 Center Drive, Room 3AN18B, Bethesda, MD 20892. 301–594–3663. *weidmanma@nigms.nih.gov.*

Name of Committee: National Institute of General Medical Sciences. Special Emphasis Panel MBRS Score.

Date: July 20–21, 2009.

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Hyatt Regency Bethesda, One Bethesda Metro Center, Bethesda, MD 20814.

Contact Person: Lisa Dunbar, PhD, Scientific Review Officer, Office of Scientific Review, National Institute of General Medical Sciences, National Institutes of Health, 45 Center Drive, Room 3AN12, Bethesda, MD 20892. 301–594–2849. *dunbarl@mail.nih.gov.*

Name of Committee: National Institute of General Medical Sciences. Special Emphasis Panel New Innovator Awards.

Date: July 21, 2009.

Time: 1 p.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Natcher Building, 45 Center Drive, Bethesda, MD 20892. (Telephone Conference Call).

Contact Person: Richard T. Okita, PhD, Program Director, Pharmacological and Physiological Sciences Branch, National Institute of General Medical Sciences, National Institutes of Health, Natcher Building, Room 2A5–49, Bethesda, MD 20892. 301–594–4469. *okitar@nigms.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.375, Minority Biomedical Research Support; 93.821, Cell Biology and Biophysics Research; 93.859, Pharmacology, Physiology, and Biological Chemistry Research; 93.862, Genetics and Developmental Biology Research; 93.88, Minority Access to Research Careers; 93.96, Special Minority Initiatives, National Institutes of Health, HHS)

Dated: June 29, 2009.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. E9–15846 Filed 7–6–09; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institutes of Health Guidelines for Human Stem Cell Research

SUMMARY: The National Institutes of Health (NIH) is hereby publishing final ''National Institutes of Health Guidelines for Human Stem Cell Research'' (Guidelines).

On March 9, 2009, President Barack H. Obama issued Executive Order 13505: *Removing Barriers to Responsible Scientific Research Involving Human Stem Cells.* The Executive Order states that the Secretary of Health and Human Services, through the Director of NIH, may support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell (hESC) research, to the extent permitted by law.

These Guidelines implement Executive Order 13505, as it pertains to extramural NIH-funded stem cell research, establish policy and procedures under which the NIH will fund such research, and helps ensure that NIH-funded research in this area is ethically responsible, scientifically worthy, and conducted in accordance with applicable law. Internal NIH policies and procedures, consistent with Executive Order 13505 and these Guidelines, will govern the conduct of intramural NIH stem cell research.

DATES: *Effective Date:* These Guidelines are effective on July 7, 2009.

Summary of Public Comments on Draft Guidelines: On April 23, 2009 the NIH published draft Guidelines for research involving hESCs in the **Federal Register** for public comment, 74 FR 18578 (April 23, 2009). The comment period ended on May 26, 2009.

The NIH received approximately 49,000 comments from patient advocacy groups, scientists and scientific societies, academic institutions, medical organizations, religious organizations, and private citizens. The NIH also received comments from members of Congress. This Notice presents the final Guidelines together with the NIH response to public comments that addressed provisions of the Guidelines.

Title of the Guidelines, Terminology, and Background

Respondents felt the title of the NIH draft guidelines was misleading, in that it is entitled ''National Institutes of Health Guidelines for Human Stem Cell Research,'' yet addresses only one type of human stem cell. The NIH notes that although the Guidelines pertain primarily to the donation of embryos for the derivation of hESCs, one Section also applies to certain uses of both hESCs and human induced pluripotent stem cells. Also, the Guidelines discuss applicable regulatory standards when research involving human adult stem cells or induced pluripotent stem cells constitutes human subject research.

Therefore, the title of the Guidelines was not changed.

Respondents also disagreed with the definition of human embryonic stem cells in the draft Guidelines, and asked that the NIH define them as originating from the inner cell mass of the blastocyst. The NIH modified the definition to say that human embryonic stem cells ''are cells that are derived from the inner cell mass of blastocyst stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers.''

Financial Gain

Respondents expressed concern that derivers of stem cells might profit from the development of hESCs. Others noted that because the stem cells eligible for use in research using NIH funding under the draft Guidelines are those cells that are subject to existing patents, there will be insufficient competition in the licensing of such rights. These respondents suggested that this could inhibit research, as well as increase the cost of any future clinical benefits. The Guidelines do not address the distribution of stem cell research material. It is, however, the NIH's expectation that stem cell research materials developed with NIH funds, as well as associated intellectual property and data, will be distributed in accordance with the NIH's existing policies and guidance, including ''Sharing Biomedical Research Resources, Principles and Guidelines for Recipients of NIH Grants and Contracts'' and ''Best Practices for the Licensing of Genomic Inventions.'' *http://ott.od.nih.gov/policy/Reports.html* Even where such policies are not directly applicable, the NIH encourages others to refrain from imposing on the transfer of research tools, such as stem cells, any conditions that hinder further biomedical research. In addition, the Guidelines were revised to state that there should be documentation that ''no payments, cash or in kind, were offered for the donated embryos.''

Respondents were concerned that donor(s) be clearly ''apprised up front by any researchers that financial gain may come from the donation and that the donor(s) should know up front if he/she will share in the financial gain.'' The Guidelines address this concern by asking that donor(s) was/were informed during the consent process that the donation was made without any restriction or direction regarding the individual(s) who may receive medical benefit from the use of the stem cells, such as who may be the recipients of cell transplants. The Guidelines also require that the donor(s) receive(s) information that the research was not intended to provide direct medical benefit to the donor(s); that the results of research using the hESCs may have commercial potential, and that the donor(s) would not receive financial or any other benefits from any such commercial development.

IRB Review Under the Common Rule

Respondents suggested that the current regulatory structure of IRB review under the Common Rule (45 CFR Part 46, Subpart A) addresses the core ethical principles needed for appropriate oversight of hESC derivation. They noted that IRB review includes a full review of the informed consent process, as well as a determination of whether individuals were coerced to participate in the research and whether any undue inducements were offered to secure their participation. These respondents urged the NIH to replace the specific standards to assure voluntary and informed consent in the draft Guidelines with a requirement that hESC research be reviewed and approved by an IRB, in conformance with 45 CFR Part 46, Subpart A, as a prerequisite to NIH funding. Respondents also requested that the NIH create a registry of eligible hESC lines to avoid burdensome and repetitive assurances from multiple funding applicants. The NIH agrees that the IRB system of review under the Common Rule provides a comprehensive framework for the review of the donation of identifiable human biological materials for research. However, in the last several years, guidelines on hESC research have been issued by a number of different organizations and governments, and different practices have arisen around the country and worldwide, resulting in a patchwork of standards. The NIH concluded that employing the IRB review system for the donation of embryos would not ameliorate stated concerns about variations in standards for hESC research and would preclude the establishment of an NIH registry of hESCs eligible for NIH funding, because there would be no NIH approval of particular hESCs. To this end and in response to comments, these Guidelines articulate policies and procedures that will allow the NIH to create a Registry. These Guidelines also provide scientists who apply for NIH funding with a specific set of standards reflecting currently recognized ethical principles and practices specific to embryo donation that took place on or after the issuance of the Guidelines, while also establishing procedures for the review of donations that took place before the effective date of the Guidelines.

Federal Funding Eligibility of Human Pluripotent Cells From Other Sources

Respondents suggested that the allowable sources of hESCs potentially available for Federal funding be expanded to include hESC lines from embryos created expressly for research purposes, and lines created, or pluripotent cells derived, following parthenogenesis or somatic cell nuclear transfer (SCNT). The Guidelines allow for funding of research using hESCs derived from embryos created using in vitro fertilization (IVF) for reproductive purposes and no longer needed for these purposes, assuming the research has scientific merit and the embryos were donated after proper informed consent was obtained from the donor(s). The Guidelines reflect the broad public support for Federal funding of research using hESCs created from such embryos based on wide and diverse debate on the topic in Congress and elsewhere. The use of additional sources of human pluripotent stem cells proposed by the respondents involve complex ethical and scientific issues on which a similar consensus has not emerged. For example, the embryo-like entities created by parthenogenesis and SCNT require women to donate oocytes, a procedure that has health and ethical implications, including the health risk to the donor from the course of hormonal treatments needed to induce oocyte production.

Respondents noted that many embryos undergo Pre-implantation Genetic Diagnosis (PGD). This may result in the identification of chromosomal abnormalities that would make the embryos medically unsuitable for clinical use. In addition, the IVF process may also produce embryos that are not transferred into the uterus of a woman because they are determined to be not appropriate for clinical use. Respondents suggested that hESCs derived from such embryos may be extremely valuable for scientific study, and should be considered embryos that were created for reproductive purposes and were no longer needed for this purpose. The NIH agrees with these comments. As in the draft, the final Guidelines allow for the donation of embryos that have undergone PGD.

Donation and Informed Consent

Respondents commented in numerous ways that the draft Guidelines are too procedurally proscriptive in articulating the elements of appropriate informed consent documentation. This over-

reliance on the specific details and format of the informed consent document, respondents argued, coupled with the retroactive application of the Guidelines to embryos already donated for research, would result in a framework that fails to appreciate the full range of factors contributing to the complexity of the informed consent process. For example, respondents pointed to several factors that were precluded from consideration by the proposed Guidelines, such as contextual evidence of the consent process, other established governmental frameworks (representing local and community influences), and the changing standards for informed consent in this area of research over time. Respondents argued that the Guidelines should be revised to allow for a fuller array of factors to be considered in determining whether the underlying ethical principle of voluntary informed consent had been met. In addition to these general issues, many respondents made the specific recommendation that all hESCs derived before the final Guidelines were issued be automatically eligible for Federal funding without further review, especially those eligible under prior Presidential policy, i.e., ''grandfathered.'' The final Guidelines seek to implement the Executive Order by issuing clear guidance to assist this field of science to advance and reach its full potential while ensuring adherence to strict ethical standards. To this end, the NIH is establishing a set of conditions that will maximize ethical oversight, while ensuring that the greatest number of ethically derived hESCs are eligible for Federal funding. Specifically, for embryos donated in the U.S. on or after the effective date of the Guidelines, the only way to establish eligibility will be to either use hESCs listed on the NIH Registry, or demonstrate compliance with the specific procedural requirements of the Guidelines by submitting an assurance with supporting information for administrative review by the NIH. Thus, for future embryo donations in the United States, the Guidelines articulate one set of procedural requirements. This responds to concerns regarding the patchwork of requirements and guidelines that currently exist.

However, the NIH is also cognizant that in the more than a decade between the discovery of hESCs and today, many lines were derived consistent with ethical standards and/or guidelines developed by various states, countries, and other entities such as the International Society for Stem Cell Research (ISSCR) and the National Academy of Sciences (NAS). These various policies have many common features, rely on a consistent ethical base, and require an informed consent process, but they differ in details of implementation. For example, some require specific wording in a written informed consent document, while others do not. It is important to recognize that the principles of ethical research, *e.g.*, voluntary informed consent to participation, have not varied in this time period, but the requirements for implementation and procedural safeguards employed to demonstrate compliance have evolved. In response to these concerns, the Guidelines state that applicant institutions wishing to use hESCs derived from embryos donated prior to the effective date of the Guidelines may either comply with Section II (A) of the Guidelines or undergo review by a Working Group of the Advisory Committee to the Director (ACD). The ACD, which is a chartered Federal Advisory Committee Act (FACA) committee, will advise NIH on whether the core ethical principles and procedures used in the process for obtaining informed consent for the donation of the embryo were such that the cell line should be eligible for NIH funding. This Working Group will not undertake a *de novo* evaluation of ethical standards, but will consider the materials submitted in light of the principles and points to consider in the Guidelines, as well as 45 CFR Part 46 Subpart A. Rather than ''grandfathering,'' ACD Working Group review will enable pre-existing hESCs derived in a responsible manner to be eligible for use in NIH funded research.

In addition, for embryos donated outside the United States prior to the effective date of these Guidelines, applicants may comply with either Section II (A) or (B). For embryos donated outside of the United States on or after the effective date of the Guidelines, applicants seeking to determine eligibility for NIH research funding may submit an assurance that the hESCs fully comply with Section II (A) or submit an assurance along with supporting information, that the alternative procedural standards of the foreign country where the embryo was donated provide protections at least equivalent to those provided by Section II (A) of these Guidelines. These materials will be reviewed by the NIH ACD Working Group, which will recommend to the ACD whether such equivalence exists. Final decisions will be made by the NIH Director. This special consideration for embryos donated outside the United States is needed because donation of embryos in foreign countries is governed by the laws and policies of the respective governments of those nations. Although such donations may be responsibly conducted, such governments may not or cannot change their national donation requirements to precisely comply with the NIH Guidelines. The NIH believes it is reasonable to provide a means for reviewing such hESCs because ethically derived foreign hESCs constitute an important scientific asset for the U.S.

Respondents expressed concern that it might be difficult in some cases to provide assurance that there was a ''clear separation'' between the prospective donor(s)' decision to create embryos for reproductive purposes and the donor(s)' decision to donate the embryos for research purposes. These respondents noted that policies vary at IVF clinics, especially with respect to the degree to which connections with researchers exist. Respondents noted that a particular clinic's role may be limited to the provision of contact information for researchers. A clinic that does not have any particular connection with research would not necessarily have in place a written policy articulating the separation contemplated by the Guidelines. Other respondents noted that embryos that are determined not to be suitable for medical purposes, either because of genetic defects or other concerns, may be donated prior to being frozen. In these cases, it is possible that the informed consent process for the donation might be concurrent with the consent process for IVF treatment. Respondents also noted that the initial consent for IVF may contain a general authorization for donating embryos in excess of clinical need, even though a more detailed consent is provided at the actual time of donation. The NIH notes that the Guidelines specifically state that consent should have been obtained at the time of donation, even if the potential donor(s) had given prior indication of a general intent to donate embryos in excess of clinical need for the purposes of research. Accordingly, a general authorization for research donation when consenting for reproductive treatment would comply with the Guidelines, so long as specific consent for the donation is obtained at the time of donation. In response to comments regarding documentation necessary to establish a separation between clinical and research decisions, the NIH has changed the language of the Guidelines to permit applicant institutions to submit consent forms,

written policies or other documentation to demonstrate compliance with the provisions of the Guidelines. This change should provide the flexibility to accommodate a range of practices, while adhering to the ethical principles intended.

Some respondents want to require that the IVF physician and the hESC researcher should be different individuals, to prevent conflict of interest. Others say they should be the same person, because people in both roles need to have detailed knowledge of both areas (IVF treatment and hESC research). There is also a concern that the IVF doctor will create extra embryos if he/she is also the researcher. As a general matter, the NIH believes that the doctor and the researcher seeking donation should be different individuals. However, this is not always possible, nor is it required, in the NIH's view, for ethical donation.

Some respondents want explicit language (in the Guidelines and/or in the consent) stating that the embryo will be destroyed when the inner cell mass is removed. In the process of developing guidelines, the NIH reviewed a variety of consent forms that have been used in responsible derivations. Several had extensive descriptions of the process and the research to be done, going well beyond the minimum expected, yet they did not use these exact words. Given the wide variety and diversity of forms, as well as the various policy, statutory and regulatory obligations individual institutions face, the NIH declines to provide exact wording for consent forms, and instead endorses a robust informed consent process where all necessary details are explained and understood in an ongoing, trusting relationship between the clinic and the donor(s).

Respondents asked for clarification regarding the people who must give informed consent for the donation of embryos for research. Some commenters suggested that NIH should require consent from the gamete donors, in cases where those individuals may be different than the individuals seeking reproductive treatment. The NIH requests consent from ''the individual(s) who sought reproductive treatment'' because this/these individual(s) is/are responsible for the creation of the embryo(s) and, therefore, its/their disposition. With regard to gamete donation, the risks are associated with privacy and, as such, are governed by requirements of the Common Rule, where applicable.

Respondents also requested clarification on the statement in the draft Guidelines noting that ''although human embryonic stem cells are derived from embryos, such stem cells are not themselves human embryos.'' For the purpose of NIH funding, an embryo is defined by Section 509, Omnibus Appropriations Act, 2009, Public Law 111–8, 3/11/09, otherwise known as the Dickey Amendment, as any organism not protected as a human subject under 45 CFR Part 46 that is derived by fertilization, parthenogenesis, cloning or any other means from one or more human gametes or human diploid cells. Since 1999, the Department of Health and Human Services (HHS) has consistently interpreted this provision as not applicable to research using hESCs, because hESCs are not embryos as defined by Section 509. This long-standing interpretation has been left unchanged by Congress, which has annually reenacted the Dickey Amendment with full knowledge that HHS has been funding hESC research since 2001. These guidelines therefore recognize the distinction, accepted by Congress, between the derivation of stem cells from an embryo that results in the embryo's destruction, for which Federal funding is prohibited, and research involving hESCs that does not involve an embryo nor result in an embryo's destruction, for which Federal funding is permitted.

Some respondents wanted to ensure that potential donor(s) are either required to put their ''extra'' embryos up for adoption before donating them for research, or are at least offered this option. The Guidelines require that all the options available in the health care facility where treatment was sought pertaining to the use of embryos no longer needed for reproductive purposes were explained to the potential donor(s). Since not all IVF clinics offer the same services, the healthcare facility is only required to explain the options available to the donor(s) at that particular facility.

Commenters asked that donor(s) be made aware of the point at which their donation decision becomes irrevocable. This is necessary because if the embryo is de-identified, it may be impossible to stop its use beyond a certain point. The NIH agrees with these comments and revised the Guidelines to require that donor(s) should have been informed that they retained the right to withdraw consent for the donation of the embryo until the embryos were actually used to derive embryonic stem cells or until information which could link the identity of the donor(s) with the embryo was no longer retained, if applicable.

Medical Benefits of Donation

Regarding medical benefit, respondents were concerned that the language of the Guidelines should not somehow eliminate a donor's chances of benefitting from results of stem cell research. Respondents noted that although hESCs are not currently being used clinically, it is possible that in the future such cells might be used for the medical benefit of the person donating them. The Guidelines are meant to preclude individuals from donating embryos strictly for use in treating themselves only or from donating but identifying individuals or groups they do or do not want to potentially benefit from medical intervention using their donated cells. While treatment with hESCs is one of the goals of this research, in practice, years of experimental work must still be done before such treatment might become routinely available. The Guidelines are designed to make it clear that immediate medical benefit from a donation is highly unlikely at this time. Importantly, it is critical to note that the Guidelines in no way disqualify a donor from benefitting from the medical outcomes of stem cell research and treatments that may be developed in the future.

Monitoring and Enforcement Actions

Respondents have expressed concern about the monitoring of funded research and the invocation of possible penalties for researchers who do not follow the Guidelines. A grantee's failure to comply with the terms and conditions of award, including confirmed instances of research misconduct, may cause the NIH to take one or more enforcement actions, depending on the severity and duration of the non-compliance. For example, the following actions may be taken by the NIH when there is a failure to comply with the terms and conditions of any award: (1) Under 45 CFR 74.14, the NIH can impose special conditions on an award, including but not limited to increased oversight/monitoring/reporting requirements for an institution, project, or investigator; and (2) under 45 CFR 74.62 the NIH may impose enforcement actions, including but not limited to withholding funds pending correction of the problem, disallowing all or part of the costs of the activity that was not in compliance, withholding further awards for the project, or suspending or terminating all or part of the funding for the project. Individuals and institutions may be debarred from eligibility for all Federal financial assistance and contracts under 2 CFR part 376 and 48

CFR subpart 9.4, respectively. The NIH will undertake all enforcement actions in accordance with applicable statutes, regulations, and policies.

National Institutes of Health Guidelines for Research Using Human Stem Cells

I. Scope of the Guidelines

These Guidelines apply to the expenditure of National Institutes of Health (NIH) funds for research using human embryonic stem cells (hESCs) and certain uses of induced pluripotent stem cells (See Section IV). The Guidelines implement Executive Order 13505.

Long-standing HHS regulations for Protection of Human Subjects, 45 CFR part 46, subpart A establish safeguards for individuals who are the sources of many human tissues used in research, including non-embryonic human adult stem cells and human induced pluripotent stem cells. When research involving human adult stem cells or induced pluripotent stem cells constitutes human subject research, Institutional Review Board review may be required and informed consent may need to be obtained per the requirements detailed in 45 CFR part 46, subpart A. Applicants should consult *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm*.

It is also important to note that the HHS regulation, *Protection of Human Subjects*, 45 CFR part 46, subpart A, may apply to certain research using hESCs. This regulation applies, among other things, to research involving individually identifiable private information about a living individual, 45 CFR 46.102(f). The HHS Office for Human Research Protections (OHRP) considers biological material, such as cells derived from human embryos, to be individually identifiable when they can be linked to specific living individuals by the investigators either directly or indirectly through coding systems. Thus, in certain circumstances, IRB review may be required, in addition to compliance with these Guidelines. Applicant institutions are urged to consult OHRP guidances at *http://www.hhs.gov/ohrp/policy/index.html#topics*.

To ensure that the greatest number of responsibly derived hESCs are eligible for research using NIH funding, these Guidelines are divided into several sections, which apply specifically to embryos donated in the U.S. and foreign countries, both before and on or after the effective date of these Guidelines. Section II (A) and (B) describe the conditions and review processes for determining hESC eligibility for NIH funds. Further information on these review processes may be found at *http://www.NIH.gov*. Sections IV and V describe research that is not eligible for NIH funding.

These guidelines are based on the following principles:

1. Responsible research with hESCs has the potential to improve our understanding of human health and illness and discover new ways to prevent and/or treat illness.

2. Individuals donating embryos for research purposes should do so freely, with voluntary and informed consent.

As directed by Executive Order 13505, the NIH shall review and update these Guidelines periodically, as appropriate.

II. Eligibility of Human Embryonic Stem Cells for Research With NIH Funding

For the purpose of these Guidelines, ''human embryonic stem cells (hESCs)'' are cells that are derived from the inner cell mass of blastocyst stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers. Although hESCs are derived from embryos, such stem cells are not themselves human embryos. All of the processes and procedures for review of the eligibility of hESCs will be centralized at the NIH as follows:

A. Applicant institutions proposing research using hESCs derived from embryos donated in the U.S. on or after the effective date of these Guidelines may use hESCs that are posted on the new NIH Registry or they may establish eligibility for NIH funding by submitting an assurance of compliance with Section II (A) of the Guidelines, along with supporting information demonstrating compliance for administrative review by the NIH. For the purposes of this Section II (A), hESCs should have been derived from human embryos:

1. That were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose;

2. That were donated by individuals who sought reproductive treatment (hereafter referred to as ''donor(s)'') and who gave voluntary written consent for the human embryos to be used for research purposes; and

3. For which all of the following can be assured and documentation provided, such as consent forms, written policies, or other documentation, provided:

a. All options available in the health care facility where treatment was sought pertaining to the embryos no longer needed for reproductive purposes were explained to the individual(s) who sought reproductive treatment.

b. No payments, cash or in kind, were offered for the donated embryos.

c. Policies and/or procedures were in place at the health care facility where the embryos were donated that neither consenting nor refusing to donate embryos for research would affect the quality of care provided to potential donor(s).

d. There was a clear separation between the prospective donor(s)'s decision to create human embryos for reproductive purposes and the prospective donor(s)'s decision to donate human embryos for research purposes. Specifically:

i. Decisions related to the creation of human embryos for reproductive purposes should have been made free from the influence of researchers proposing to derive or utilize hESCs in research. The attending physician responsible for reproductive clinical care and the researcher deriving and/or proposing to utilize hESCs should not have been the same person unless separation was not practicable.

ii. At the time of donation, consent for that donation should have been obtained from the individual(s) who had sought reproductive treatment. That is, even if potential donor(s) had given prior indication of their intent to donate to research any embryos that remained after reproductive treatment, consent for the donation for research purposes should have been given at the time of the donation.

iii. Donor(s) should have been informed that they retained the right to withdraw consent for the donation of the embryo until the embryos were actually used to derive embryonic stem cells or until information which could link the identity of the donor(s) with the embryo was no longer retained, if applicable.

e. During the consent process, the donor(s) were informed of the following:

i. That the embryos would be used to derive hESCs for research;

ii. What would happen to the embryos in the derivation of hESCs for research;

iii. That hESCs derived from the embryos might be kept for many years;

iv. That the donation was made without any restriction or direction regarding the individual(s) who may receive medical benefit from the use of the hESCs, such as who may be the recipients of cell transplants;

v. That the research was not intended to provide direct medical benefit to the donor(s);

vi. That the results of research using the hESCs may have commercial potential, and that the donor(s) would not receive financial or any other benefits from any such commercial development;

vii. Whether information that could identify the donor(s) would be available to researchers.

B. Applicant institutions proposing research using hESCs derived from embryos donated in the U.S. before the effective date of these Guidelines may use hESCs that are posted on the new NIH Registry or they may establish eligibility for NIH funding in one of two ways:

1. By complying with Section II (A) of the Guidelines; or

2. By submitting materials to a Working Group of the Advisory Committee to the Director (ACD), which will make recommendations regarding eligibility for NIH funding to its parent group, the ACD. The ACD will make recommendations to the NIH Director, who will make final decisions about eligibility for NIH funding.

The materials submitted must demonstrate that the hESCs were derived from human embryos: (1) That were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose; and (2) that were donated by donor(s) who gave voluntary written consent for the human embryos to be used for research purposes.

The Working Group will review submitted materials, *e.g.*, consent forms, written policies or other documentation, taking into account the principles articulated in Section II (A), 45 CFR part 46, subpart A, and the following additional points to consider. That is, during the informed consent process, including written or oral communications, whether the donor(s) were: (1) Informed of other available options pertaining to the use of the embryos; (2) offered any inducements for the donation of the embryos; and (3) informed about what would happen to the embryos after the donation for research.

C. For embryos donated outside the United States before the effective date of these Guidelines, applicants may comply with either Section II (A) or (B). For embryos donated outside of the United States on or after the effective date of the Guidelines, applicants seeking to determine eligibility for NIH research funding may submit an assurance that the hESCs fully comply with Section II (A) or submit an assurance along with supporting information, that the alternative procedural standards of the foreign country where the embryo was donated provide protections at least equivalent to those provided by Section II (A) of these Guidelines. These materials will be reviewed by the NIH ACD Working Group, which will recommend to the ACD whether such equivalence exists. Final decisions will be made by the NIH Director.

D. NIH will establish a new Registry listing hESCs eligible for use in NIH funded research. All hESCs that have been reviewed and deemed eligible by the NIH in accordance with these Guidelines will be posted on the new NIH Registry.

III. Use of NIH Funds

Prior to the use of NIH funds, funding recipients should provide assurances, when endorsing applications and progress reports submitted to NIH for projects using hESCs, that the hESCs are listed on the NIH registry.

IV. Research Using hESCs and/or Human Induced Pluripotent Stem Cells That, Although the Cells May Come From Eligible Sources, Is Nevertheless Ineligible for NIH Funding

This section governs research using hESCs and human induced pluripotent stem cells, *i.e.*, human cells that are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers. Although the cells may come from eligible sources, the following uses of these cells are nevertheless ineligible for NIH funding, as follows:

A. Research in which hESCs (even if derived from embryos donated in accordance with these Guidelines) or human induced pluripotent stem cells are introduced into non-human primate blastocysts.

B. Research involving the breeding of animals where the introduction of hESCs (even if derived from embryos donated in accordance with these Guidelines) or human induced pluripotent stem cells may contribute to the germ line.

V. Other Research Not Eligible for NIH Funding

A. NIH funding of the derivation of stem cells from human embryos is prohibited by the annual appropriations ban on funding of human embryo research (Section 509, Omnibus Appropriations Act, 2009, Pub. L. 111–8, 3/11/09), otherwise known as the Dickey Amendment.

B. Research using hESCs derived from other sources, including somatic cell nuclear transfer, parthenogenesis, and/or IVF embryos created for research purposes, is not eligible for NIH funding.

Dated: June 30, 2009.

Raynard S. Kington,

Acting Director, NIH.

[FR Doc. E9–15954 Filed 7–6–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HOMELAND SECURITY

U.S. Customs and Border Protection

Agency Information Collection Activities: Importer's ID Input Record

AGENCY: U.S. Customs and Border Protection, Department of Homeland Security.

ACTION: 30-Day notice and request for comments; Extension of an existing information collection: 1651–0064.

SUMMARY: U.S. Customs and Border Protection (CBP) of the Department of Homeland Security has submitted the following information collection request to the Office of Management and Budget (OMB) for review and approval in accordance with the Paperwork Reduction Act: Importer's ID Input Record (Form 5106). This is a proposed extension of an information collection that was previously approved. CBP is proposing that this information collection be extended with no change to the burden hours. This document is published to obtain comments from the public and affected agencies. This proposed information collection was previously published in the **Federal Register** (74 FR 16226) on April 9, 2009, allowing for a 60-day comment period. This notice allows for an additional 30 days for public comments. This process is conducted in accordance with 5 CFR 1320.10.

DATES: Written comments should be received on or before August 6, 2009.

ADDRESSES: Interested persons are invited to submit written comments on the proposed information collection to the Office of Information and Regulatory Affairs, Office of Management and Budget. Comments should be addressed to the OMB Desk Officer for Customs and Border Protection, Department of Homeland Security, and sent via electronic mail to *oira_submission@omb.eop.gov* or faxed to (202) 395–5806.

SUPPLEMENTARY INFORMATION: U.S. Customs and Border Protection (CBP) encourages the general public and affected Federal agencies to submit written comments and suggestions on

Federal Register

Friday,
August 25, 2000

Part IV

Department of Health and Human Services

National Institutes of Health

National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells and Notification of Request for Emergency Clearance; Modification of OMB No. 0925–0001/Exp. 2/01, "PHS 398 Research and Research Training Grant Applications and Related Forms"; Notices

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells

SUMMARY: The National Institutes of Health (NIH) is hereby publishing final ''National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells.'' The Guidelines establish procedures to help ensure that NIH-funded research in this area is conducted in an ethical and legal manner.

EFFECTIVE DATE: These Guidelines are effective on August 25, 2000. The moratorium on research using human pluripotent stem cells derived from human embryos and fetal tissue put in place by the Director, NIH, in January 1999, will be lifted on August 25, 2000.

SUMMARY OF PUBLIC COMMENTS ON DRAFT GUIDELINES: On December 2, 1999 (64 FR 67576), the NIH published Draft Guidelines for research involving human pluripotent stem cells (hPSCs) in the **Federal Register** for public comment. The comment period ended on February 22, 2000.

The NIH received approximately 50,000 comments from members of Congress, patient advocacy groups, scientific societies, religious organizations, and private citizens. This Notice presents the final Guidelines together with NIH's response to the substantive public comments that addressed provisions of the Guidelines.

Scope of Guidelines and General Issues

Respondents asked for clarification of terminology used in the Guidelines and some commented that the language was not appropriate or was too technical, particularly the informed consent sections. The NIH agrees that these Guidelines should be clear and understandable. Changes, including some reorganization of the sections, were made to this end. The Guidelines are written primarily for the purpose of informing investigators of the conditions that must be met in order to receive NIH funding for research using hPSCs and, therefore, some technical language is required. The Guidelines do not define the precise language that should appear in informed consent documents because these should be developed by the investigator/clinician specifically for a particular study protocol or procedure for which the consent is being sought. Existing regulatory provisions require (45 CFR 46.116) that the language in informed consent documents be understandable to prospective participants in the study.

Respondents suggested that NIH funding for research using hPSCs would be in violation of the DHHS appropriations law and that derivation of hPSCs cannot be distinguished from their use. For this reason, a number of respondents asked that the NIH withdraw the draft Guidelines. The NIH sought the opinion of the DHHS General Counsel, who determined that ''federally funded research that utilizes hPSCs would not be prohibited by the HHS appropriations law prohibiting human embryo research, because such cells are not human embryos.'' Comments questioning this conclusion did not present information or arguments that justify reconsideration of the conclusion.

Respondents commented that the Guidelines are too restrictive or that there is no need for Federal Guidelines for this arena of research. Comments asserted that federally funded research using hPSCs should go forward without formal requirements, in the same manner as in the private sector. In order to help ensure that the NIH-funded research using hPSCs is conducted in an ethical and legal manner, the NIH felt it was advisable to develop and implement guidelines. To this end, the NIH Director convened a Working Group of the Advisory Committee to the Director, NIH (ACD), to advise the ACD on the development of guidelines and an oversight process for research involving hPSCs. The NIH Director charged the Working Group with developing appropriate guidelines to govern research involving the derivation and use of hPSCs from fetal tissue and research involving the use of hPSCs derived from human embryos that are in excess of clinical need.

Respondents commented regarding the sources of stem cells. Some respondents stated that research on hPSCs was unnecessary because stem cells from adults, umbilical cords, and placentas could be used instead. Other respondents asked the NIH to restrict Federal funding for hPSC research to those cells derived from fetal and adult tissue but not embryos. Other respondents asked that the Guidelines encompass research using stem cells from adult tissues.

As stated under Section I. *Scope of Guidelines*, the Guidelines apply to the use of NIH funds for research using hPSCs derived from human embryos or human fetal tissue. The Guidelines do not impose requirements on Federal funding of research involving stem cells from human adults, umbilical cords, or placentas.

Given the enormous potential of stem cells to the development of new therapies for the most devastating diseases, it is important to simultaneously pursue all lines of promising research. It is possible that no single source of stem cells is best or even suitable/usable for all therapies. Different types or sources of stem cells may be optimal for treatment of specific conditions. In order to determine the very best source of many of the specialized cells and tissues of the body for new treatments and even cures, it is vitally important to study the potential of adult stem cells for comparison to that of hPSCs derived from embryos and fetuses. Unless all stem cell types are studied, the differences between adult stem cells and embryo and fetal-derived hPSCs will not be known.

Moreover, there is evidence that adult stem cells may have more limited potential than hPSCs. First, stem cells for all cell and tissue types have not yet been found in the adult human. Significantly, cardiac stem cells or pancreatic islet stem cells have not been identified in adult humans.

Second, stem cells in adults are often present in only minute quantities, are difficult to isolate and purify, and their numbers may decrease with age. For example, brain cells from adults that may be neural stem cells have been obtained only by removing a portion of the brain of an adult with epilepsy, a complex and invasive procedure that carries the added risk of further neurological damage. Any attempt to use stem cells from a patient's own body for treatment would require that stem cells would first have to be isolated from the patient and then grown in culture in sufficient numbers to obtain adequate quantities for treatment. This would mean that for some rapidly progressing disorders, there may not be sufficient time to grow enough cells to use for treatment.

Third, in disorders that are caused by a genetic defect, the genetic error likely would be present in the patient's stem cells, making cells from such a patient inappropriate for transplantation. In addition, adult stem cells may contain more DNA abnormalities caused by exposure to daily living, including sunlight, toxins, and errors made during DNA replication than will be found in fetal or embryonic hPSCs.

Fourth, there is evidence that stem cells from adults may not have the same capacity to multiply as do younger cells. These potential weaknesses may limit the usefulness of adult stem cells.

Respondents were concerned that these are guidelines and not requirements or regulations. Although these are guidelines and not regulations, they prescribe the documentation and assurances that must accompany requests for NIH funding for research utilizing hPSCs. If the funding requests do not contain the prescribed information, funding for hPSC research will not be provided. Compliance with the Guidelines will be imposed as a condition of grant award.

Respondents commented that there had not been enough widespread public disclosure/discussion of this research or the Guidelines. Prior to the development of draft Guidelines, there were two Congressional hearings on hPSCs. In a further effort to ensure substantial discussion and comment, the NIH convened a Working Group of the Advisory Committee to the Director, NIH (ACD), to advise the ACD on the development of these Guidelines. The Working Group was composed of scientists, patients and patient advocates, ethicists, clinicians, and lawyers. The Working Group met in public session on April 8, 1999, and heard from members of the public, as well as professional associations and Congress. In developing the draft Guidelines, the NIH also considered advice from the National Bioethics Advisory Commission (NBAC). Draft Guidelines were published for public comment in the **Federal Register** on December 2, 1999, for 60 days, and, in response to public interest, the comment period was extended an additional 28 days. Approximately 50,000 comments were received. NIH issued a national press release announcing the **Federal Register** notice and many of the Nation's newspapers carried articles on this area of research and on the Guidelines. Patient groups, scientific societies, and religious organizations convened meetings and discussion groups and disseminated materials about this area of research and about the Guidelines.

Comment was received about whether the Guidelines apply to hPSC lines developed outside of the United States. The Guidelines make no distinction based upon the country in which an hPSC line is developed. All lines to be used in hPSC cell research funded by NIH must meet the same requirements.

Derivation and Use of hPSCs From Fetal Tissue

Respondents made the point that the NIH has specified certain requirements for the use of human fetal tissue to derive hPSCs in addition to those imposed on other areas of human fetal tissue research. These respondents suggested that the section of the Guidelines pertaining to fetal tissue sources be omitted. In order to ensure uniformity in NIH's oversight of research using hPSCs, the Guidelines were extended to govern hPSCs derived from both human embryos and fetal tissue.

Use of hPSCs Derived From Human Embryos

Respondents suggested that the Guidelines refer to ''fertility treatment'' rather than to ''infertility treatment'' in order to clarify that they allow the use of human embryos from treatments that employ assisted reproductive technologies to facilitate reproduction in fertile, as well as in infertile, individuals. The Guidelines have been changed accordingly.

Respondents suggested dropping the word ''early'' throughout the document or more clearly defining ''early.'' The word ''early'' in reference to human embryos has been deleted; the Guidelines make it clear that NIH funding of research using hPSCs derived in the private sector from human embryos can involve only embryos that have not reached the stage at which the mesoderm is formed.

Some respondents were concerned that embryos might be created for research purposes. Other respondents stated there should be no distinction between embryos created for research purposes and those created for fertility treatment. Investigators seeking NIH funds for research using hPSCs are required to provide documentation, prior to the award of any NIH funds, that embryos were created for the purposes of fertility treatment. President Clinton, many members of Congress, the NIH Human Embryo Research Panel, and the NBAC have all embraced the distinction between embryos created for research purposes and those created for reproductive purposes.

Respondents were concerned about the creation of a ''black market'' for human embryos, and expressed concerns that individuals will be coerced into donating embryos. The Guidelines state that there can be no incentives for donation and that a decision to donate must be made free of coercion. In addition, the Guidelines set forth conditions that will help ensure all donations are voluntary. For example, with regard to hPSCs derived from embryos, research using Federal funds may only be conducted if the cells were derived from frozen embryos that were created for the purpose of fertility treatment and that were in excess of clinical need.

Respondents commented on the requirement that human embryos be frozen in order to qualify for derivation of hPSCs to be used in NIH-funded research. Respondents suggested that the freezing requirement would preclude the use of hPSCs derived from embryos that are genetically and chromosomally abnormal, since such embryos are usually not frozen for reproductive purposes. While the NIH acknowledges that research on hPSCs derived from such embryos could yield important scientific information, limiting research to hPSCs derived from frozen human embryos will help ensure that the decision to donate the embryo for hPSC research is distinct and separate from the fertility treatment.

Financial Issues

Respondents expressed concern regarding the sale of fetal tissue for profit and whether hPSC research would encourage such activity. Respondents also were concerned about whether clinics or doctors would profit from the derivation of hPSCs and/or their sale. Section 498B of the Public Health Service Act prohibits any individual from knowingly acquiring or selling human fetal tissue for ''valuable consideration.'' In addition, the Guidelines prohibit any inducement for the donation of human embryos for research purposes. The Guidelines also call for an assurance that the hPSCs to be used in NIH-funded research were obtained through a donation or through a payment that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of the hPSCs. All grantees must sign an assurance that they are in compliance with all applicable Federal, State, and local laws. Each funded research institution is responsible for monitoring compliance by individual investigators with any such applicable laws.

Respondents questioned the prohibition against embryo donors benefitting financially from their donation. This clause was retained in the final Guidelines to help ensure that the donating individuals are offered no inducements to donate and that all donations are voluntary.

Respondents suggested that the Guidelines be strengthened to include a waiver of intellectual property rights. This proposed change would be inconsistent with 45 CFR 46.116 of the regulation for the protection of human subjects of research, which provides that no informed consent may include

language through which the subject waives or appears to waive any of the subject's legal rights.

Respondents questioned the reference in the requirements for informed consent related to the commercial potential of donated material. The paragraphs providing for disclosure in the informed consent of the possibility that the donated material could have commercial potential were modified. The reference in these paragraphs to ''donated material'' did not accurately reflect the intent of the provision. The Guidelines now make clear that the ''results of research on the human pluripotent stem cells may have commercial potential.''

Ineligible Research

Respondents objected to the areas of research that the NIH has deemed ineligible, particularly research that is not restricted by statute or regulation, such as research utilizing hPSCs that were derived using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human egg. The NIH determined that, at this time, research using hPSCs derived from such sources has not received adequate discussion and consideration by the public and is, therefore, ineligible for NIH funding.

Separation of Fertility Treatment and Abortion From Research

Respondents were concerned that hPSC research would encourage abortion. The law and the Guidelines guard against encouraging abortion by requiring that the decision to have an abortion be made apart from and prior to the decision to donate tissue.

Respondents objected to the condition in the Guidelines that the fertility physician could not be the same person as the researcher deriving stem cells. Some respondents stated that the Institutional Review Board (IRB) or an independent physician would be able to guard against this conflict of interest. The restriction was designed so that the person treating the individuals seeking fertility treatment, who is involved in decisions such as how many embryos to produce, is not the person seeking to derive hPSCs. This separation will help ensure that embryos will not be created in numbers greater than necessary for fertility treatment.

Respondents suggested that the clauses regarding donation of fetal tissue or human embryos for derivation of stem cells for eventual use in transplantation be changed explicitly to prevent directed donation. This change has been made.

Identifiers

Respondents were concerned about removing identifiers. There was concern that the investigator would not be able to document compliance with the Guidelines requirements without identifiers, or that the removal of identifiers would make it impossible to conduct certain genetic studies or develop therapeutic materials. The Guidelines have been modified to clarify that the term ''identifier'' refers to any information from which the donor(s) can be identified, directly or through identifiers linked to the donors. However, since information identifying the donor(s) may be necessary if the tissue or cells are to be used in transplantation, the Guidelines have also been modified to state that the informed consent should notify donor(s) whether or not identifiers will be retained.

Respondents commented that DNA is an identifier and that all donors of human embryos or fetal tissue should be told that identifiers such as DNA will be retained with the samples. Although DNA can be used to determine the individual from whom a tissue sample was taken, this can be done only when one has a sample from both the tissue in question and the putative donor; it cannot be used to identify an individual out of a population. Moreover, it is difficult to identify a donor using tissue derived from a fetus or embryo, since the tissue is not genetically identical to the donor.

Informed Consent and IRB Review

Respondents asked why investigators were expected to provide documentation of IRB review of derivation from human embryos, but not for derivation from fetal tissue. Respondents suggested that the requirements be changed so that protocols for both sources of hPSCs must be approved by an IRB. The Guidelines have been changed to make clear that the IRB review requirements regarding the derivation of cells from fetal tissue and human embryos are the same.

Comment was received expressing concern that the informed consent explicitly state that the donor will have no dispositional authority over derived pluripotent stem cells. The Guidelines state that donation of human embryos should have been made without any restriction regarding the individual(s) who may be the recipient of the cells derived from the hPSCs for transplantation. Such a statement is consistent with the statutory provision applicable to the donor informed consent for the use of fetal tissue for transplantation. The Guidelines now provide for the inclusion of a statement to this effect in the informed consent.

Respondents urged that the Guidelines be revised to remove the prohibition on potential donors receiving information regarding subsequent testing of donated tissue in the situation when physicians deem disclosure to be in the donors' best interest. This change has been made.

Respondents requested clarification regarding the persons from whom consent for donation of embryos for research must be obtained. The Guidelines call for informed consent from individual(s) who have sought fertility treatment. Only the individual(s) who were part of the decision to create the embryo for reproductive purposes should have been part of the decision to donate for the derivation of hPSCs.

Respondents urged that fertility clinics should be able to discuss with patients the option of donating embryos for research at the beginning of the IVF process. The Guidelines do not delineate the timeframe during which the general option of donating embryos for research can be discussed. However, according to the Guidelines, obtaining consent for donation of embryos for the purpose of deriving hPSCs should not occur until after the embryos are determined to be in ''excess of clinical need.''

Oversight

Respondents stated that the NIH's oversight in this area of research was very important to the legal and ethical conduct of this research, and asked for more information regarding the oversight process. Information about the operations of the Human Pluripotent Stem Cell Review Group (HPSCRG) can be found in the final Guidelines and on the NIH Web page.

Respondents were concerned about whether and how NIH would monitor research after a researcher receives NIH funds. Compliance with the Guidelines will be largely determined prior to the award of funds. Follow-up to ensure continued compliance with the Guidelines will be conducted in the same manner as for all other conditions of all other NIH grant awards. It is the responsibility of the investigator to file progress reports, and it is the responsibility of the funded institution to ensure compliance with the NIH Guidelines. NIH staff will also monitor the progress of these investigators as part of their regular duties.

Respondents asked about penalties for not following the Guidelines. The following actions may be taken by the NIH when there is a failure to comply with the terms and conditions of any award: (1) Under 45 CFR 74.14, the NIH can impose special conditions on an award, including increased oversight/monitoring/reporting requirements for an institution, project or investigator; and (2) under 45 CFR 74.62, if a grantee materially fails to comply with the terms and conditions of the award, the NIH may withhold funds pending correction of the problem or, pending more severe enforcement action, disallow all or part of the costs of the activity that was not in compliance, withhold further awards for the project, or suspend or terminate all or part of the funding for the project. Individuals and institutions may be debarred from eligibility for all Federal financial assistance and contracts under 45 CFR Part 76 and 48 CFR Subpart 9.4, respectively. Because these sanctions pertain to all conditions of grant award, the NIH did not reiterate them in the Guidelines.

Respondents suggested that the HPSCRG hold periodic Stem Cell Policy Conferences (similar to the Gene Therapy Policy Conferences conducted by the Recombinant DNA Advisory Committee (''RAC'')) in order to solicit and consider public comment from interested parties on the scientific, medical, legal, and ethical issues arising from stem cell research. Members of the HPSCRG will serve as a resource for recommending to the NIH any need for Human Pluripotent Stem Cell Policy Conferences.

Other Changes

Because compliance materials may be made public prior to funding decisions, we have added a sentence requiring the principal investigator's written consent to the disclosure of such material necessary to carry out public review and other oversight procedures.

The draft Guidelines required HPSCRG review of proposals from investigators planning to derive hPSCs from fetal tissue. Because the Guidelines address proposals for NIH funding for the use of hPSCs, this requirement has been removed from the Guidelines.

The text of the final Guidelines follows.

National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells

I. Scope of Guidelines

These Guidelines apply to the expenditure of National Institutes of Health (NIH) funds for research using human pluripotent stem cells derived from human embryos (technically known as human embryonic stem cells) or human fetal tissue (technically known as human embryonic germ cells). For purposes of these Guidelines, ''human pluripotent stem cells'' are cells that are self-replicating, are derived from human embryos or human fetal tissue, and are known to develop into cells and tissues of the three primary germ layers. Although human pluripotent stem cells may be derived from embryos or fetal tissue, such stem cells are not themselves embryos. NIH research funded under these Guidelines will involve human pluripotent stem cells derived: (1) From human fetal tissue; or (2) from human embryos that are the result of *in vitro* fertilization, are in excess of clinical need, and have not reached the stage at which the mesoderm is formed.

In accordance with 42 Code of Federal Regulations (CFR) 52.4, these Guidelines prescribe the documentation and assurances that must accompany requests for NIH funding for research using human pluripotent stem cells from: (1) Awardees who want to use existing funds; (2) awardees requesting an administrative or competing supplement; and (3) applicants or intramural researchers submitting applications or proposals. NIH funds may be used to derive human pluripotent stem cells from fetal tissue. NIH funds may not be used to derive human pluripotent stem cells from human embryos. These Guidelines also designate certain areas of human pluripotent stem cell research as ineligible for NIH funding.

II. Guidelines for Research Using Human Pluripotent Stem Cells That Is Eligible for NIH Funding

A. Utilization of Human Pluripotent Stem Cells Derived From Human Embryos

1. Submission to NIH

Intramural or extramural investigators who are intending to use existing funds, are requesting an administrative supplement, or are applying for new NIH funding for research using human pluripotent stem cells derived from human embryos must submit to NIH the following:

a. An assurance signed by the responsible institutional official that the pluripotent stem cells were derived from human embryos in accordance with the conditions set forth in section II.A.2 of these Guidelines and that the institution will maintain documentation in support of the assurance;

b. A sample informed consent document (with patient identifier information removed) and a description of the informed consent process that meet the criteria for informed consent set forth in section II.A.2.e of these Guidelines;

c. An abstract of the scientific protocol used to derive human pluripotent stem cells from an embryo;

d. Documentation of Institutional Review Board (IRB) approval of the derivation protocol;

e. An assurance that the stem cells to be used in the research were or will be obtained through a donation or through a payment that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of the stem cells;

f. The title of the research proposal or specific subproject that proposes the use of human pluripotent stem cells;

g. An assurance that the proposed research using human pluripotent stem cells is not a class of research that is ineligible for NIH funding as set forth in section III of these Guidelines; and

h. The Principal Investigator's written consent to the disclosure of all material submitted under Paragraph A.1 of this section, as necessary to carry out the public review and other oversight procedures set forth in section IV of these Guidelines.

2. Conditions for the Utilization of Human Pluripotent Stem Cells Derived From Human Embryos

Studies utilizing pluripotent stem cells derived from human embryos may be conducted using NIH funds only if the cells were derived (without Federal funds) from human embryos that were created for the purposes of fertility treatment and were in excess of the clinical need of the individuals seeking such treatment.

a. To ensure that the donation of human embryos in excess of the clinical need is voluntary, no inducements, monetary or otherwise, should have been offered for the donation of human embryos for research purposes. Fertility clinics and/or their affiliated laboratories should have implemented specific written policies and practices to ensure that no such inducements are made available.

b. There should have been a clear separation between the decision to create embryos for fertility treatment and the decision to donate human embryos in excess of clinical need for research purposes to derive pluripotent stem cells. Decisions related to the creation of embryos for fertility treatment should have been made free

from the influence of researchers or investigators proposing to derive or utilize human pluripotent stem cells in research. To this end, the attending physician responsible for the fertility treatment and the researcher or investigator deriving and/or proposing to utilize human pluripotent stem cells should not have been one and the same person.

c. To ensure that human embryos donated for research were in excess of the clinical need of the individuals seeking fertility treatment and to allow potential donors time between the creation of the embryos for fertility treatment and the decision to donate for research purposes, only frozen human embryos should have been used to derive human pluripotent stem cells. In addition, individuals undergoing fertility treatment should have been approached about consent for donation of human embryos to derive pluripotent stem cells only at the time of deciding the disposition of embryos in excess of the clinical need.

d. Donation of human embryos should have been made without any restriction or direction regarding the individual(s) who may be the recipients of transplantation of the cells derived from the human pluripotent stem cells.

e. Informed Consent

Informed consent should have been obtained from individuals who have sought fertility treatment and who elect to donate human embryos in excess of clinical need for human pluripotent stem cell research purposes. The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether or not to donate their embryos for research purposes.

Informed consent should have included:

(i) A statement that the embryos will be used to derive human pluripotent stem cells for research that may include human transplantation research;

(ii) A statement that the donation is made without any restriction or direction regarding the individual(s) who may be the recipient(s) of transplantation of the cells derived from the embryo;

(iii) A statement as to whether or not information that could identify the donors of the embryos, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;

(iv) A statement that derived cells and/or cell lines may be kept for many years;

(v) Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development;

(vi) A statement that the research is not intended to provide direct medical benefit to the donor; and

(vii) A statement that embryos donated will not be transferred to a woman's uterus and will not survive the human pluripotent stem cell derivation process.

f. Derivation protocols should have been approved by an IRB established in accord with 45 CFR 46.107 and 46.108 or FDA regulations at 21 CFR 56.107 and 56.108.

B. Utilization of Human Pluripotent Stem Cells Derived From Human Fetal Tissue

1. Submission to NIH

Intramural or extramural investigators who are intending to use existing funds, are requesting an administrative supplement, or are applying for new NIH funding for research using human pluripotent stem cells derived from fetal tissue must submit to NIH the following:

a. An assurance signed by the responsible institutional official that the pluripotent stem cells were derived from human fetal tissue in accordance with the conditions set forth in section II.A.2 of these Guidelines and that the institution will maintain documentation in support of the assurance;

b. A sample informed consent document (with patient identifier information removed) and a description of the informed consent process that meet the criteria for informed consent set forth in section II.B.2.b of these Guidelines;

c. An abstract of the scientific protocol used to derive human pluripotent stem cells from fetal tissue;

d. Documentation of IRB approval of the derivation protocol;

e. An assurance that the stem cells to be used in the research were or will be obtained through a donation or through a payment that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of the stem cells;

f. The title of the research proposal or specific subproject that proposes the use of human pluripotent stem cells;

g. An assurance that the proposed research using human pluripotent stem cells is not a class of research that is ineligible for NIH funding as set forth in section III of these Guidelines; and

h. The Principal Investigator's written consent to the disclosure of all material submitted under Paragraph B.1 of this section, as necessary to carry out the public review and other oversight procedures set forth in section IV of these Guidelines.

2. Conditions for the Utilization of Human Pluripotent Stem Cells Derived From Fetal Tissue.

a. Unlike pluripotent stem cells derived from human embryos, DHHS funds may be used to support research to derive pluripotent stem cells from fetal tissue, as well as for research utilizing such cells. Such research is governed by Federal statutory restrictions regarding fetal tissue research at 42 U.S.C. 289g–2(a) and the Federal regulations at 45 CFR 46.210. In addition, because cells derived from fetal tissue at the early stages of investigation may, at a later date, be used in human fetal tissue transplantation research, it is the policy of NIH to require that all NIH-funded research involving the derivation or utilization of pluripotent stem cells from human fetal tissue also comply with the fetal tissue transplantation research statute at 42 U.S.C. 289g–1.

b. Informed Consent

As a policy matter, NIH-funded research deriving or utilizing human pluripotent stem cells from fetal tissue should comply with the informed consent law applicable to fetal tissue transplantation research (42 U.S.C. 289g–1) and the following conditions. The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether to donate fetal tissue for research purposes.

Informed consent should have included:

(i) A statement that fetal tissue will be used to derive human pluripotent stem cells for research that may include human transplantation research;

(ii) A statement that the donation is made without any restriction or direction regarding the individual(s) who may be the recipient(s) of transplantation of the cells derived from the fetal tissue;

(iii) A statement as to whether or not information that could identify the donors of the fetal tissue, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;

(iv) A statement that derived cells and/or cell lines may be kept for many years;

(v) Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development; and

(vi) A statement that the research is not intended to provide direct medical benefit to the donor.

c. Derivation protocols should have been approved by an IRB established in accord with 45 CFR 46.107 and 46.108 or FDA regulations at 21 CFR 56.107 and 56.108.

III. Areas of Research Involving Human Pluripotent Stem Cells That Are Ineligible for NIH Funding

Areas of research ineligible for NIH funding include:

A. The derivation of pluripotent stem cells from human embryos;

B. Research in which human pluripotent stem cells are utilized to create or contribute to a human embryo;

C. Research utilizing pluripotent stem cells that were derived from human embryos created for research purposes, rather than for fertility treatment;

D. Research in which human pluripotent stem cells are derived using somatic cell nuclear transfer, *i.e.,* the transfer of a human somatic cell nucleus into a human or animal egg;

E. Research utilizing human pluripotent stem cells that were derived using somatic cell nuclear transfer, *i.e.,* the transfer of a human somatic cell nucleus into a human or animal egg;

F. Research in which human pluripotent stem cells are combined with an animal embryo; and

G. Research in which human pluripotent stem cells are used in combination with somatic cell nuclear transfer for the purposes of reproductive cloning of a human.

IV. Oversight

A. The NIH Human Pluripotent Stem Cell Review Group (HPSCRG) will review documentation of compliance with the Guidelines for funding requests that propose the use of human pluripotent stem cells. This working group will hold public meetings when a funding request proposes the use of a line of human pluripotent stem cells that has not been previously reviewed and approved by the HPSCRG.

B. In the case of new or competing continuation (renewal) or competing supplement applications, all applications shall be reviewed by HPSCRG and for scientific merit by a Scientific Review Group. In the case of requests to use existing funds or applications for an administrative supplement or in the case of intramural proposals, Institute or Center staff should forward material to the HPSCRG for review and determination of compliance with the Guidelines prior to allowing the research to proceed.

C. The NIH will compile a yearly report that will include the number of applications and proposals reviewed and the titles of all awarded applications, supplements or administrative approvals for the use of existing funds, and intramural projects.

D. Members of the HPSCRG will also serve as a resource for recommendations to the NIH with regard to any revisions to the NIH Guidelines for Research Using Human Pluripotent Stem Cells and any need for human pluripotent stem cell policy conferences.

Dated: August 17, 2000.

Ruth L. Kirschstein,

Principal Deputy Director, NIH.

[FR Doc. 00–21760 Filed 8–23–00; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Notification of Request for Emergency Clearance; Modification of OMB No. 0925–0001/Exp. 2/01, ''PHS 398 Research and Research Training Grant Applications and Related Forms''

SUMMARY: In accordance with section 3507(j) of the Paperwork Reduction Act of 1995, the National Institutes of Health (NIH) hereby publishes notification of a request for Emergency Clearance for modification of the information collection related to the National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, published elsewhere in today's **Federal Register**. The currently approved information collection OMB No. 0925–0001 permits the NIH to request from applicant institutions information related to application, award, and continued compliance with the terms of Federal assistance for research and research-related training. The approval also covers the information collection authorized in accordance with 42 CFR 52, specifically the obtaining of ''[o]ther pertinent information the Secretary may require to evaluate the proposed project.'' (42 CFR 52.4(f))

The final National Institutes of Health Guidelines for Research Using Pluripotent Stem Cells requires submission of additional documentation in the form of additional institutional records from a limited number of institutions to enable an independent panel of non-Government experts to ascertain institutional compliance with the Guidelines. Compliance with the requirements of existing law and regulations is authorized under OMB No. 0925–0418, Exp. 1/01, ''Protection of Human Subjects: Assurance Identification/Certification/ Declaration.''

The present modification relates to the added reporting requirement of submission of documentation to permit the agency to exercise the oversight responsibility established under the Guidelines.

This modification is essential to the mission of NIH (42 USC 241 and 282(b)) and is of the highest scientific priority as determined by both internal review and external review by a panel of scientific and other experts in the field of stem cell research. After extensive consultation with the public and a public meeting, the NIH published proposed National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells in the **Federal Register** on December 2 , 1999 (**Federal Register**, Vol. 64, No. 231, pages 67576–67579). The comment period was extended to February 22, 2000. (**Federal Register**, February 3, 2000, Vol. 65, No. 23, page 539). Following the period of comment, NIH has proceeded to finalize the Guidelines, which are published elsewhere in this issue of the **Federal Register**.

These Guidelines are essential to ensure that NIH-funded research in this area is conducted in an ethical and legal manner. The NIH has determined that the oversight process stipulated in the Guidelines will achieve this objective. The Guidelines will require that institutions requesting or using NIH funds for research using human pluripotent stem cells submit additional documentation to the NIH in the form of institutional records that will permit NIH oversight in accordance with the Guidelines.

NIH has taken all practicable steps to consult with the scientific community and the public, through the process described above and through the careful consideration of all comments received from the public.

In view of the extensive period of comment and the thorough consideration of all views, both prior to the publication of the proposed Guidelines in December 1999 and subsequently, NIH is herewith requesting that OMB approve the modification of the collection of information simultaneously with the publication of the **Federal Register**

notice and the publication of the Guidelines in the **Federal Register**.

Proposed Collection

Title: Research and Research Training Grant Applications and Related Forms PHS–398 and PHS–2590.

Type of Information Collection Request: Revision.

Need and Use of Information Collection: The additional NEW reporting requirement is needed to ascertain compliance with the National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells. PHS–398 and PHS–2590 are used to apply for research project grants, Research Career Awards (RCA), and Institutional National Research Service Awards (NRSA).

Frequency of Response: On occasion and annually.

Affected Public: Individuals or households; business or other for-profit; not-for-profit institutions; Federal Government; and State, local or tribal government.

Type of Respondents: Research institutions.

The annual reporting burden was:

Estimated Number of Respondents: 111,482.

Estimated Number of Responses per Respondent: 1.05.

Average Burden Hours Per Response: 16.34.

Estimated Total Annual Burden Hours Requested: 1,913,166.

The NEW annual reporting burden is as follows:

Estimated Number of Respondents: 111,582.

Estimated Number of Responses per Respondent: 1.05.

Average Burden Hours Per Response: 16.33.

Estimated Total Annual Burden Hours Requested: 1,913,466.

There are no Capital Costs to report. There are no Operating or Maintenance Costs to report.

FOR FURTHER INFORMATION CONTACT: The Office of Management and Budget, Office of Information and Regulatory Affairs, New Executive Office Building, Room 10235, Washington, D.C. 20503, Attention: Desk Officer for NIH.

Dated: August 17, 2000.

Ruth L. Kirschstein,

Principal Deputy Director, National Institutes of Health.

[FR Doc. 00–21761 Filed 8–23–00; 8:45 am]

BILLING CODE 4140–01–P

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, 64 Grove Street, Watertown, MA 02472; DR. THERESA DEISHER, 1420 Fifth Avenue, Suite 2650, Seattle, WA 98101; NIGHTLIGHT CHRISTIAN ADOPTIONS, individually and as next friend for PLAINTIFF EMBRYOS, 801 East Chapman Avenue, Suite 106, Fullerton, CA 92831; SHAYNE AND TINA NELSON, 3908 Martinez Way, Riverton, UT 84065; WILLIAM AND PATRICIA FLYNN, 8 Nottingham Dr., East Sandwich, MA 02537; CHRISTIAN MEDICAL ASSOCIATION, 2604 Highway 421, Bristol, TN 37620, Plaintiffs, v. KATHLEEN SEBELIUS, in her official capacity as Secretary of the Department of Health and Human Services, 200 Independence Avenue, S.W., Washington, D.C. 20201; DEPARTMENT OF HEALTH AND HUMAN SERVICES; DR. FRANCIS S. COLLINS, in his official capacity as Director of the National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892; NATIONAL INSTITUTES OF HEALTH, Defendants.	Civil Action No. ____

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiffs, by their attorneys, allege as follows:

I. INTRODUCTION

1. For over 13 years, Congress has explicitly prohibited the use of federal monies to fund research in which embryos are destroyed or knowingly subjected to harm. *See* Balanced Budget Downpayment Act, Pub. L. No. 144-99, § 128, 110 Stat. 26, 34 (1996). This prohibition on the use of federal funds for embryonic stem cell research remains in place today. *See* Omni-

bus Appropriations Act, 2009, Pub. L. No. 111-8, § 509, 123 Stat. 524, 803 (2009) ("Federal Funding Ban" or "Dickey-Wicker Amendment"). Despite the explicit federal ban on funding embryonic stem cell research, on July 7, 2009, Defendants promulgated the Guidelines for Human Stem Cell Research ("Guidelines"). 74 Fed. Reg. 32,170. These Guidelines authorize public funding of research that depends upon and, indeed, requires the destruction of living human embryos. As a result, these Guidelines violate the Federal Funding Ban, and are therefore invalid. *See* 5 U.S.C. § 706(2)(A).

2. Furthermore, in promulgating the Guidelines, Defendants failed to follow the procedures required by the Administrative Procedure Act. *See* 5 U.S.C. § 706(2)(D). Contrary to the rulemaking procedures set forth in 5 U.S.C. § 553, Defendants entered the rulemaking proceedings with an unalterably closed mind, having prejudged the relevant issues; did not allow a sufficient time period for commenting on the draft guidelines, proposed on April 23, 2009, 74 Fed. Reg. 18,578 ("Draft Guidelines"); refused to respond to or even consider comments asking NIH to reconsider its decision to fund embryonic stem cell research; and did not properly consider or respond to the more than 49,000 comments that were submitted regarding the Draft Guidelines.

3. The implementation of the Guidelines also constitutes arbitrary and capricious agency action under 5 U.S.C. § 706(2)(A) because the Defendants have repeatedly and improperly dismissed or ignored substantial scientific research that demonstrates that adult stem cells and induced pluripotent stem cells ("iPSCs") provide ethically and medically superior alternatives to medical experimentation on stem cells derived from human embryos; the Guidelines fail to implement proper and necessary safeguards ensuring that embryo donors give truly informed consent; the Guidelines fail to protect against conflicts of interest among the fertility clinic that

creates the embryo, the destroyer of the embryo, and the recipient of federal funding; and the Defendants have failed to take into account long-established state laws and policies protecting human embryos.

4. For these reasons, Plaintiffs bring this action against Defendants Kathleen Sebelius, in her official capacity as Secretary of the Department of Health and Human Services ("HHS"), HHS, Dr. Francis S. Collins, in his official capacity as Director of the National Institutes of Health ("NIH"), and NIH (collectively, the "Defendants"), and seek an order (a) declaring that the Guidelines are contrary to law, were promulgated without observing the procedures required by law, and constitute arbitrary and capricious agency action; and (b) enjoining Defendants from applying the Guidelines or otherwise funding research involving the destruction of human embryonic stem cells.

II. JURISDICTION AND VENUE

5. This action arises under 5 U.S.C. § 706(2) and the Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, § 509, 123 Stat. 524, 803 (2009), and therefore presents a federal question, giving this Court jurisdiction over the matter pursuant to 28 U.S.C. § 1331. Venue is proper in this Court under 28 U.S.C. § 1391(e) because this is an action against officers and agencies of the United States, defendant HHS resides in this judicial district, defendant Kathleen Sebelius performs her official duties in this judicial district, and a substantial part of the events or omissions giving rise to this action occurred in this judicial district.

III. PARTIES

A. Plaintiffs

6. Plaintiff Dr. James L. Sherley is a senior scientist currently working at the Boston Biomedical Research Institute where he and his research team are pursuing the study of normal molecular and biochemical processes in adult stem cells that are involved in cancer initiation and

contribute to aging. Dr. Sherley, a Massachusetts resident, received his B.A. in Biology from Harvard University, and his M.D. and Ph.D. in Molecular Biology from John Hopkins University. Prior to joining the Boston Biomedical Research Institute, Dr. Sherley worked in the Department of Molecular Oncology at the Fox Chase Cancer Center in Philadelphia, Pennsylvania, and served as an associate professor in the Department of Biological Engineering at the Massachusetts Institute of Technology. Dr. Sherley does not conduct research on embryonic stem cells. His research focuses on improving methods for identifying adult stem cells and producing them in large numbers for therapeutic development. Dr. Sherley has received funding from NIH for research aimed at developing new methods for identification and production of human adult stem cells that have the potential for human cell therapy. Since 1999, Dr. Sherley has applied for NIH funding approximately 41 times. Twelve of these proposals have received NIH funding, and one proposal is currently pending. Dr. Sherley will continue to seek NIH funding for adult stem cell research in the future. The Guidelines, which unlawfully authorize federal funding of research using stem cells derived from human embryos, will result in increased competition for limited federal funding and will thereby injure Dr. Sherley's ability to compete successfully for the NIH stem cell research funds that he seeks.

7. Plaintiff Dr. Theresa Deisher, a resident of the State of Washington, is the founder, managing member, and research and development director of AVM Biotechnology. Dr. Deisher received her B.A. in Human Biology and Ph.D. in Molecular and Cellular Physiology from Stanford University. Dr. Deisher has seventeen years of experience in scientific and corporate leadership positions involving research, discovery, production, and commercialization of human therapeutics. After obtaining her Ph.D., Dr. Deisher was employed by Repligen Corporation as a Research Scientist where she managed a staff of associates and scientists and di-

rected the development of research and clinical tests in support of Phase I and Phase II clinical trials for various Repligen developmental efforts. Thereafter, Dr. Deisher served as Senior Scientist of Cardiovascular Biology at ZymoGenetics, Inc., Senior Staff Scientist of Vascular Biology at Immunex, and Principal Scientist at Amgen, Inc. Most recently, Dr. Deisher served as Vice President of Research and Development for Cellcyte Genetics Corp., a post she held prior to founding AVM Biotechnology in 2007. Dr. Deisher does not conduct research using embryonic stem cells. She specializes in adult stem cell therapies and regenerative medicine, and her research has resulted in the issuance of twenty-three patents. In order to continue her research, Dr. Deisher and AVM Biotechnology will require federal funding, and are in the process of applying for NIH grants for research on adult stem cells. The Guidelines, which unlawfully authorize federal funding of research using stem cells derived from human embryos, will result in increased competition for limited federal funding and will thereby injure Dr. Deisher's ability to successfully compete for the NIH stem cell research funds that she requires.

8. Plaintiff Nightlight Christian Adoptions ("Nightlight") is a non-profit, licensed adoption agency located in the States of California and South Carolina that is dedicated to protecting human embryos conceived through *in vitro* fertilization. Through its "Snowflakes" Program, Nightlight enables adoptive parents to adopt human embryos that are being stored in fertilization clinics. Nightlight has assisted many adoptive parents in successfully adopting and implanting these embryos, resulting in numerous births. Nightlight currently has a waiting list of families seeking to adopt embryos, and often these families must wait several months. The Guidelines permit federal funding for research on stem cells that are derived from embryos that, while no longer needed for the donors' reproductive purposes, could have been donated to an adoption agency such as Nightlight. Therefore, the Guidelines, in unlawfully utilizing federal

monies to fund human embryonic stem cell research, decrease the number of embryos available for adoption. The Guidelines pose a recurring threat to embryos that adoption agencies such as Nightlight could otherwise place for adoption with waiting families, and impose a consequent burden on the resources that Nightlight devotes to facilitating embryo adoption. Moreover, by perpetuating the myth that embryos are a more promising source of human therapies and cures than adult stem cells, Defendants effectively discourage families with frozen embryos from considering embryo donation and adoption because they are led to believe that there is a high moral purpose in donating the embryos for research. Nightlight brings this action on behalf of itself and, pursuant to Fed. R. Civ. P. 17(c), as guardian ad litem of the Plaintiff Embryos, who are minor persons that qualify for representation under Rule 17(c).

9. Plaintiff Embryos include all individual human embryos that are or will be "created using in vitro fertilization (IVF) for reproductive purposes and [are] no longer needed for these purposes." 74 Fed. Reg. at 32,171. The Embryos are persons that qualify for representation under Fed. R. Civ. P. 17(c). NIH's violation of the Federal Funding Ban will place the lives of these Embryos under a recurring risk of destruction.

10. Plaintiffs Shayne and Tina Nelson, residents of the State of Utah, are clients of Plaintiff Nightlight. The Nelsons have two children, both adopted embryos, and are currently seeking to adopt additional embryos for implantation. Defendants' promulgation of the Guidelines in violation of federal law jeopardizes the likelihood that embryos will become available in a timely manner for adoption and implantation.

11. Plaintiffs William and Patricia Flynn, residents of the State of Massachusetts, are clients of Plaintiff Nightlight. The couple have one child, an adopted embryo, and seek to adopt

additional human embryos. Defendants' promulgation of the Guidelines jeopardizes the likelihood that human embryos will become available for Mr. and Mrs. Flynn to adopt in the future.

12. Plaintiff Christian Medical Association ("CMA") is located in Bristol, Tennessee. CMA is a non-profit association of doctors that is dedicated to improving the ethical standards of health care in the United States and abroad. CMA is opposed to federal funding of human embryonic stem cell research, and expends approximately $300,000 a year in an ongoing effort to promote high ethical standards in the field of medical research, to assist its members in dealing with the issues posed by the development of medical practice and research, and to encourage legal reform. If Defendants are not enjoined from illegally funding research using stem cells derived from human embryos, the Guidelines will frustrate CMA's purpose and require CMA to devote significant resources to address and counteract the grave ethical problems posed by illegal public funding of embryo research.

B. Defendants

13. Defendant Kathleen Sebelius is the Secretary of HHS. She was confirmed by the Senate and sworn in as Secretary on April 28, 2009. Her official address is 200 Independence Avenue, S.W., Washington, D.C. 20201. She is sued in her official capacity. In this capacity, Secretary Sebelius has overall responsibility for the operation and management of HHS, of which NIH is an agency. Ms. Sebelius exercises cabinet-level oversight and supervisory authority over the management and policy of NIH. Ms. Sebelius is thus responsible, in her official capacity, for NIH's unlawful promulgation of the Guidelines and for related acts and omissions alleged herein.

14. Defendant HHS is, and was at all times relevant hereto, an executive agency of the U.S. government subject to the Administrative Procedure Act. *See* 5 U.S.C. § 551(1). HHS is located at 200 Independence Avenue, S.W., Washington, D.C. 20201.

15. Defendant Dr. Francis S. Collins is the Director of NIH and has served in that position since August 7, 2009. Dr. Collins is sued in his official capacity. His official address is 9000 Rockville Pike, Bethesda, MD 20892. Dr. Collins has the overall responsibility for the operation and management of NIH.

16. Defendant NIH is, and was at all times relevant hereto, an agency within HHS subject to the Administrative Procedure Act. *See* 5 U.S.C. § 551(1). NIH conducts, regulates, and supports federally funded biomedical scientific research. NIH is responsible for issuing and administering the Guidelines that are the subject matter of this suit. NIH is located at 9000 Rockville Pike, Bethesda, MD 20892.

17. Defendants, and those subject to their supervision, direction, and control are responsible for the actions complained of herein. The relief requested in this action is sought against each Defendant, as well as against each Defendant's officers, employees, and agents, and against all persons acting in cooperation with Defendant(s), under their supervision, at their direction, or under their control.

IV. BACKGROUND

A. Congress's Ban On The Federal Funding Of Human Embryo Research

18. For more than a decade, Congress has explicitly banned federal funding of research in which embryos are destroyed or knowingly subject to harm. *See* Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, § 509, 123 Stat. 524, 803 (2009). This prohibition was a direct response to efforts on the part of NIH to begin funding stem cell research that utilized human embryos. Specifically, in early 1993, NIH Director Harold Varmus convened the Human Embryo Research Panel, which recommended that NIH fund research using "surplus" human embryos. 59 Fed. Reg. 28,874, 28,875 (June 3, 1994). The Human Embryo Research Panel submitted its report to the NIH Advisory Committee to the Director, and the report was subse-

quently transmitted to NIH Director Varmus, who approved implementing the Panel's recommendations.

19. Before any grants were made under NIH's new standards, however, Congress enacted an appropriations rider to override Director Varmus's decision and prevent federal funding of human embryo research. *See* Balanced Budget Downpayment Act, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996). The rider provided in relevant part: "None of the funds made available by [this Act] may be used for—(1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 C.F.R. § 46.208(a)(2) and 42 U.S.C. 289g(b)."

20. This congressional prohibition on the use of HHS funds for human embryo[1] research has been renewed every year since the enactment of the initial rider. Most recently, Congress renewed the rider, without any material change, in the HHS appropriations bill that was signed into law on March 11, 2009. *See* Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, § 509, 123 Stat. 524, 803 (2009).[2]

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[1] The Federal Funding Ban defines "human embryo" as "any organism, not protected as a human subject under 45 C.F.R. 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

[2] The new version of the rider cross-references 45 C.F.R. § 46.204(b), which requires that any research-related risk to a human fetus be "caused solely by interventions or procedures that hold out the prospect of direct benefit for . . . the fetus; or if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means," and 42 U.S.C. § 289g(b), which demands that the "risk standard . . . be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term."

21. Under the Human Subject Protection Regulations—cited by Congress in the Dickey-Wicker amendment—"research" is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." 45 C.F.R. § 46.102(d). And according to HHS's own guidance, an institution that receives federal funding is generally engaged in human subjects research "even where all activities involving human subjects are carried out by agents of another institution." Final Guidance on Engagement of Institutions in Human Subjects Research, 73 Fed. Reg. 63,151 (Oct. 23, 2008).

22. The rider therefore evinces a clear congressional intent to prohibit federal funding for research that is dependent on harming or destroying human embryos. Because the process by which human embryonic stem cells are extracted from human embryos necessarily destroys the embryos, the Federal Funding Ban expressly prohibits federal funding of human embryonic stem cell research.

23. In addition, the Federal Funding Ban prohibits "knowingly subject[ing embryos] to risk of injury or death." Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, § 509(a)(2). Because funding and conducting embryonic stem cell research will inevitably create a substantial risk—indeed, a virtual certainty—that more human embryos will be destroyed in order to derive embryonic stem cells for research purposes, the Federal Funding Ban clearly prohibits the federal government from knowingly funding and/or conducting such research.

24. Researchers conducting embryonic stem cell research know that embryos were destroyed as a necessary part of the research process needed to create the stem cells.

25. In funding the research, Defendants know that they are creating incentives for and acting as the direct and foreseeable cause of the destruction of embryos. Indeed, the Guidelines function to regulate the process by which these embryos will be destroyed.

B. The NIH's 2000 Funding Guidelines

26. Despite the Federal Funding Ban, in 2000 NIH nonetheless issued guidelines that would permit the federal funding of human embryonic stem cell research. On December 2, 1999, NIH published a Notice of its Draft Guidelines for Research Involving Human Pluripotent Stem Cells in the Federal Register and invited public comment for a period of 60 days. *See* 64 Fed. Reg. 67,576 (Dec. 2, 1999). NIH received approximately 50,000 comments from members of Congress, patient advocacy groups, scientific societies, religious organizations, and private citizens. The vast majority of these comments were opposed to the draft guidelines.

27. NIH finalized and made effective "Guidelines for Research Using Human Pluripotent Stem Cells" ("2000 Guidelines") on August 25, 2000. 65 Fed. Reg. 51,976. The 2000 Guidelines "appl[ied] to the expenditure of [NIH] funds for research using human pluripotent stem cells derived from human embryos." *Id.* at 51,979. Contrary to Congress's plainly expressed intent, the 2000 Guidelines, like the current Guidelines, would have allowed federal funding of research using embryonic stem cells derived from the destruction of human embryos.

C. NIH's Withdrawal Of The 2000 Guidelines

28. In 2001, NIH delayed implementation of the 2000 Guidelines pending a review of their legality under federal law. As a result of that review, NIH issued new guidelines that provided funding to researchers who either already had derived "stem cell lines" from human embryos, or who proposed to use such existing stem cell lines in their own research. NIH determined that this approach complied with the Dickey-Wicker Amendment because with respect to those cell lines, the life and death decision had already been made, leaving no incentive to de-

stroy more embryos. But NIH withdrew the 2000 Guidelines and refused to fund research on those "excess" embryos that were cryopreserved in *in vitro* fertilization banks. 66 Fed. Reg. 57,107 (Nov. 14, 2001).

29. NIH has acknowledged the benefits of medically and ethically superior alternatives to human embryonic stem cells and appropriately allocated federal funds to the research and development of such alternatives. On June 22, 2007, then-President Bush issued Executive Order 13,435, which expressed a policy of "expanding approved stem cell lines in ethically responsible ways" to include "alternative sources of pluripotent stem cells" that were "derived without creating a human embryo for research purposes or destroying, discarding, or subjecting to harm a human embryo or fetus." 72 Fed. Reg. 34,591. Such "alternative sources" included induced pluripotent stem cells ("iPSCs")—pluripotent cells (or cells that are able to develop into most cell types) that are derived from adult stem cells and reprogrammed in such a way as to achieve the characteristics of embryonic stem cells. In 2007, NIH characterized the research advances relating to iPSCs as "very exciting." National Institutes of Health, Plan for Implementation of Executive Order 13,435: Expanding Approved Stem Cell Lines in Ethically Responsible Ways, Sept. 18, 2007, *available at* http://stemcells.nih.gov/staticresources/policy/eo13435.pdf. By federally funding iPSC research and other alternatives to human embryonic stem cell research that would not result in the destruction of human embryos, NIH supported the most current and promising science while adhering to the mandate of the Federal Funding Ban.

D. The NIH's New Funding Guidelines

30. On March 9, 2009, President Obama issued Executive Order 13,505, which required that "within 120 days . . . the Secretary [of HHS], through the Director of NIH, shall review existing NIH guidance and other widely recognized guidelines on human stem cell re-

search . . . and issue new NIH guidance on such research that is consistent with [the] order." Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 11, 2009).

31. Additionally, Executive Order 13,505 revoked, without explanation, Executive Order 13,435, which had expanded approved stem cell lines to include iPSCs. As a result, there is no longer any guarantee that federal funds will be allocated to alternative sources of stem cells that do not require the creation or destruction of embryos.

32. After the issuance of Executive Order 13,505, but even before the issuance of the Draft Guidelines or the public comment period, Defendants evinced a preconceived intent to expand federally funded stem cell research to include newly derived human embryonic stem cells. For instance, after the issuance of Executive Order 13,505, on April 17, 2009, then-acting Director Raynard S. Kington reported to the press that NIH "*will* expand greatly the number of cell lines eligible for funding." Guatam Naik, *NIH Offers Rules for Embryonic Stem Cell Research*, Wall St. J., Apr. 17, 2009, *available at* http://online.wsj.com/article/SB123999343505429693.html (emphasis added). Additionally, even prior to issuing the Draft Guidelines, NIH announced that it would begin accepting applications for grants funding human embryonic stem cell research. *See* Implementation of Executive Order on Removing Barriers to Responsible Scientific Research Involving Human Stem Cells, NOT-OD-09-085 (Apr. 17, 2009), *available at* http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-085.html. Such actions demonstrate that Defendants entered the rulemaking process having already prejudged the merits of human embryonic stem cell research, thus limiting or foreclosing their ability to fully and fairly consider the comments they received.

33. Defendants promulgated the Draft Guidelines for Human Stem Cell Research on April 23, 2009, 74 Fed. Reg. 18,578, and invited public comment. The comment period, howev-

er, lasted for a mere 34 days, which did not afford interested parties an adequate opportunity to comprehensively review and comment on the Draft Guidelines—especially given the scientific complexity and ethical ramifications of the issues raised by the Draft Guidelines. This was in violation of 5 U.S.C. § 553.

34. After receiving 49,015 comments, Defendants issued the final Guidelines only six weeks after the close of the comment period, on July 7, 2009. 74 Fed. Reg. 32,170. This time period did not allow Defendants adequate time to consider fully and respond appropriately to the vast number of comments they received during the comment period.

35. In order to fit within this rushed timeframe, Defendants disregarded *more than 60 percent* of the public comments on the Guidelines. *See* Jeffrey Young, *Administration Unveils Stem Cell Rules*, The Hill, July 6, 2009, *available at* http://thehill.com/leading-the-news/obama-administration-unveils-stem-cell-rules-2009-07-06.html (reporting that NIH's Acting Director admitted the agency ignored approximately 30,000 comments as "unresponsive" to the Guidelines because NIH "did not ask the public whether we should fund research on human embryonic stem cells. We asked the public how we should fund human embryonic stem cell research.").

36. Even before submitting the Guidelines for notice and comment, Defendants had prejudged the issues involved in funding embryonic stem cell research. Specifically, Defendants had already decided, before considering the comments, that they would fund hESC research. *See id.* This pre-judgment allowed Defendants to label approximately 60 percent of the comments to the Guidelines unresponsive, but it did not satisfy their burden to consider any comments with an open mind.

37. Defendants also failed to respond adequately—or respond at all—to many significant comments received in opposition to the Guidelines. NIH's response to the nearly 50,000 comments is contained in a mere 3.5 pages of text. *See* 74 Fed. Reg. 32,170, 32,170–74.

38. This meager response did *not*: provide a rational connection between the facts found and the choice to fund embryonic stem cell research to the detriment of adult stem cell research; consider viable alternatives such as induced pluripotent stem cell research; take into account relevant considerations such as the inherent flaws of embryonic stem cells; consider the effects of the Guidelines on state statutory regimes; cogently justify the provisions addressing conflicts of interest and informed consent; or fulfill Defendants' responsibility to respond to significant arguments made during the public comment period.

39. Because the Guidelines permit federal funds to be used for research in which embryos are destroyed, Defendants' actions to implement the Guidelines violate federal law.

40. Although the Guidelines set out to create the appearance of protection against conflicts of interest, the vagueness of the procedural requirements creates an unacceptable risk that these conflicts will survive. As described by NIH, the Guidelines purport to fund only "ethically responsible" research and explicitly fund only research for cells that were "created . . . for reproductive purposes" and "were no longer needed for this purpose." 74 Fed. Reg. at 32,170, 32,174. But notwithstanding the serious ethical concerns associated with embryonic stem cell research, the Guidelines require merely that "[t]he attending physician responsible for reproductive clinical care and the research deriving and/or proposing to utilize hESCs should not have been the same person *unless separation was not practicable*." *See id.* at 32,174 (emphasis added). This makes it possible for the *in vitro* fertilization facility to create and destroy the embryo, and then utilize the derived embryonic stem cell as a research subject. By allowing the same

person or clinic to be involved in the creation of embryos "for reproductive purposes" and the research using the embryos that are "no longer needed," the Guidelines allow researchers to evade the substantive requirements by creating more embryos at the outset to ensure that there are "spares" left for research. This risk was made known to NIH during the public comment period, but NIH nonetheless failed to explain how the Guidelines' conflict of interest provisions can possibly ensure that federally funded embryonic stem cell research is conducted in an ethical manner.

41. The Guidelines do not ensure that potential donors will be adequately informed of the relevant scientific, legal, and practical implications of donating human embryos for research purposes. Potential donors are not told that many scientists believe that human embryos are human life or that many States hold that human life begins at conception. *See, e.g.*, Ark. Const. amend. 68, § 2 ("The policy of Arkansas is to protect the life of every unborn child from conception until birth . . . ."); La. Rev. Stat. Ann. § 14:2(7) (defining "person" for purposes of criminal code to include "a human being from the moment of fertilization and implantation"). Indeed, in some of these States, the "donation" of human embryos for research may be deemed a criminal action, and the potential donor is left without any knowledge of this fact. A researcher is required to include only information about "[w]hat would happen to the embryos in the derivation of [human embryonic stem cells] for research." 74 Fed. Reg. at 32,174.

42. Finally, the informed consent procedures fail to notify potential donors that to the extent the embryos are no longer needed, it is now possible for them to place each embryo up for adoption as an alternative to having the human embryo destroyed for research purposes. *See, e.g.*, Natalie Lester, *Embryo Adoption Becoming the Rage*, Wash. Times, Apr. 19, 2009, *available at* http://washingtontimes.com/news/2009/apr/19/embryo-adoption-becoming-rage.

E. Current Scientific Knowledge About Stem Cell Research

43. NIH's decision to use federal funds to support research that destroys human embryos is unethical, scientifically unnecessary, fiscally irresponsible, and counterproductive. Although the Guidelines purport to "ensure that NIH-funded research in this area is ethically responsible [and] scientifically worthy," 74 Fed. Reg. at 32,170, the Guidelines' true effect is to divert limited federal dollars away from the most ethically responsible and scientifically promising forms of stem cell research—without even explaining such an irrational decision. Indeed, not only is embryonic stem cell research ethically problematic, it has shown no promise of safe, effective human therapies.

44. Only research with adult stem cells has yielded any successes in the treatment of human disease. Moreover, even if NIH had reason to believe that research involving human embryonic stem cells ("hESCs") would be as valuable as research involving adult stem cells, it has not offered an adequate explanation for choosing not to focus funds on iPSC research, which offers the same benefits without the ethical difficulties.

1. Scientific Evidence In The Administrative Record Shows That Embryonic Stem Cell Research Cannot Develop Safe Or Effective Human Therapies

45. Human embryonic stem cells are neither required nor useful components of modern scientific research aimed at discovering "new ways to prevent and/or treat illness." 74 Fed. Reg. at 32,174. hESCs are plagued by a multitude of shortcomings that limit their scientific efficacy and potential to be used successfully and safely in human therapies. Indeed, even NIH recognizes that embryonic stem cells are "not currently being used clinically." 74 Fed. Reg. at 32,172–74. Indeed, hESCs have never been utilized in human therapy, let alone successfully treated human disease. In promulgating the Guidelines, NIH ignored evidence in the Administrative Record about these shortcomings, ignored the advantages of non-hESC research, and has

therefore failed to consider adequately that federal funds would be better utilized in research that does not present the same problems.

46. The problems associated with hESC research are a function of the fact that hESCs are inherently abnormal cells. hESCs are derived from the inner cell mass of an early stage embryo. Typically, the cells of this inner cell mass would give rise to a fetus during normal embryonic development. However, the removal of the inner cell mass generates cells—the hESCs—that are not normal. The cells, for instance, universally exhibit genetic instability. *See* Comments of Do No Harm et al. at I-1, *available at* http://www.advocatesinternational.org/sites/www.advocatesinternational.org/files/webfm/DoNoHarm_20090526.pdf ("Comments").

47. This genetic instability is an inherent characteristic of hESCs, and one that inevitably causes hESCs injected into organisms to cause tumors. Scientists have been unable to develop methods to prevent this tumor formation. *Id*. at I-2. Research indicates that the tumor-causing characteristics of hESCs cannot be dismissed as a normal quality of a pluripotent cell removed from its endogenous environment. *Id*. at I-1. As a result of these abnormalities, hESCs have not shown promise of offering a safe or effective component of human therapy or medical treatments. Defendants have failed to address this defect inherent in hESC therapy.

48. Embryonic stem cells are also problematic candidates for safe and effective human therapies because they do not come from the patient, and are often rejected by the patient's immune system. *See* Comments, at G-8. iPSCs do not pose this problem.

49. The therapeutic utility of other pluripotent cells does not require the use of hESCs. Specifically, hESCs are not needed in order to test the pluripotent properties of other stem cells, such as iPSCs. The only test needed to establish the pluripotency of a stem cell is the tumor-forming test—hESCs are not needed at any step in the process. Moreover, in testing the

differentiation capacity of other pluripotent stem cells, adult stem cells—and not hESCs—are required. Thus, hESCs cannot contribute to the development of research that utilizes other types of pluripotent stem cells. *Id.* at I-3.

50. In promulgating the Guidelines, Defendants ignored important information on the promise and utility of hESC research that was contained in the Administrative Record. The Guidelines, the product of this uninformed and arbitrary decisionmaking process, will result in the allocation of fewer resources to research that utilizes more promising alternatives, including adult stem cells and induced pluripotent stem cells, while devoting scarce public resources to research that will not yield effective medical treatment, thereby defeating the very goals that Defendants claim to advance.

2. Defendants Ignored Evidence In The Administrative Record That Adult Stem Cell Research Is Scientifically And Ethically Superior To Embryonic Stem Cell Research

51. Adult stem cells do not possess hESCs' inherent shortcomings, and are therefore superior to hESCs. The Guidelines, by permitting federal funding of hESC research, unnecessarily direct resources away from the more scientifically promising adult stem cell research.

52. Unlike embryonic stem cells, adult stem cells provide a readily available, flexible, and safe source of stem cells for the treatment of diseases. They can be harvested from various tissue sources, including virtually all body tissues, as well as tissues normally discarded after birth. In addition, adult stem cells can be harvested and grown in numbers sufficient for patient treatment. *See* Comments, at G-2.

53. Unlike the transplantation of hESCs, which carries with it the risk of immune rejection, re-transplantation of a patient's own adult stem cells does not pose the same risks because the patient's own cells can be used. Adult stem cells also avoid tumor formation. And

adult stem cells have shown an ability to home in on damaged tissue, allowing the development of minimally invasive administration techniques. *Id*. at G-8.

54. Adult stem cells are currently being used to treat clinically many diseases in human patients. Successful clinical trials include the use of adult stem cells, in conjunction with chemotherapy or radiation, in treatments for various cancers, including ovarian cancer, brain tumors, testicular cancer, breast cancer, and various lymphomas. Similar methodology has utilized adult stem cells in treatments for sickle cell anemia and Fanconi's anemia. Adult stem cells have also successfully been used to treat patients with certain autoimmune diseases, including multiple sclerosis, systemic lupus, Crohn's disease, rheumatoid arthritis, and juvenile diabetes. *Id*. at G-4–G-8.

55. Preclinical studies also reveal the significant potential of adult stem cells for use in regenerative medicine, repairing damaged and diseased tissue, and improving health. These studies demonstrate that adult stem cells are effective in treating animal models of disease, including diabetes, stroke, spinal cord injury, Parkinson's disease, retinal degeneration, amyotrophic lateral sclerosis, and cardiac damage. *Id*. at G-2.

56. Defendants ignored the voluminous current scientific research record and comments in the Administrative Record indicating the impressive scientific and medical potential of adult stem cell research. Unlike hESCs, adult stem cells have already shown the ability to deliver therapeutic benefit to countless patients suffering from a wide array of diseases.

57. In the interest of improving patient well-being, federal funding should be directed at research that is actually improving the lives of patients. By failing to recognize the comparative strength of adult stem cell research, NIH's decision to direct federal funds toward hESC research is uninformed, misleading, inaccurate, arbitrary, and capricious, and unnecessarily diverts

funding away from more promising alternatives. Defendants abdicated their duty to exercise reasoned decisionmaking and issue fair and informed rules regarding research funding.

3. Defendants Ignored Another Ethically And Scientifically Superior Alternative, Induced Pluripotent Stem Cell Research

58. Similarly, Defendants did not properly consider that induced pluripotent stem cells have the ability to achieve the scientific and medical goals identified in the Guidelines, while avoiding the moral and ethical problems posed by the use of human embryonic stem cells. Within the last several years, scientists discovered how to use adult stem cells to create iPSCs. These cells "meet the defining criteria [that were] originally proposed for human [embryonic stem] cells, with the significant exception that the [induced pluripotent stem] cells are not derived from embryos." Junying Yu et al., *Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells*, 318 Science 1917 (2007). In addition, unlike embryonic stem cells, NIH has stated that "tissues derived from [induced pluripotent stem cells] will be a nearly identical match to the cell donor and thus probably avoid rejection by the immune system." National Institutes of Health, *Stem Cell Basics* 14 (2009), *available at* http://stemcells.nih.gov/staticresources/info/basics/SCprimer2009.pdf.

59. The development of iPSCs essentially eliminates the need for hESCs. Dr. James Thomson, the first scientist to isolate and culture hESCs, was also one of the first scientists to produce iPSCs. In referring to the effect that the discovery of iPSCs will have on hESC research, Dr. Thomson stated: "Isn't it great to start a field and then to end it?" Gina Kolata, *Man Who Helped Start Stem Cell War May End It*, N.Y. Times, Nov. 22, 2007, *available at* http://www.nytimes.com/2007/11/22/science/22stem.html?_r=1. Others have similarly recognized that induced pluripotent stem cells offer all of the scientific possibilities of embryonic stem cells—and more. For instance, Professor Ian Wilmut—whose research brought about the first

cloned sheep, Dolly—has declared that the induced pluripotent "technique to obtain stem cells is now the most efficient technique for researchers" and that "[induced pluripotent] cells are more useful than embryonic cells." Comments, at H-3.

60. Not only do iPSCs offer an ethically superior alternative to hESCs, they also offer scientific advantages. iPSC lines can be created more easily and less expensively than embryonic stem cell lines, and iPSC lines can be derived from virtually any cell type, including human hair and human blood cells. *Id.* at H-3. To date, over 500 human iPSC lines have been created. *Id*. at H-4.

61. Additionally, scientists can create iPSC lines from a specific individual, allowing the creation of patient-specific cell lines. *Id*. Several such lines have already been created from individuals with specific diseases so that the disease mechanism and potential drug-based therapies can be studied in the laboratory. As NIH has recognized, unlike embryonic stem cells, "tissues derived from iPSCs will be a nearly identical match to the cell donor and thus probably avoid rejection by the immune system." National Institutes of Health, *Stem Cell Basics*, *supra*, at 14.

62. Thus, iPSC research offers a superior alternative to embryonic stem cell research and does not require the destruction of human embryos. By failing to consider the scientific and ethical advantages of iPSC research compared to embryonic stem cell research and choosing to fund hESC research, which will necessarily result in less funding available for adult and iPSC research, NIH's decision to make public funds available for embryonic stem cell research is uninformed, arbitrary, and capricious.

F. Defendants Failed To Consider The Guidelines' Effect On State Law And Policy

63. The Guidelines fail to account for, and substantially undermine, the laws of numerous States that protect human life from the moment of conception, or otherwise protect hu-

man embryos from being destroyed or placed at risk for the purpose of medical experimentation. Indeed, state protection of human embryos is pervasive: Numerous States have fetal homicide statutes that apply without regard to gestational age and/or wrongful death statutes that apply regardless of gestational age; various States expressly prohibit nontherapeutic human embryonic stem cell research; still others prohibit the destruction of embryos for any purpose; and a number of state laws provide that life begins at conception. Moreover, under evolving state tort laws, parents or other surrogates in some States have limited capacity to consent to hazardous biomedical experiments on human subjects under their care who are incapable of voluntary consent. Despite the fact that a number of the comments on the Draft Guidelines make this plain, the Guidelines fail to inform potential donors that some States consider embryos to be living human beings, and that donating an embryo for research may constitute criminal conduct under these States' laws.

64. Furthermore, the Guidelines erroneously presume that the parents of the human embryo have the legal right under applicable state law, as well as the moral and ethical authority, to substitute their judgment for the interests and judgment of the human embryo, which is recognized in some States as an independent human life.

65. Although Defendants have a statutory mandate to "assist States" in the enforcement of state health regulations, 42 U.S.C. § 243(a), the adoption and implementation of the Guidelines will substantially undermine state laws and policies that protect embryonic human life from destruction through medical experimentation. Defendants, however, have wholly failed to consider, address, or acknowledge the effect of authorizing and implementing the Guidelines on these coordinate state laws and policies.

V. CLAIMS FOR RELIEF

CLAIM ONE: AGENCY ACTION NOT IN ACCORDANCE WITH LAW— 5 U.S.C. § 706(2)(A)

66. Plaintiffs repeat and reallege paragraphs 1–65.

67. Defendants' promulgation and implementation of the Guidelines are not in accordance with law within the meaning of 5 U.S.C. § 706(2)(A). Such funding authorizations violate the Omnibus Appropriations Act, 2009, Pub. L. No. 111-8, § 509 (2009), which prohibits federal funding of "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 C.F.R. § 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b))."

68. Therefore, the Defendants' actions are contrary to law, and Plaintiffs are entitled to relief pursuant to 5 U.S.C. § 706(2)(A).

CLAIM TWO: AGENCY ACTION NOT IN OBSERVANCE OF PROCEDURES REQUIRED BY LAW—5 U.S.C. § 706(2)(D)

69. Plaintiffs repeat and reallege paragraphs 1–65.

70. The Guidelines were not promulgated in observance of the procedures required by law within the meaning of 5 U.S.C. § 706(2)(D). In violation of 5 U.S.C. § 553(c)'s requirement that an agency "give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments," Defendants did not permit sufficient time for the submission of comments on the Draft Guidelines.

71. Additionally, in violation of 5 U.S.C. § 553(c)'s requirements that interested persons have the opportunity to comment and that the agency issue a final rule only after it completes a meaningful "consideration of the relevant matter presented," Defendants prejudged the

merits of matters critical to the rulemaking proceeding and did not even consider, much less respond to, the voluminous comments they received in opposition to the proposed Guidelines.

72. Therefore, Defendants have undertaken agency action not in observance with procedures required by law, and Plaintiffs are entitled to relief pursuant to 5 U.S.C. § 706(2)(D).

CLAIM THREE: ARBITRARY AND CAPRICIOUS AGENCY ACTION—5 U.S.C. § 706(2)(A)

73. Plaintiffs repeat and reallege paragraphs 1–65.

74. Defendants' issuance of the Guidelines was arbitrary and capricious within the meaning of 5 U.S.C. § 706(2)(A) because the Guidelines lack necessary and sufficient informed consent safeguards, do not adequately prohibit conflicts of interest, and ignore, contradict, or are otherwise inconsistent with scientific knowledge regarding the relative research and therapeutic potential of embryonic, adult, and induced pluripotent stem cells, and with numerous state laws and ethical rules regarding the protection of human embryos. Defendants failed to consider and utilize alternative research methods that offer similar or even superior medical promises without giving rise to the difficult ethical issues posed by hESC research, and failed to respond to evidence in the administrative record demonstrating that hESC research is neither ethically responsible nor scientifically worthy (NIH's stated criteria for funding hESC research).

75. Therefore, Defendants' agency action is arbitrary and capricious, and Plaintiffs are entitled to relief pursuant to 5 U.S.C. § 706(2)(A).

VI. IRREPARABLE INJURY

76. Plaintiffs repeat and reallege paragraphs 1–75.

77. Plaintiffs are now severely and irreparably injured by the Guidelines. Plaintiffs' injuries will be redressed only if this Court declares that the Guidelines are not in accordance

with law, fail to observe procedures required by law, and/or are arbitrary and capricious, and enjoins the Defendants from implementing them.

78. An actual and judicially cognizable controversy exists between Plaintiffs and Defendants regarding whether the Guidelines are not in accordance with law, fail to observe procedures required by law, and/or are arbitrary and capricious. Once an embryo is destroyed it cannot be revived. It is gone forever. Moreover, adult stem cell researchers like Drs. Sherley and Deisher will likely experience increased competition for already-scarce funds for their research, and may be unable to continue their work with adult stem cells. Also as a result of the Guidelines, which will likely cause many more embryos to be donated for research purposes, adoptive parents like Mr. and Mrs. Flynn, and Mr. and Mrs. Nelson, may find it more difficult to secure an embryo for adoption, and Nightlight will likely be less able to match the clients on their waiting list with embryos. Defendants are presently implementing the Guidelines to the detriment of the Plaintiffs.

VII. PRAYER FOR RELIEF

79. WHEREFORE, Plaintiffs pray for an order and judgment:

(a) Declaring that the NIH Guidelines authorizing the funding of research involving human embryonic stem cells are not in accordance with law within the meaning of 5 U.S.C. § 706(2)(A); declaring that the NIH Guidelines authorizing the funding of research involving human embryonic stem cells were promulgated by Defendants without observing procedures required by law within the meaning of 5 U.S.C. § 706(2)(D); declaring that the NIH Guidelines authorizing the funding of research involving human embryonic stem cells are arbitrary and capricious within the meaning of 5 U.S.C. § 706(2)(A);

(b) Declaring that any action previously taken by Defendants pursuant to the Guidelines is null and void, including any grants of funds for research involving human embryonic stem cells;

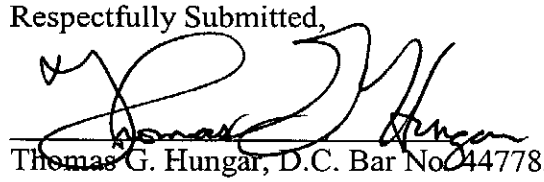
(c) Enjoining Defendants and their officers, employees, and agents from implementing, applying, or taking any action whatsoever pursuant to the Guidelines, or otherwise funding research involving human embryonic stem cells as contemplated by the Guidelines;

(d) Awarding Plaintiffs their reasonable costs, including attorney's fees, incurred in bringing this action; and

(e) Granting such other and further relief as this Court deems just and proper.

Dated: August 19, 2009

Respectfully Submitted,



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Complaint.DOC

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DR. JAMES L. SHERLEY, et al.	)	
Plaintiffs,	)	Civil Action No. 1:09-cv-01575 (RCL)
v.	)	
KATHLEEN SEBELIUS, et al.	)	
Defendants.	)	

DECLARATION OF SARAH JEAN ROCKEY, PH.D.

I, Sarah Jean Rockey, Ph.D., pursuant to 28 U.S.C. § 1746, declare under penalty of perjury as follows:

1. I am the Acting Deputy Director for Extramural Research, National Institutes of Health ("NIH") and Acting Director, Office of Extramural Research, NIH. The NIH Office of Extramural Research (OER) provides leadership, oversight, tools and guidance needed to manage NIH's grants policies and operations. Prior to assuming the roles of Acting Deputy Director for Extramural Research and Acting Director, OER, NIH, in November 2008, I had served as the Deputy Director, OER, since January 2005.

2. In these positions, I am familiar with the process used by NIH to review applications for research grants, and I make this declaration based upon information within my personal knowledge or provided to me in my official capacity.

3. NIH funds grants, cooperative agreements and contracts that support biomedical and behavioral research leading to the advancement of fundamental knowledge about the nature and

behavior of living organisms and the application of that knowledge to the causes, diagnosis, prevention and cure of human diseases.

4. Extramural research accounts for approximately 80 percent of the NIH's budget. NIH supports such research through twenty-four Institutes and Centers (ICs), which award grants, as well as the Office of the Director. See List of Institutes, Centers and Offices, at http://www.nih.gov/icd/.

5. Each IC within NIH which provides research grants receives an independent appropriation from Congress to support the IC's mission. Accordingly, each IC maintains an independent budget. For example, the National Cancer Institute has a budget for fiscal year 2009 (FY 09) of about $5 billion. It expects to award approximately $3 billion in research grants in FY 09 consistent with its statutory mission to conduct and support cancer research, including cellular and molecular studies as well as interventions and treatments. 42 U.S.C. § 285 et seq.

6. NIH strongly encourages investigator-initiated (also termed "unsolicited") research. Over 80 percent of applications fall into this category. NIH, through its funding components, also uses specific funding or "targeted" announcements to stimulate research in particular areas of science through use of an announcement called a "Request for Applications" (RFA). In the 2008 fiscal year (FY), 11 percent of funding went to "targeted" research.

7. The regulations governing grants for research projects are found at 42 C.F.R. Part 52. Eligible projects may consist of laboratory, clinical, population, field, statistical, basic, applied or other types of investigations, studies or experiments or combinations thereof, and may either be limited to one, or a particular aspect of a problem or subject, or may consist of two or more related problems or subjects for concurrent or consecutive investigation and involving multiple

disciplines, facilities and resources. 42 C.F.R. 52.3(b). All applications filed in accordance with prescribed procedures are evaluated. 42 C.F.R. 52.5(a).

8. All grant applications for research funding undergo evaluation through two-tier peer review, as required by provisions of the Public Health Service Act (PHS Act). See sections 402(b)(9), 406(a)(3), 492 and 492A(a)(2) of the PHS Act (codified at 42 U.S.C. §§ 282(b)(9), 284a(a)(3), 289a and 289a-1(a)(2)) and implementing regulations at 42 C.F.R. Part 52h.

9. An applicant for a research grant submits the application to the Center for Scientific Review (CSR) at NIH. CSR refers the application to one or more Institutes or Centers (ICs) at NIH for funding consideration based on the relationship of the subject area of the application to the focus and mission of the ICs.

10. In addition, CSR assigns the application to a Scientific Review Group (SRG) that conducts the first level of peer review within CSR or an IC. The SRG is primarily composed of nongovernment experts qualified by training and experience in particular scientific or technical fields, or as authorities knowledgeable in the various disciplines and fields related to the subject areas of the application under review, to give expert advice on the scientific and technical merit of grant applications. See 42 C.F.R. 52h.2(k).

11. The peer reviewers that comprise the SRG assign preliminary scores to grant applications. Based on these preliminary scores, the reviewers then generally discuss only the applications in the top half of the scores at a meeting of the group. Applications scoring in the bottom half may also be considered on the motion of a reviewer. The discussion concerning the applications involves the following general criteria for determining the scientific and technical merit of an application: significance [Does the study address an important problem?], approach [Are the concepts and methods well thought out and appropriate to the aim of the research?],

innovation [Does the project develop or use novel concepts?], investigators [Are the investigators appropriately trained and capable of carrying out the project], and environment [Will the setting for the research (facilities, resources, institutional support) contribute to the probability of success?]. Each reviewer then scores the applications, which are then ranked according to their scores.

12. The scored applications then proceed to the second level of peer review. This review is performed by the National Advisory Councils or Boards of each component that is considering whether to fund an application relevant to its mission. Taking into account the ranking of the applications and the needs and mission of the particular funding component (such as the National Cancer Institute), the Council or Board then recommends certain applications for funding.

13. Only applications that are favorably recommended by both levels of peer review are considered eligible for funding. In very rare circumstances, an IC Director may decide based on programmatic reasons to fund an application without a numerical priority score if it was found to have merit by the SRG and is approved for funding by the responsible advisory council.

14. Only about 20 percent of applicants are successful in having their research proposals funded by NIH. For example, 43,467 applications for research project grants were received in fiscal year 2008 and there were 9,460 awards for a success rate of about 22%. However, an unsuccessful applicant may be given an opportunity to amend his or her application and to resubmit it.

15. Within their individual budgets as set by Congress, most ICs establish a "payline" for the overall amount that they will spend on research grants. The "payline" is a percentile-based funding cutoff point determined at the beginning of a fiscal year by balancing the projected number of applications coming to an IC and the projected average cost of an application with the

amount of funds determined to be available to fund research projects. This payline is not, however, set according to the expected focus of the individual research projects or the type of tools or methods expected to be used in the research. Other ICs, which don't publicly make known a payline, go down as far as their money will allow in funding research projects.

16. To my knowledge, no IC has ever established within its payline a specific amount to be used only for stem cell projects, be they embryonic or nonembryonic. Instead, stem cell research, as with all other methodologies, is included within the overall payline and funded on a case-by-case basis according to the particular proposals received and the funding available to the particular IC.

17. IC Directors, who have the authority to make funding decisions, may also decide to fund research projects outside of any announced payline so long as they have been recommended by the peer review groups.

18. Using text mining procedures to locate key words in conjunction with funded research projects, NIH annually attempts to estimate past, current and future support levels for various diseases, conditions and research categories based on grants, contracts and other funding mechanisms. Two of the listed categories are "Stem Cell Research - Embryonic - Human" and "Stem Cell Research - Nonembryonic - Human," the latter of which includes adult stem cells and induced pluripotent stem cells. See http://www.report.nih.gov/rcdc/categories/PFSummaryTable.aspx. NIH estimates that the expenditure for human embryonic stem cell research was approximately $88 million in FY 08, and estimated to rise to $91 million in FY 09 and $92 million in FY 10. The same table estimates that the NIH expenditure for human nonembryonic stem cell research was

approximately $297 million in FY 08, and estimated to rise to $305 million in FY 09 and $311 million in FY 10.

19. As the table reveals, NIH remains committed to the funding of eligible research applications involving nonembryonic stem cells. The funding is not mutually exclusive with funding for eligible research proposals involving embryonic stem cells.

20. NIH does not set individual budgets by research category or methodology, and the awarding of a grant in response to an application is made on a case-by-case basis. Accordingly, it is impossible to accurately predict whether, how, or to what degree an application will compete with another for funding.

21. A "principal investigator" (PI) on a research project means an individual designated by the grantee in the grant application who is responsible for the scientific and technical direction of the project if the grant is made. See 42 C.F.R. 52.2. While a PI conceives and writes a grant application, the applicant institution or employer of the PI is the entity typically recognized as the grantee for most grant types.

22. Plaintiff Dr. James Sherley has been the PI on prior research grants from NIH. In 2006, the Massachusetts Institute of Technology, with Dr. Sherley as PI, received the first year of a five year grant totaling $2.5 million in direct costs under the NIH Director's Pioneer Award (NDPA) Program that will continue through 2011. In 2007, the NDPA was transferred to Dr. Sherley's current employer, the Boston Biomedical Research Institute. A grant supplement to the NDPA was also made on July 20, 2009, under the American Recovery and Investment Act of 2009.

23. While plaintiff Dr. Theresa Deisher received training support from NIH in the early 1990s, she has to my knowledge not received any NIH research grants either individually or as PI for her institutions.

I declare under penalty of perjury that the foregoing is true and correct.

Executed at Bethesda, Maryland, this 14 day of September, 2009.

SARAH JEAN ROCKEY, PH.D.
Acting Deputy Director for Extramural Research
National Institutes of Health