ORAL ARGUMENT SCHEDULED FOR APRIL 23, 2012
No. 11-5241

IN THE UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

DR. JAMES L. SHERLEY, et al.,

Plaintiffs-Appellants,

v.

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

Defendants-Appellees.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BRIEF FOR APPELLEES

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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 appellants 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 appellees in this appeal, are Kathleen Sebelius, in her official capacity as 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.

An ad hoc coalition of bioethics scholars, comprising Robert P. George, Donald W. Landry, Michael J. Birrer, Eric Cohen, Farr A. Curlin, Austin L. Hughes, William B. Hurlbut, Peter Augustine Lawler, Yuval Levin, Paul R. McHugh, Gilbert C. Meilaender, Charles T. Rubin, Diana J. Schaub, O. Carter Snead, Meir Y. Soloveichik, and Christopher O. Tollefsen, are amici supporting Plaintiffs-Appellants in this appeal.

The Coalition for the Advancement of Medical Research and the Genetics

Policy Institute, Inc., intend to appear as amici supporting Defendants-Appelleess in this appeal.

The Coalition for the Advancement of Medical Research, Genetics Policy Institute, Inc., and State of Wisconsin appeared as amici in the district court.

Regents of the University of California, Coalition for the Advancement of Medical Research, Genetics Policy Institute, State of Wisconsin, Maureen L. Condic, and Boston Biomedical Research Institute appeared as amici in a prior appeal.

B. Rulings Under Review.

The ruling under review is the July 27, 2011, order and memorandum opinion of the district court. *Sherley* v. *Sebelius*, No. 1:09-cv-1575 (D.D.C.) (Chief Judge Royce C. Lamberth). The district court's opinion is available at 776 F. Supp. 2d 1.

C. Related Cases.

This matter has previously come before this Court in *Sherley* v. *Sebelius,* No. 09-5374 (June 25, 2010), and in *Sherley* v. *Sebelius,* No. 10-5287 (Apr. 29, 2011). The opinions are available at 610 F.3d 69 and 644 F.3d 388, respectively. Counsel is aware of no other related cases within the meaning of D.C. Circuit Rule 28(a)(1)(c).

Respectfully Submitted,

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GLOSSARY

Term	Definition
APA	Administrative Procedure Act
Guidelines	National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009)
HHS	Department of Health and Human Services
IVF	*in vitro* fertilization
JA	Joint Appendix
NIH	National Institutes of Health
Pl. Br.	Plaintiffs' Brief
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Sherley II	*Sherley* v. *Sebelius,* 644 F.3d 388 (D.C. Cir. 2011)

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BRIEF FOR APPELLEES

STATEMENT OF JURISDICTION

Plaintiffs invoked the court's jurisdiction under 28 U.S.C. § 1331. JA 18 (Complaint ¶ 5). The district court entered summary judgment for the government on July 27, 2011, JA 693, and plaintiffs filed a timely notice of appeal on September 19, 2011, JA 694; Fed. R. App. P. 4(a). This Court has jurisdiction pursuant to 28 U.S.C. § 1291.

STATEMENT OF THE ISSUES

1. Whether the district court properly held that the human embryonic stem cell research Guidelines issued by the National Institutes of Health in 2009 do not violate governing appropriations restrictions.

2. Whether the district court properly held that the human embryonic stem cell research Guidelines issued by the National Institutes of Health in 2009 were promulgated in accord with the Administrative Procedure Act.

STATUTES AND REGULATIONS

All applicable regulatory and statutory provisions are contained in the Brief for Appellants.

STATEMENT OF THE CASE

Plaintiffs Dr. James L. Sherley and Dr. Theresa Deisher are scientists who perform research using adult stem cells. Together with several other plaintiffs, they filed suit to enjoin application of the National Institutes of Health ("NIH") Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170 (July 7, 2009) ("Guidelines"). JA 41-42 (Complaint ¶ 79). Plaintiffs asserted that the Guidelines violate an appropriations restriction — known as the Dickey-Wicker amendment — that was in effect at the time of suit, was reenacted as an appropriations restriction in the subsequent years as well, and remains in effect as part of the 2012 Consolidated Appropriations Act. Pub. L. No. 112-74, Div. F, § 508, 125 Stat. 786, 1112 (2011).

The Dickey-Wicker amendment bars federal funding for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death . . . ." Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112. Plaintiffs also claimed that adoption of the Guidelines was arbitrary and capricious in violation of the Administrative Procedure Act. JA 17-18 (Complaint ¶ 2-3).

The district court dismissed the complaint for lack of standing in October 2009. JA 189. Plaintiffs appealed the standing ruling with respect to the two scientists. This Court reversed, holding 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." JA 222 (*Sherley* v. *Sebelius,* 610 F.3d 69, 72-73 (D.C. Cir. 2010) (internal quotations omitted) (alteration in original) (hereinafter *Sherley I*)). This 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." JA 224-25 (*Sherley I*, at 74).

The district court then entered a preliminary injunction against NIH and the other defendants. JA 228. The court enjoined them 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." JA 228. This Court entered a stay pending appeal, JA 490, and, after full briefing and argument, vacated the preliminary injunction. This Court held that NIH had reasonably interpreted the Dickey-Wicker amendment to permit the funding of research involving human embryonic stem cells. JA 509 (*Sherley* v. *Sebelius,* 644 F.3d 388, 390 (D.C. Cir. 2011)) (hereinafter *Sherley II*).

The district court then denied plaintiffs' motion for summary judgment and granted the government's motion for summary judgment. JA 693. The court held that NIH had reasonably interpreted the Dickey-Wicker amendment to permit the funding of research involving human embryonic stem cells. JA 678, 685. The court also held that the Guidelines were promulgated in accord with the Administrative Procedure Act. JA 691-92.

STATEMENT OF THE FACTS

I. Human Stem Cell Research.

"[S]tem cells have the potential of yielding treatments for a wide range of afflictions because scientists can cause them to function as any one of a number of specific types of cell." JA 510 (*Sherley II*, at 390); *see* also National Academies, *Understanding Stem Cells: An Overview of the Science and the Issues from the National Academies,* at 3, *available at* http://dels-old.nas.edu/bls/stemcells/basics.shtml. Scientists currently perform research using essentially three types of human stem

cells: adult stem cells, embryonic stem cells, and induced pluripotent stem cells. NIH funds all three types of human stem cell research.

A. Adult stem cells can be found in various tissues and organs of the human body, although they have not been identified in all of the various different types of tissue. National Academies, *Understanding Stem Cells,* at 8-9; NIH, *Stem Cell Basics: What Are Adult Stem Cells?*, *available at* http://stemcells.nih.gov/info/basics/basics4.asp. Adult stem cells are not "pluripotent," *i.e.*, they cannot differentiate into any of the approximately 200 types of cells in the human body. Blood stem cells usually produce more blood cells, and nerve stem cells can make only the various types of nervous system cells. National Academies, *Understanding Stem Cells,* at 8. To date, it has also been difficult to grow large quantities of adult stem cells in cell culture. *Ibid.*

Despite these limitations, various research using adult stem cells has been of value and has led to successful treatments including those "that reconstitute the immune system after leukemia, lymphoma, and various blood or autoimmune disorders have been treated with chemotherapy." JA 249 (Declaration of Dr. Francis S. Collins, ¶ 7).

B. 1. Embryonic stem cells, unlike adult stem cells, are pluripotent. They exist for a brief period in human embryos as undifferentiated stem cells, and they then begin to differentiate into all the different types of cells that exist in the human

body. National Academies, *Understanding Stem Cells*, at 4-5. Unlike adult cells, embryonic stem cells can readily be identified, isolated, grown, and maintained in a laboratory indefinitely.

The human embryonic stem cell research that is funded under the NIH Guidelines uses stem cells that are taken from stem cell lines, and many of those lines are very longstanding. The NIH Guidelines do not authorize use of federal funding to derive such lines, and the Guidelines allow use of cells only from lines that were derived from an embryo that was produced as part of an *in vitro* fertilization ("IVF") process for reproductive purposes.

As a general matter, to derive embryonic stem cells in the most commonly used method, scientists remove cells from the inner cell mass of an embryo after approximately five days of development, when the embryo is known as a "blastocyst." National Academies, *Understanding Stem Cells,* at 4-5; JA 510 (*Sherley II*, at 390). "The stem cells among the 30 or so cells in the inner cell mass are then placed in a culture[.]" JA 510 (*Sherley II*, at 390). Some of those cells are pluripotent stem cells and are identified as such by scientists based on specific criteria such as the appearance of the cells, their ability to self-renew, and the presence of particular cell surface markers. NIH, *Stem Cell Basics: What Are Embryonic Stem Cells?*, *available at* http://stemcells.nih.gov/info/basics/basics3.asp. Those cells that continue to divide for a prolonged period of time without differentiating, and are shown to be

pluripotent, constitute embryonic stem cells. Those cells will continue to divide if kept in the appropriate conditions, and all the cells created through the continuing division of the stem cells constitute a stem cell line — a propagating collection of genetically identical cells. National Academies, *Understanding Stem Cells*, at 10. "An individual [embryonic stem cell] may be removed from the line without disrupting either the multiplication process or the durability of the line." JA 510 (*Sherley II*, at 390). The stem cells that are removed can also continue to divide and may be used by scientists conducting a range of research to create different types of specialized human cells.

Stem cells that are derived from a single embryo to form a stem cell line may multiply over a period of years and provide stem cells for a broad range of subsequent research. For example, one stem cell line, known as "H9," was created by a researcher at the University of Wisconsin in 1998, and has been used in more than 360 published research studies and remains one of the most highly requested stem cell lines from the Wisconsin stem cell bank. Lines H1 and H7, also developed at the University of Wisconsin, have been used in approximately 300 and 100 research studies, respectively. *See* Peter Loser et al., *Human Embryonic Stem Cell Lines and Their Use in International Research,* 28 Stem Cells 240, 244 (2010), *available at* http://onlinelibrary.wiley.com/doi/10.1002/stem.286/full.

2. Stem cell lines are generally managed by a university or associated research institute, or a private entity. In the typical case, a researcher chooses an existing stem cell line for use in her research based on scientific experience with that cell line in other research; for example, the H9 cell line is known to be particularly good at differentiating into nerve cells. The researcher may obtain thousands, or even millions, of cells from the owner or provider of the stem cell line. The provider often charges a fee; for example, the research institute associated with the University of Wisconsin charges $1,000 per line to researchers engaged in non-commercial research. This fee covers the cost to the institute of culturing, maintaining, and handling the stem cell lines. *See, e.g.,* WiCell, Frequently Asked Questions For Requesting Cells, https://www.wicell.org/index.php?option=com_content&task=blogcategory&id=124&Itemid=197.

3. Once a researcher obtains the necessary stem cells from the stem cell line, she may differentiate the stem cells into the kind of cell she needs for her research. National Academies, *Understanding Stem Cells,* at 10. For example, a researcher studying Parkinson's disease might develop the stem cells into a specific kind of nerve cell that produces dopamine. *Id.* at 16.

Researchers have made substantial progress toward treating disease, and are using these differentiated cells to develop new therapeutic drugs to treat conditions such as spinal muscular atrophy and amyotrophic lateral sclerosis ("ALS"). JA 248

(Decl. ¶ 6). Two studies in which cells differentiated from human embryonic stem cells were transplanted into patients with serious eye diseases have reported that patients had no ill effects after 4 months and at least one patient described improved eyesight. *See* Steven D. Schwartz et al., *Embryonic Stem Cell Trials For Macular Degeneration: A Preliminary Report*, The Lancet, at 1, published online Jan. 23, 2012, http://download.thelancet.com/flatcontentassets/pdfs/S0140673612600282.pdf.

4. As noted above, NIH's Guidelines allow federally funded researchers to use human embryonic stem cells only if the original cell line was derived from an embryo that was produced as part of an IVF process for reproductive purposes. In many cases, when couples participate in an IVF process, they create more embryos than they will ultimately use to meet their reproductive goals.

No uniform procedure governs the treatment of these embryos, which varies from clinic to clinic. Some embryos are deemed not suitable for implantation from the outset, such as embryos with a genetic defect or embryos that are failing to develop normally, and thus will never be used for implantation and are typically discarded. Stem cell lines derived from embryos with genetic defects may be particularly valuable to scientists, however, because they allow the study of a particular genetic disease, such as cystic fibrosis or Marfan syndrome, and its potential therapies. *See* K. D. Sermon, et al*., Creation of a Registry For Human Embryonic*

Stem Cells Carrying An Inherited Defect, 24 Human Reproduction 1156, 1557 (2009), *available at* http://humrep.oxfordjournals.org/content/24/7/1556.full.

With regard to the embryos created through IVF that are suitable for implantation, excess embryos (*i.e.,* embryos other than the ones that are implanted) are almost always frozen so patients can implant them later, if the first implantation attempt fails or if the patient desires additional pregnancies. Ann Drapkin Lyerly et al., *Fertility Patients' Views About Frozen Embryo Disposition: Results of a Multi-institutional U.S. Survey*, 93 Fertility and Sterility 499 (2010)*; see also* Andrea D. Gurmankin et al., *Embryo Disposal Practices in IVF Clinics in the United States*, 22 Politics and the Life Sciences, Aug. 2004, at 4 (describing variations among IVF clinics), *available at* http://repository.upenn.edu/bioethics_papers/7/. One recent study found that nearly half of the patients who have embryos currently held in a frozen state no longer intend to use them for reproductive purposes. Lyerly et al., at 506. Patients who have embryos remaining that they do not intend to use may thaw and discard the embryos, donate the embryos to another woman for implantation, donate the embryos for scientific research, or continue to freeze the embryos indefinitely, which often involves a continuing fee. *Id.* at 501; *see also, e.g.,* Cost Sheet, Advanced Fertility Center of Chicago, http://www.advancedfertility.com/ivfprice.htm.

C. The third type of human stem cells are induced pluripotent stem cells, which were recently developed by researchers. Scientists have developed a procedure

to reprogram adult cells to assume a state similar to embryonic stem cells. JA 249-50 (Decl. ¶ 7). Scientists are still investigating whether induced pluripotent stem cells differ from embryonic stem cells in clinically significant ways that would limit their usefulness. NIH, *Stem Cell Basics: What Are Induced Pluripotent Stem Cells?*, *available at* http://stemcells.nih.gov/info/basics/basics10.asp; *see also* JA 249-50 (Decl. ¶ 7). A recent study found that mice rejected induced pluripotent cells and counseled further evaluation of pluripotent stem cells before their use in human patients. Tongbiao Zhao et al., *Immunogenicity of Induced Pluripotent Stem Cells*, 474 Nature 212 (2011).

II. Regulatory Background.

A. In 1996, Congress enacted the Dickey-Wicker amendment to limit the scope of federal research funding in response to the report of a 1994 NIH panel that recommended funding for research to be done directly on human embryos in order to improve IVF techniques and to screen embryos for genetic defects before implantation, among other things. *See* NIH, Report of the Human Embryo Research Panel 75-76, *available at* http://bioethics.georgetown.edu/pcbe/reports /past_commissions/; *see also* JA 511 (*Sherley II*, at 390) ("The historical record suggests the Congress passed the Amendment chiefly to preclude President Clinton from acting upon an NIH report recommending federal funding for research using embryos that had been created for the purpose of in vitro fertilization."). The amendment, which has been reenacted without substantive change in subsequent

annual appropriations, provides that no funds 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. 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b))." Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112.

When the amendment was first enacted in 1996, human embryonic stem cells had not yet been isolated for use in research. *See* JA 247 (Decl. ¶ 6) (embryonic stem cells were first isolated in 1998); *see also* JA 511 (*Sherley II*, at 390) ("In 1996, when the Congress first passed Dickey-Wicker, scientists had taken steps to isolate [embryonic stem cells] but had not yet been able to stabilize them for research in the laboratory.").

B. The Court in *Sherley II* explained that "Dickey-Wicker became directly relevant to [embryonic stem cells] only in 1998, when researchers at the University of Wisconsin succeeded in generating a stable line of [embryonic stem cells], which they made available to investigators who might apply for NIH funding." JA 511-12 (*Sherley II*, at 391). In light of these developments, the Director of NIH requested a legal opinion from the General Counsel of the Departmenf of Health and Human Services ("HHS") regarding the applicability of the Dickey-Wicker amendment to research using embryonic stem cells. The 1999 opinion letter concluded that "[t]he

statutory prohibition on the use of funds appropriated to HHS for human embryo research would not apply to research utilizing human pluripotent stem cells because such cells are not a human embryo within the statutory definition." *See* JA 163 (Rabb Memorandum); *see also* JA 512 (*Sherley II*, at 391) (quoting Rabb Memorandum).

Citing the General Counsel's legal opinion, NIH issued proposed guidelines to "ensure that NIH-funded research in this area is conducted in an ethical and legal manner," 64 Fed. Reg. 67,576 (Dec. 2, 1999), and issued final guidelines in 2000, 65 Fed. Reg. 51,976 (Aug. 25, 2000) (final guidelines).

In 2001, President Bush determined to continue federal support for research using embryonic stem cells. *See* Address to the Nation on Stem Cell Research From Crawford, Texas, 37 Weekly Comp. Pres. Doc. 1149 (Aug. 9, 2001) (noting that "most scientists, at least today, believe that research on embryonic stem cells offer the most promise because these cells have the potential to develop in all of the tissues in the body"). Observing, however, that "we must proceed with great care," President Bush decided to limit funding to research using cells from existing stem cell lines. *Id.* at 1151. He observed, that "[a]s a result of private research, more than 60 genetically diverse stem cell lines already exist," and that these lines "have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research." *Ibid.* He concluded "that we should allow Federal funds to be used for research on these existing stem cell lines." *Ibid.*

NIH issued new guidance to implement President Bush's policy. The agency noted that the President had decided "to allow Federal funds to be used for research on existing human embryonic stem cell lines" derived "prior to his announcement," and announced that it was creating a "Human Embryonic Stem Cell Registry that will list the human embryonic stem cells that meet the eligibility criteria," in "order to facilitate research using human embryonic stem cells[.]" *See* NIH, Notice of Criteria for Federal Funding of Research on Existing Human Embryonic Stem Cells and Establishment of NIH Human Embryonic Stem Cell Registry (Nov. 7, 2001), *available at* http://grants.nih.gov/grants/guide/notice-files/not-OD-02-005.html.

When Congress reenacted the Dickey-Wicker amendment after President Bush's announcement of his policy, the relevant Committees made clear that the legislative language did not impose a ban on research using embryonic stem cells and that President Bush's policy was consistent with the amendment. *See* H.R. Rep. No. 107-229, at 180 (Oct. 9, 2001) ("The Committee continues a provision to prohibit the use of funds in the Act concerning research involving human embryos. However, this language should not be construed to limit federal support for research involving human embryonic stem cells listed on an NIH registry and carried out in accordance with policy outlined by the President."); *see also* S. Rep. No. 107-84, at 18 (Oct. 11, 2001) ("The Committee urges the NIH to move quickly to support all types of stem

cell research, including embryonic [and] adult . . . ."). Congress continued to express this view throughout the Bush administration. *See* H.R. Rep. No. 110-231, at 288 (2007); H.R. Rep. No. 108-636, at 199 (2004).

C. "Upon assuming office in 2009, President Obama lifted the temporal restriction imposed by President Bush and permitted the NIH to 'support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law.'" JA 512 *(Sherley II*, at 391) (quoting Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (2009) (reproduced at JA 493)). The President stated that he would "remove . . . limitations on scientific inquiry" involving stem cells, "expand NIH support for the exploration of human stem cell research," and thereby "enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind." JA 493, § 1. The President further 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." JA 493, § 3.

After notice-and-comment, NIH issued the 2009 Guidelines, which are currently in effect. JA 44 (74 Fed. Reg. 32,170 (July 7, 2009)). "In the Guidelines, the NIH noted 'funding of the derivation of stem cells from human embryos is

prohibited by . . . the Dickey-Wicker Amendment.'" JA 512-13 (*Sherley II*, at 391) (quoting 74 Fed. Reg. at 32,175). The Guidelines further explained that "[s]ince 1999, the Department of Health and Human Services (HHS) has consistently interpreted [Dickey–Wicker] as not applicable to research using [embryonic stem cells], because [embryonic stem cells] are not embryos . . . . This longstanding interpretation has been left unchanged by Congress, which has annually reenacted the . . . Amendment with full knowledge that HHS has been funding [embryonic stem cell] research since 2001." JA 513 (*Sherley II*, at 391) (quoting 74 Fed. Reg. at 32,173) (some alterations in original).

As the agency explained, its 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 [human embryonic stem cells] that does not involve an embryo nor result in an embryo's destruction, for which Federal funding is permitted." JA 47 (74 Fed. Reg. at 32,173).

NIH's 2009 Guidelines set forth strict standards that researchers must meet when choosing the stem cell lines to use in research funded by NIH. Research funded by NIH may use stem cell lines derived from human embryos only if they

"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." JA 47 (74 Fed. Reg. at 32,174). For stem cell lines derived from embryos donated after the Guidelines, the donor must also have been informed of all options available at the facility for the disposition of embryos. *Ibid.* NIH maintains a registry of stem cell lines that meet these criteria and are therefore eligible to be used in federally funded research. *See* NIH Human Embryonic Stem Cell Registry, http://grants.nih.gov/stem_cells/registry/current.htm.

When Congress reenacted the Dickey-Wicker amendment for FY 2010, after issuance of NIH's 2009 Guidelines, Congress again noted that the amendment "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) (Conf. Rep.) ("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.").

Congress reenacted the Dickey-Wicker amendment for FY 2011 and FY 2012. *See* Department of Defense and Full-Year Continuing Appropriations Act, 2011, Pub. L. No. 112-10, Div. B, §§ 1101, 1104, 125 Stat. 38, 102-03 (2011); Consolidated Appropriations Act, 2012, Pub. L. No. 112-74, Div. F, § 508, 125 Stat. 786, 1112 (2011).

III. Prior Proceedings.

A. *Sherley I*.

1. Plaintiffs filed suit on August 19, 2009, challenging the 2009 NIH Guidelines on two grounds. JA 16. Their first claim asserted that the 2009 Guidelines violate the Dickey-Wicker amendment, which prohibits federal funding for "research in which a human embryo or embryos are destroyed." Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112; JA 39 (Complaint ¶¶ 66-68). Their second and third claims asserted that the Guidelines were promulgated in violation of the Administrative Procedure Act's procedural requirements, JA 39-40 (Complaint ¶¶ 69-72), and that the Guidelines constitute arbitrary and capricious agency action, JA 40 (Complaint ¶¶ 73-75).

The plaintiffs include Dr. James L. Sherley and Dr. Theresa Deisher, two scientists who perform research using adult stem cells. JA 18-20 (Complaint ¶¶ 6, 7). The original plaintiffs also included Nightlight Christian Adoptions, an agency facilitating the adoption of frozen embryos, and its clients Shayne Nelson, Tina Nelson, William Flynn, and Patricia Flynn, JA 20-22 (Complaint ¶¶ 8, 10, 11); Christian Medical Association, a non-profit association "dedicated to improving the ethical standards of health care in the United States and abroad," JA 22 (Complaint ¶ 12); and all embryos created using *in vitro* fertilization and no longer needed for reproduction, JA 21 (Complaint ¶ 9). Those plaintiffs have been dismissed for lack of standing. JA 664.

Plaintiffs filed a motion for a preliminary injunction and a motion to appoint a guardian ad litem for the plaintiff embryos. They argued that if an injunction were not granted, the plaintiff embryos might be destroyed and the two plaintiff research scientists would suffer injury because their grant proposals to NIH would be in competition with those of embryonic stem cell researchers.

The government opposed the preliminary injunction and filed a motion to dismiss for lack of subject matter jurisdiction or, in the alternative, for failure to state a claim. The district court granted the government's motion and dismissed the

complaint on October 27, 2009, on the ground that plaintiffs lacked standing. JA 180. The district court rejected the scientists' claim that increased competition resulted in their injury in fact and their invocation of the "competitor standing doctrine." JA 188.

2. Plaintiffs appealed the ruling with respect to the standing of the two plaintiff scientists. This Court reversed, holding that the two scientists have standing under 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." JA 222 (*Sherley I*, at 72-73) (internal quotations omitted) (alteration in original). The Court reasoned that the increase in grant applications for embryonic stem cell research resulting from the Guidelines would "intensif[y] the competition for a share in a fixed amount of money." JA 224-25 (*Sherley I*, at 74). The Court declined plaintiffs' invitation to reach the merits of their claims and remanded to the district court. JA 227.

B. *Sherley II*.

On August 23, 2010, the district court issued a preliminary injunction, concluding that the plaintiffs were likely to show that the 2009 NIH Guidelines

violated the Dickey-Wicker amendment. JA 228, 237. The government appealed. JA 244. After hearing argument, this Court granted the government's request for a stay pending appeal. JA 490. Then, after full briefing and oral argument, the Court vacated the district court's order, with Judge Henderson dissenting from the ruling. JA 509-10.

The Court began its inquiry with the statutory language, which precludes funding of "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death[.]" Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112. The Court observed that "[t]he district court held, and the plaintiffs argue on appeal" that the statute "unambiguously bars funding for any project using an [embryonic stem cell]." JA 517 (*Sherley II*, at 393). In plaintiffs' view, "because an embryo had to be destroyed in order to yield an [embryonic stem cell], any later research project that uses an [embryonic stem cell] is necessarily 'research' in which the embryo is destroyed." JA 517-18 (*Sherley II*, at 393-94). But the Court rejected plaintiffs' contention, noting that "[t]he use of the present tense in a statute strongly suggests it does not extend to past actions," and that "the present tense generally does not include the past." JA 518 (*Sherley II*, at 394) (quoting *Carr* v. *United States*, — U.S. —, 130 S. Ct. 2229, 2236 (2010)). The Court also rejected the dissent's

view that "[t]he context here . . . indicate[s] a different understanding." JA 518 (*Sherley II*, at 394). The Court emphasized, "[t]o the contrary, as amicus the University of California urges in its brief, and as the Government emphasized at oral argument, NIH funding decisions are forward-looking, requiring the NIH to 'determine whether what is proposed to be funded meets with its requirements.' Therefore, a grant application to support research that includes the derivation of stem cells would have to be rejected." JA 518 (*Sherley II*, at 394).

Moreover, the Court rejected plaintiffs' contention that "'research' using an [embryonic stem cell] includes derivation of the [embryonic stem cell]" on the theory that derivation "is an integral part of the 'research.'" JA 519 (*Sherley II*, at 394). The Court explained that this "conclusion does not follow from the premise; at best it shows Dickey-Wicker is open to more than one possible reading." *Ibid.* It also rejected plaintiffs' contention that if "Congress had [ ] intended a narrower reading [of research], [it] would have used a term identifying a particular action, as it did in subsection (1) of Dickey-Wicker, which specifically bars the 'creation' of an embryo for 'research purposes.'" *Ibid.* The Court found "no basis for that inference." It explained that "[t]he definition of research is flexible enough to describe either a

discrete project or an extended process," and that "this flexibility only reinforces our conclusion that the text is ambiguous." *Ibid.*

Turning to the reasonableness of the agency's construction of the statute under *Chevron* step 2, the Court rejected plaintiffs' contention that "NIH is not entitled to deference because it never offered an interpretation of the term 'research.'" JA 520 (*Sherley II*, at 395). The Court noted that the 2009 Guidelines "expressly distinguished between the derivation of [embryonic stem cells] and 'research involving [embryonic stem cells] that does not involve an embryo nor result in an embryo's destruction.'" *Ibid.* (quoting 74 Fed. Reg. at 32,173). The Court noted that "although the Guidelines do not define the term 'research,' they do make clear the agency's understanding that 'research involving [embryonic stem cells]' does not necessarily include the antecedent process of deriving the cells." JA 520 (*Sherley II*, at 395).

The Court concluded that "it is entirely reasonable for the NIH to understand Dickey-Wicker as permitting funding for research using cell lines derived without federal funding, even as it bars funding for the derivation of additional lines." JA 523 (*Sherley II*, at 396). Indeed, the Court observed, "Congress has reenacted Dickey-Wicker unchanged year after year 'with full knowledge that HHS has been funding [embryonic stem cell] research since 2001.'" JA 523 (*Sherley II*, at 396) (quoting 74

Fed. Reg. at 32,173). The Court held that the balance of the equities also weighed against granting a preliminary injunction, but made clear that it would have vacated the injunction even "if likelihood of success on the merits is an independent requirement." JA 528 (*Sherley II*, at 399).

Judge Henderson dissented, and would have held that the Dickey-Wicker amendment unambiguously prohibits funding research using human embryonic stem cells. JA 531 (*Sherley II*, at 400). Judge Henderson stated that "the plain meaning of 'research'" in the amendment is a "systematic inquiry or investigation" and includes both the derivation of stem cells and their subsequent use. JA 532 (*Sherley II*, at 401) (internal quotations omitted). Judge Henderson also would have held that, because plaintiffs "made an unusually strong showing" on their likelihood of success on the merits, the district court did not abuse its discretion in balancing the remaining preliminary injunction factors in favor of granting the injunction. JA 541 (*Sherley II*, at 406).

C. *Sherley III*.

On remand, the district court granted the government's motion for summary judgment and denied plaintiffs' motion for summary judgment. JA 693.

The district court explained that plaintiffs' statutory claim was foreclosed by the holding and reasoning of this Court's decision in *Sherley II*. JA 675, 677. The district court noted that the issues had been "carefully briefed and argued before both this Court and the Court of Appeals" and that "plaintiffs haven't offered any new information or reasoning that was unavailable to the D.C. Circuit." JA 675, 677.

The district court also held that the 2009 Guidelines were promulgated in accordance with the Administrative Procedure Act ("APA"). The court rejected plaintiffs' claim that the agency had violated the APA because it failed to respond to public comments and entered the rulemaking with an "unalterably closed mind." The court held that "NIH's notice of proposed rulemaking did not invite (and therefore the NIH wasn't obligated to respond to) comments on the topic of whether to fund human embryonic stem cell research." JA 687 (emphasis removed). The court explained that the President's Executive Order 13,505 "required the promulgation of Guidelines for funding embryonic stem cell research," JA 687, and that "NIH reasonably concluded . . . that the fundamental policy question of whether to provide federal funds for embryonic stem cell research wasn't a question for it to decide," JA 691. Therefore, the court held, "the NIH wasn't obligated to consider comments that, if adopted, would cause it to disobey the President and create an unlawful rule."

JA 687. The court noted that comments by the Acting NIH Director did not show an "unalterably closed mind" but "merely indicate[d] [the Acting Director's] reasonable understanding of the scope of the rulemaking as specified in" the President's Executive Order. JA 691-92.

SUMMARY OF ARGUMENT

I. Congress first enacted the Dickey-Wicker amendment in 1996, two years before human pluripotent stem cells derived from embryos became available for laboratory research. The amendment prohibits funding of "research *in which* a human embryo or embryos *are* destroyed, discarded, or knowingly subjected to risk of injury or death[.]" Pub. L. No. 112-74, Div. F, § 508, 125 Stat. at 1112 (emphasis added). The language reflects the type of research that animated enactment of the amendment — a federally funded research project in which embryos would be destroyed or harmed.

Since 1999, HHS has repeatedly explained that embryonic stem cells are not embryos within the meaning of the statute and that research using stem cells from human stem cell lines is therefore not "research in which a human embryo or embryos" are destroyed or discarded. NIH guidance under the Clinton, Bush, and Obama Administrations has thus advised grant applicants that research using human stem cell lines derived from embryos may be conducted with federal support. The

policy adopted by President Bush in August 2001 provided that federal funds could be used only for research using already existing stem cell lines. President Obama lifted that restriction and directed that NIH consider funding applications without regard to the date on which a stem cell line was derived. These policy differences did not, however, reflect different understandings of the Dickey-Wicker amendment. As this Court observed, plaintiffs have conceded that their reading of the statute would condemn not only the 2009 NIH Guidelines but also the federal funding authorized under the Bush Administration. JA 523 (*Sherley II*, at 396). Aware of this consistent understanding of the amendment, Congress has reenacted the provision each year without substantive change.

In *Sherley II*, this Court, after briefing and oral argument, rejected plaintiffs' contention that the plain language of the statute nevertheless requires the Court to reject the longstanding understanding of the statute that has repeatedly been ratified by Congress. The Court recognized that the statute applies to research in which embryos are destroyed; it does not extend to antecedent projects in which a stem cell line was originally created. Equally, plaintiffs cannot expand the scope of the amendment by arguing that funding of research using stem cell lines will provide an incentive to scientists to create new stem cell lines. This hypothetical future research is not the research funded by NIH.

Although plaintiffs characterize the Court's opinion as a "tentative assessment" of their claims, Pl. Br. 16, they offer the same arguments, often verbatim, that they presented to the Court in *Sherley II*. Where, as here, a panel has addressed a legal issue after full briefing and argument, the principles of the law of the case doctrine strongly weigh against a plenary reconsideration of plaintiffs' arguments. In any event, plaintiffs offer no basis on which to depart from the Court's prior decision.

II. Plaintiffs are on no firmer ground in claiming that NIH violated the Administrative Procedure Act in its responses to comments on its draft guidelines. NIH received "approximately 49,000 comments," JA 44 (74 Fed. Reg. at 32,170), and responded appropriately to comments that were relevant to establishing the policies and procedures under which NIH will fund human embryonic stem cell research. *See* JA 44-48 (74 Fed. Reg. at 32,170-74). As the district court noted, "the fundamental policy question of whether to provide federal funds for embryonic stem cell research wasn't a question for [NIH] to decide." JA 690. That question had been answered by "three Presidential administrations" that all determined "to permit federal funding." JA 691. The 2009 Executive Order "required the promulgation of Guidelines for funding embryonic stem cell research, and the NIH wasn't obligated to consider comments that, if adopted, would cause it to disobey the President and create an unlawful rule." JA 687.

STANDARD OF REVIEW

This Court reviews grants of summary judgment de novo. *Sierra Club* v. *Van Antwerp*, 661 F.3d 1147, 1150 (D.C. Cir. 2011).

ARGUMENT

I. The NIH Guidelines Do Not Violate The Dickey-Wicker Amendment.

A. NIH Has Consistently Interpreted The Dickey-Wicker Amendment To Permit Federal Funding of Research That Uses Embryonic Stem Cells, And Congress Has Repeatedly Ratified That Interpretation.

1. Congress first enacted the Dickey-Wicker amendment in 1996. At that time, "scientists had taken steps to isolate [embryonic stem cells] but had not yet been able to stabilize them for research in the laboratory." JA 511 (*Sherley II*, at 390). The legislation responded to a 1994 NIH panel report that had advocated federal funding of research that would have involved the use of human embryos. JA 511 (*Sherley II*, at 390-91). The research was designed to improve the process of *in vitro* fertilization, to determine whether embryos carried genetic abnormalities, and to isolate embryonic stem cells. Embryos would have been destroyed or subject to risk of being destroyed during that research. *See* NIH, Report of the Human Embryo Research Panel 75-76, *available at* http://bioethics.georgetown.edu/pcbe/reports/past_commissions/. The Dickey-Wicker amendment created a ban on federal funding of that type of research, specifically prohibiting federal funding of "research in which a human embryo or

embryos are destroyed, discarded, or knowingly subjected to risk of injury or death . . . ." Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112.

A 1996 letter from NIH to researchers at Georgetown University, cited by plaintiffs, illustrates the nature of the research to which the statute was directed. *See* JA 507; Pl. Br. 35. The research at issue involved pre-implantation genetic diagnosis, which is a procedure used on embryos fertilized *in vitro* to determine if they carry genetic disorders predisposing them to hereditary diseases. JA 679 n.3. Pre-implantation genetic diagnosis requires the removal of one cell from the embryo. HHS, Regenerative Medicine 82 (2006), *available at* http://stemcells.nih.gov/info/scireport/2006report.htm. NIH explained to the researchers that federal dollars could not be used to fund the project. JA 507. In 1996, as today, federal funding for such research was unavailable, because it poses a risk of harm to embryos involved in the procedure that is greater than that allowed for research on fetuses in utero and is thus prohibited by the Dickey-Wicker amendment.[1]

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[1] Plaintiffs mistakenly suggest that NIH was actually concerned with tests on the DNA removed from an embryo, rather than with experimentation on human embryos. Pl. Br. 35-36 & n.6. They cite testimony from a congressional hearing, however, that makes plain that the researchers performed pre-implantation genetic diagnosis on embryos, which requires the removal of a cell from an embryo to test that embryo for genetic abnormalities and thereby subjects the embryo to a risk of harm. *See Continued Management Concerns at the National Institutes of Health: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Commerce*, 105th Cong. 29 (1997) ("Rep. Barton: Well, can you do preimplantation genetic diagnosis without

2. "Dickey-Wicker became directly relevant to [embryonic stem cells] only in 1998, when researchers at the University of Wisconsin succeeded in generating a stable line of [embryonic stem cells], which they made available to investigators who might apply for NIH funding." JA 511-12 (*Sherley II,* at 391).[2] When funding for research using human embryonic stem cells first became an issue in 1999, the General Counsel of HHS issued an opinion letter that concluded that research using embryonic stem cells is not prohibited by the amendment because an embryonic stem cell is not an "embryo" and is not capable of developing into a human being. *See* JA 163 (Rabb Memorandum).

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doing human embryo research? Dr. Varmus [then Director of NIH]: Pre-implantation genetic diagnosis, no."); *id.* at 2-3 (stating that the prohibited research "at the NIH campus involved a misdiagnosis that resulted in the birth of an infant with cystic fibrosis"). In 1996, as today, the Dickey-Wicker amendment precludes federal funding for such research because it is research in which an embryo is subject to a risk of injury or death that is greater than that allowed for research on fetuses in utero.

[2] Plaintiffs assert that human embryonic stem cells were isolated in 1994, relying on a citation to Ariff Bongso et al., *Isolation and Culture of Inner Cell Mass Cells from Human Blastocysts*, 9 Human Reproduction 2110 (1994). Pl. Br. 39-40 (citing JA 358, 360). Although this paper reported isolating human embryonic stem cells, it did not generate a stem cell line that could be maintained and used in future research. *See* JA 360 ("However, after the second subculture, the cells differentiated into fibroblasts or died."). Only in 1998 did scientists isolate and maintain human embryonic stem cell lines, *see* James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 Science 1145 (1998), and it is commonly accepted among the scientific community that human embryonic stem cells were successfully isolated at that time, *see, e.g.*, JA 247 (Decl. ¶ 5).

Citing the General Counsel's legal opinion, NIH issued proposed guidelines to "ensure that NIH-funded research in this area is conducted in an ethical and legal manner," 64 Fed. Reg. at 67,576, and issued final guidelines in 2000, 65 Fed. Reg. 51,976 (Aug. 25, 2000) (final guidelines).

3. NIH has never departed from its interpretation of the Dickey-Wicker amendment — set out in the 2000 guidelines — to not bar research using human embryonic stem cells. In the subsequent decade, that understanding formed the premise of the policies of both the Bush Administration and the Obama Administration. Those policies differ in the scope of embryonic stem cell lines that could be used in federally funded research, but both recognize that NIH may fund research using embryonic stem cells. Thus, "[a]s the plaintiffs conceded at oral argument, because [President Bush's policy permitted the NIH to fund projects using [embryonic stem cells], it would have been prohibited under their proposed reading of Dickey-Wicker." JA 523 (*Sherley II*, at 396).[3]

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[3] Plaintiffs mistakenly suggest that NIH's longstanding interpretation is at odds with a 2002 memorandum from the General Counsel of HHS to the Acting Director of NIH that evaluated whether President Bush's policy on stem cell research was consistent with the Dickey-Wicker amendment. Pl. Br. 36; JA 122. The memorandum concluded that funding research using stem cells was not funding of research "in which" an embryo was destroyed. JA 125-26. The memorandum also noted that "[t]he President's policy provides no incentives for the destruction of additional embryos," but did not suggest that the statute imposed such a requirement and did not suggest that the policy in place before President Bush's announcement

The NIH guidance issued to implement President Bush's policy explained that the President had decided "to allow Federal funds to be used for research on existing human embryonic stem cell lines" derived "prior to his announcement," and announced that it was creating a "Human Embryonic Stem Cell Registry that will list the human embryonic stem cells that meet the eligibility criteria," in "order to facilitate research using human embryonic stem cells[.]" *See* NIH, Notice of Criteria for Federal Funding of Research On Existing Human Embryonic Stem Cells and Establishment of NIH Human Embryonic Stem Cell Registry (Nov. 7, 2001), *available at* http://grants.nih.gov/grants/guide/notice-files/not-OD-02-005.html.

When Congress reenacted the Dickey-Wicker amendment for FY 2002, it approved that research, noting that the prohibition on the destruction of embryos "should not be construed to limit federal support for research involving human embryonic stem cells listed on an NIH registry and carried out in accordance with policy outlined by the President." H.R. Rep. No. 107-229, at 180 (Oct. 9, 2001); *see also* S. Rep. No. 107-84, at 18 (Oct. 11, 2001) ("The Committee urges the NIH to move quickly to support all types of stem cell research, including embryonic [and] adult . . . ."). Congress continued to express this view throughout the Bush

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was infirm. JA 125.

administration. *See* H.R. Rep. No. 110-231, at 288 (2007); H.R. Rep. No. 108-636, at 199 (2004).

4. President Obama lifted "the temporal restriction imposed by President Bush and permitted the NIH to 'support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by law.'" JA 512 *(Sherley II*, at 391) (quoting Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (reproduced at JA 493)). The President stated that he would "remove . . . limitations on scientific inquiry" involving stem cells, "expand NIH support for the exploration of human stem cell research," and thereby "enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind." JA 493, § 1. The President further 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." JA 493, § 3.

Under the 2009 NIH Guidelines, research using human embryonic stem cells is eligible for federal funding only if the cells are from stem cell lines 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

individuals . . . who gave voluntary written consent for the human embryos to be used for research purposes." JA 48.

When Congress included the Dickey-Wicker amendment in the FY 2010 appropriations bill, it was fully aware of the 2009 NIH Guidelines that had been promulgated to govern funding of research grants. The relevant Committee Report, like the 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 273 (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) (Conf. Rep.) ("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.").

After this Court's decision in *Sherley II*, entered April 29, 2011, that upheld the 2009 NIH Guidelines, Congress reenacted the Dickey-Wicker amendment for FY 2012. *See* Consolidated Appropriations Act, 2012, Pub. L. No. 112-74, Div. F, § 508, 125 Stat. 786, 1112 (2011).

5. The agency's consistent understanding of the Dickey-Wicker amendment, as it relates to research using embryonic stem cells, is rooted in the language of the amendment which speaks in the present tense and prohibits funding of "research *in which* a human embryo or embryos *are* destroyed, discarded, or knowingly subjected to risk of injury or death[.]" Pub. L. No. 112-74, Div. F, § 508, 125 Stat. at 1112 (emphasis added); *see* JA 518 (*Sherley II* at 394) (noting that "[t]he use of the present tense in a statute strongly suggests it does not extend to past actions," and that "the present tense generally does not include the past" (quoting *Carr* v. *United States*, — U.S. —, 130 S. Ct. 2229, 2236 (2010))). The amendment does not bar funding for research that uses embryonic stem cells from a stem cell line that may have been derived a dozen years earlier and used in hundreds of other types of research, as is the case, for example, with the H9 stem cell line.

Moreover, even if plaintiffs' interpretation could be reconciled with the statutory language, NIH's interpretation of the statute, set out in 1999, and reaffirmed

in 2009, is plainly entitled to judicial deference. Congress's reenactment of the statute with knowledge of the existing Executive Branch interpretation counsels special hesitation in setting that longstanding agency interpretation aside. The Supreme Court explained in *NLRB* v. *Bell Aerospace Co.*, 416 U.S. 267, 274-75 (1974), that "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." *See also Lorillard* v. *Pons*, 434 U.S. 575, 580-81 (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.").[4]

Where Congress repeatedly reenacts an appropriations restriction accompanied by clear expressions of legislative intent, those statements are "worthy of considerable

[4] Plaintiffs offer the unfounded speculation that the Dickey-Wicker amendment may be subject to conflicting interpretations because the provision appears as a restriction on appropriations for the Departments of Labor and Education as well as HHS. Pl. Br. 42. Congress enacted Dickey-Wicker in response to proposed funding by NIH of research in which a human embryo would be destroyed. HHS interpreted the relevance of the provision in 1999, and NIH has established and implemented stem cell research policy under three administrations. President Obama's Executive Order thus recognized that the "authority of [HHS], including [NIH], to fund and conduct human embryonic stem cell research has been limited by Presidential actions," and that "[t]he purpose of this order is to remove these limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research." JA 493, § 1.

respect from the coordinate branches," and this Court has made clear that consideration should be given to such statements in interpreting the language of the appropriations restriction. *Nat'l Senior Citizens Law Ctr.* v. *Legal Servs. Corp.*, 751 F.2d 1391, 1397 (D.C. Cir. 1985) (R.B. Ginsburg, J.); *see also Brooks* v. *Dewar*, 313 U.S. 354, 360-61 (1941) (Congress's "repeated appropriations" with knowledge of the agency's practice "not only confirms the departmental construction of the statute, but constitutes a ratification of the action of the Secretary as the agent of Congress in the administration of the act"); *FDIC* v. *Phila. Gear Co.,* 476 U.S. 426, 437-38 (1986) (citing reports of both Houses as evidence that Congress "has expressly incorporated [agency regulations] into the statutory scheme"). In reenacting the amendment, Congress has repeatedly approved the funding of research using embryonic stem cell lines and declared that such research is not precluded by the Dickey-Wicker amendment.

B. Plaintiffs Offer No Basis For Setting Aside This Court's Holding That The Guidelines Do Not Violate The Dickey-Wicker Amendment.

1. Plaintiffs offer no arguments or evidence not previously presented to this Court. This Court has made clear that in such instances, "the same issue presented a second time in the same case in the same court should lead to the same result."

LaShawn A. v. *Barry*, 87 F.3d 1389, 1393 (D.C. Cir. 1996) (en banc). Although plaintiffs characterize the Court's opinion as a "tentative assessment" of their claims, Pl. Br. 16, the Court examined at length the same arguments that plaintiffs offer on this appeal. Indeed, much of plaintiffs' brief on this appeal is taken verbatim from their brief in *Sherley II*. Plaintiffs ask, in effect, that their claim be reheard.

Although the law of the case doctrine generally does not preclude reconsideration of a decision rendered on a preliminary injunction appeal, *see Berrigan* v. *Sigler*, 499 F.2d 514, 518 (D.C. Cir. 1974), the policies animating the law of the case doctrine are implicated when the Court is asked to hear the same legal claim that it has already addressed and in fact resolved on preliminary injunction after full briefing and oral argument. "[T]he doctrine posits that when a court decides upon a rule of law, that decision should continue to govern the same issues in subsequent stages in the same case." *Pepper* v. *United States,* 131 S. Ct. 1229, 1250 (2011) (quoting *Arizona* v. *California*, 460 U.S. 605, 618 (1983)). "This doctrine directs a court's discretion, it does not limit the tribunal's power" and thus "does not apply if the court is convinced that [its prior decision] is clearly erroneous and would work a manifest injustice." *Pepper*, 131 S. Ct. at 1250-51 (citations omitted) (alteration in original).

This Court has also observed that "the same issue presented in a later case in the same court should lead to the same result." *LaShawn A.*, 87 F.3d at 1393. The law of the circuit doctrine is "much more exacting" because it is "derived from legislation and from the structure of the federal courts of appeal." *Id.*, at 1395. This Court has explained that "when both [the law of the case and the law of the circuit] doctrines are at work, the law-of-the-circuit doctrine should increase a panel's reluctance to reconsider a decision made in an earlier appeal in the same case." *Ibid.*

Several courts of appeals have applied the discretionary principles of the law of the case doctrine when a party has raised legal issues fully addressed on a prior appeal from a preliminary injunction. *See, e.g., Naser Jewelers, Inc.* v. *City of Concord*, 538 F.3d 17, 20 (1st Cir. 2008); *Preminger* v. *Peake*, 552 F.3d 757, 765 (9th Cir. 2008); *ACLU* v. *Mukasey*, 534 F.3d 181, 187-90 (3d Cir. 2008); *This That &The Other Gift & Tobacco, Inc.* v. *Cobb Cty.*, 439 F.3d 1275, 1284-85 (11th Cir. 2006); *Nat'l Hockey League Players Ass'n* v. *Plymouth Whalers Hockey Club*, 419 F.3d 462, 470–71 (6th Cir. 2005); *Entergy, Ark., Inc.* v. *Nebraska*, 241 F.3d 979, 987 (8th Cir. 2001); *Royal Ins. Co. of Am.* v. *Quinn-L Capital Corp.*, 3 F.3d 877, 880–81 (5th Cir. 1993); *see also* 18B Charles Alan Wright et al., *Federal Practice & Procedure* § 4478.5 (2d ed. 1982 & Supp. 2011) ("A fully considered appellate ruling on an issue of law made on a preliminary injunction

appeal, however, does become the law of the case for further proceedings in the trial court on remand and in any subsequent appeal.").

University of Texas v. *Camenisch*, 451 U.S. 390 (1981), is not to the contrary. The Supreme Court did not definitively bar application of the law of the case doctrine to a decision vacating a preliminary injunction, holding only that "it is *generally* inappropriate for a federal court at the preliminary-injunction stage to give a final judgment on the merits" due to special "considerations." *Id.* at 395 (emphasis added). Those considerations are the "haste that is often necessary" in preliminary injunction proceedings, which result in "procedures that are less formal and evidence that is less complete than in a trial on the merits." *Ibid.*

None of those considerations apply here. In *Sherley II,* the Court vacated the preliminary injunction based on a resolution, after full briefing and oral argument, of the same statutory question at issue in this appeal, and plaintiffs merely recite the same arguments already rejected by this Court.

In any event, even if the Court were to determine that the law of the case doctrine did not apply, the Court's earlier decision is "persuasive" and should be followed here. *Berrigan*, 499 F.2d at 518. Plaintiffs' reiteration of their arguments does not diminish that fact. We have already discussed most of their contentions.

We briefly respond to some statements in plaintiffs' brief not fully addressed in the prior discussion.

2. a. Plaintiffs again argue that the Dickey-Wicker amendment incorporates the definition of "research" contained in the Human Subject Protection regulations. The amendment does not, however, incorporate that definition but merely references those regulations as the standard of risk that is prohibited, stating that federal funding is prohibited of research in which embryos are 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) of the Human Subject Protection regulations and section 498(b) of the Public Health Service Act, 42 U.S.C. § 289g(b). Pub. L. No. 112-74, Div. F, § 508(a), 125 Stat. at 1112. Congress thus applied the same risk standards to research on human embryos applicable to fetuses in utero under those provisions. It did not thereby incorporate the definition of "research" contained in the Human Subject Protection regulations.

But, as we explained in *Sherley II*, the definition of research contained in those regulations would not advance plaintiffs' argument even if it were applicable. Those regulations define research 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). The fact that research is "systematic" does not mean that it includes acts or processes that predated the federally funded research.[5]

Plaintiffs note that this Court did not resolve whether the Dickey-Wicker amendment incorporated the definition of research in the Human Protection Subject regulations. Pl. Br. 21. But the Court declared that it "need not resolve this debate" precisely because plaintiffs' argument would fail even if the definition of research had been made part of Dickey-Wicker. JA 518 (*Sherley II*, at 394 n*). The Court explained that "as the Government also argues, that a project involves 'research development' or is 'systematic' does not mean that it includes acts or processes,' such as deriving [embryonic stem cells], 'that predated the federally funded research.'" *Ibid.*

b. Plaintiffs argue that even if research using cells from stem lines is not "research" within the meaning of Dickey-Wicker, it is still subject to the statute's restriction on funding. The amendment admits of no such interpretation. The

[5] Other NIH regulations underscore that "systematic" research can consist of a single study or a single experiment. For example, the regulation that governs the extramural grant process defines "research" as "a systematic investigation, study or experiment designed to contribute to general knowledge relating broadly to public health." 42 C.F.R. § 52.2.

amendment prohibits funding for "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death[.]" Pub. L. No. 112-74, Div. F, § 508, 125 Stat. at 1112. This Court sustained NIH's longstanding understanding that research involving the use of cells from stem cell lines is *not* such research.

Plaintiffs nevertheless argue that funding research using stem cells "provides a strong incentive for researchers to develop additional human embryonic stem-cell lines." Pl. Br. 27. In *Sherley II*, the Court stated that "[t]o the extent this argument is distinct from the plaintiffs' principal argument," it had not been presented to the district court and therefore would not be considered. JA 525 (*Sherley II*, at 397).

On remand, the district court correctly held that plaintiffs' "incentive" argument is without basis in the statute. The statutory restriction applies to research *"in which"* an embryo is destroyed, discarded or knowingly subjected to risk of death or serious injury. As the district court observed, the words "'in which' restrict the types of research for which funding is prohibited to research that knowingly subjects a human embryo or embryos to risk of injury or death *within* the research." JA 680-81. The court observed that "[a]n example of such a prohibited piece of research would be, as defendants note, preimplantation genetic diagnosis," which "doesn't

necessarily destroy human embryos, but . . . subjects them to some risk of injury or death *inside* that research." JA 681.

Plaintiffs' argument posits that funding research in which an embryo is *not* destroyed or endangered will provide an incentive to other scientists to undertake different research in order to derive new stem cell lines. Even if plaintiffs' premise were accurate, it would not bring stem cell research within the scope of the statute.

The premise is, in any event, not correct. The NIH Guidelines impose strict limitations on the stem cell lines that may be used in federally funded research. NIH funded research may use stem cell lines derived from human embryos only if the stem cell lines "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." JA 48. There is no reason to conclude that embryos donated for stem cell derivation would otherwise be implanted.[6]

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[6] Plaintiffs' theory of causation is attenuated in the extreme. Human embryonic stem cells have been, and would continue to be, derived from human embryos even in the absence of federal funding for embryonic stem cell research. Plaintiffs declare that NIH has approved two stem cell lines derived from embryos donated after the Guidelines were promulgated. Pl. Br. 27. But approval by NIH of a stem cell line does not suggest that embryos were donated because of the availability of government funding or that the stem cell lines were derived because of the availability of federal funding.

II. The District Court Correctly Rejected Plaintiffs' APA Claim Because NIH Implemented The President's Executive Order And Responded To Relevant Comments.

President Obama issued Executive Order No. 13,505 on March 9, 2009. *See* JA 493. The President stated that the purpose of the Order was to "remove . . . limitations" on the "authority of the Department of Health and Human Services, including the National Institutes of Health, to fund and conduct human embryonic stem cell research . . . ." JA 493, § 1. These "limitations" were the result of "Presidential actions," *ibid.*, — specifically, President Bush's policy that limited funding of human embryonic stem cell research to research that used stem cell lines that had been created before his policy was announced on August 9, 2001. *See* Exec. Order No. 13,435, 72 Fed. Reg. 34,591 (2007); Address to the Nation on Stem Cell Research From Crawford, Texas, 37 Weekly Comp. Pres. Doc. 1149 (Aug. 9, 2001).

The 2009 Executive Order removed these temporal limitations on the stem cell lines that could be used in federally funded human embryonic stem cell research, and noted the "broad agreement in the scientific community that [human embryonic stem cell] research should be supported by Federal funds." JA 493 § 1. To that end, the President 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." JA 493, § 2. The President further 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." JA 493, § 3.

The President thereby directed NIH to prepare guidance that would describe standards for the responsible conduct of federally funded human embryonic stem cell research. NIH was not free to disregard the Executive Order and to reimpose the limitations that the President had withdrawn. *See Bldg. & Constr. Trades Dep't, AFL-CIO* v. *Allbaugh*, 295 F.3d 28, 32 (D.C. Cir. 2002) ("[Executive Branch] officers are duty-bound to give effect to the policies embodied in the President's direction, to the extent allowed by the law."); *see also Sierra Club* v. *Costle*, 657 F.2d 298, 406 n.524 (D.C. Cir. 1981).

The 2009 Guidelines were issued to "implement Executive Order 13505." JA 44 (74 Fed. Reg. at 32,170). On April 23, 2009, NIH requested public comments on draft guidelines that would "implement Executive Order 13505," "establish policy and procedures under which NIH will fund research in this area, and [ ] help ensure that NIH-funded research in this area is ethically responsible, scientifically worthy, and conducted in accordance with applicable law." JA 495 (74 Fed. Reg. 18,578 (Apr. 23, 2009)). The draft guidelines stated that their scope was to "describe the

circumstances under which human embryonic stem cells are eligible for use in . . . NIH-funded research." JA 496 (74 Fed. Reg. at 18,579).

As the district court explained, NIH did not suggest in its notice of proposed rulemaking that it was free to depart from the President's directive and did not seek comments on the wisdom of such a course. The Executive Order was not "an invitation from President Obama to adopt a policy even more restrictive than his predecessor's by categorically prohibiting funding for any embryonic stem cell research projects." JA 690 (emphasis removed). The district court recognized that "the fundamental policy question of whether to provide federal funds for embryonic stem cell research wasn't a question for [NIH] to decide." JA 691. That question had been answered by "three Presidential administrations" that all determined "to permit federal funding." *Ibid.*

Plaintiffs concede that NIH was bound to issue guidelines in line with the Executive Order, *see* Pl. Br. 52, and the proposed guidelines were thus limited to examining "the circumstances under which human embryonic stem cells are eligible for use" in NIH-funded research. JA 496 (74 Fed. Reg. at 18,579).

NIH received "approximately 49,000 comments," JA 44 (74 Fed. Reg. at 32,170), and responded appropriately to comments that were relevant to establishing

the policies and procedures under which NIH would fund human embryonic stem cell research. *See* JA 44-48 (74 Fed. Reg. at 32,170-74). The agency fully discharged its obligation to respond to comments that were "relevant to the agency's decision and which, if adopted, would require a change in an agency's proposed rule." *Home Box Office, Inc.* v. *FCC*, 567 F.2d 9, 35 n.58 (D.C. Cir. 1977). This requirement is not "particularly demanding," *Pub. Citizen, Inc.* v. *FAA*, 988 F.2d 186, 197 (D.C. Cir. 1993), and "[t]he failure to respond to comments is significant only insofar as it demonstrates that the agency's decision was not based on a consideration of the relevant factors," *Covad Commc'ns Co.* v. *FCC*, 450 F.3d 528, 550 (D.C. Cir. 2006) (internal quotations omitted). *See also Nat'l Mining Ass'n* v. *Mine Safety & Health Admin.,* 116 F.3d 520, 549 (D.C. Cir. 1997) (upholding agency's reasonable rejection of comments that were outside the scope of the rulemaking).

The district court correctly reasoned that "NIH's notice of proposed rulemaking did not invite (and therefore the NIH wasn't obligated to respond to) comments on the topic of whether to fund human embryonic stem cell research[.]" The Executive Order "required the promulgation of Guidelines for funding embryonic stem cell research, and the NIH wasn't obligated to consider comments

that, if adopted, would cause it to disobey the President and create an unlawful rule." JA 687 (emphasis removed).

The Executive Order did not, of course, determine whether any research proposal had scientific merit and should be approved. The Order noted that it could not be construed "to impair or otherwise affect" the statutory scheme under which the merits of individual research proposals must be decided on an application-by-application basis by expert reviewers. JA 493, § 4(b); *see also* 42 U.S.C. §§ 282(b)(9), 284a(a)(3), 289a, 289a-1(a)(2). Those procedures are established for the express purpose of ensuring that scientifically unworthy or poorly designed research proposals will not receive federal funding. The Executive Order removed previous constraints that prohibited NIH from considering the scientific merit of proposals that involved the use of certain stem cell lines. With those constraints lifted, NIH is obliged to consider proposals in accordance with the governing statutory regime. That regime did not contemplate that NIH decide the merits of a class of proposals through rulemaking.

Plaintiffs observe that the Executive Order did not remove the agency's obligation to comply with the APA. Pl. Br. 54-55. The APA does not establish the subject matter of a rulemaking, however, and does not require an agency to respond

to comments that do not bear on the issue posed by a proposed rule. JA 687-88. NIH responded to comments that addressed the substance of the proposed informed consent procedures, *see* JA 44-48 (74 Fed. Reg. at 32,170-74), and was not required to address comments regarding the scientific merits of human embryonic stem cell research generally.

Plaintiffs are on no firmer ground in declaring that Acting NIH Director Kington was predisposed toward federal funding for human embryonic stem cell research. Pl. Br. 48. The President had already made the determination to fund such research and no predisposition of the Acting Director could properly alter that determination.

In any event, the comment attributed to the Acting Director in a newspaper noted only that the number of cell lines eligible for funding would increase. As the district court observed, the comment "merely states the obvious." JA 691-92. It was common knowledge that many additional stem cell lines were created after President Bush's proclamation, *see, e.g.,* JA 464 (Declaration of Dr. Story Landis, ¶ 14), and that those lines would now be eligible for review under the processes established by the Guidelines.

CONCLUSION

For the foregoing reasons, the judgment of the district court should be affirmed.

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CERTIFICATE OF COMPLIANCE

Pursuant to Rule 32(a)(7)(C) of the Federal Rules of Appellate Procedure, I hereby certify that this brief complies with the type-volume limitation in Rule 32(a)(7)(B). The foregoing brief is presented in proportionally-spaced font typeface using Corel WordPerfect X4 in 14-point Garamond font. The brief, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii), contains 11,599 words, as counted by Corel WordPerfect X5.

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CERTIFICATE OF SERVICE

I hereby certify that on February 27, 2012, I filed and served the foregoing Brief for Appellees by using the CM/ECF system. I also hereby certify that I will have eight copies hand delivered to the Court within two business days.

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