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HOUSE OF REPRESENTATIVES
REPORT
116–513

NATIONAL CENTERS OF EXCELLENCE IN CONTINUOUS PHARMACEUTICAL MANUFACTURING ACT OF 2020

SEPTEMBER 17, 2020.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. PALLONE, from the Committee on Energy and Commerce, submitted the following

R E P O R T

[To accompany H.R. 4866]

The Committee on Energy and Commerce, to whom was referred the bill (H.R. 4866) to amend the 21st Century Cures Act to provide for designation of institutions of higher education that provide research, data, and leadership on continuous manufacturing as National Centers of Excellence in Continuous Pharmaceutical Manufacturing, and for other purposes, having considered the same, reports favorably thereon with an amendment and recommends that the bill as amended do pass.

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The amendment is as follows:

Strike all after the enacting clause and insert the following:

SECTION 1. SHORT TITLE.

This Act may be cited as the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2020".

SEC. 2. NATIONAL CENTERS OF EXCELLENCE IN CONTINUOUS PHARMACEUTICAL MANUFACTURING.

(a) IN GENERAL.—Section 3016 of the 21st Century Cures Act (21 U.S.C. 399h) is amended to read as follows:

"SEC. 3016. NATIONAL CENTERS OF EXCELLENCE IN CONTINUOUS PHARMACEUTICAL MANUFACTURING.

"(a) IN GENERAL.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs—

"(1) shall solicit and, beginning not later than one year after the date of enactment of the National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2020, receive requests from institutions of higher education to be designated as a National Center of Excellence in Continuous Pharmaceutical Manufacturing (in this section referred to as a 'National Center of Excellence') to support the advancement and development of continuous manufacturing; and

"(2) shall so designate any institution of higher education that—

"(A) requests such designation; and

"(B) meets the criteria specified in subsection (c).

"(b) REQUEST FOR DESIGNATION.—A request for designation under subsection (a) shall be made to the Secretary at such time, in such manner, and containing such information as the Secretary may require. Any such request shall include a description of how the institution of higher education meets or plans to meet each of the criteria specified in subsection (c).

"(c) CRITERIA FOR DESIGNATION DESCRIBED.—The criteria specified in this subsection with respect to an institution of higher education are that the institution has, as of the date of the submission of a request under subsection (a) by such institution—

"(1) physical and technical capacity for research and development of continuous manufacturing;

"(2) manufacturing knowledge-sharing networks with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other entities;

"(3) proven capacity to design and demonstrate new, highly effective technology for use in continuous manufacturing;

"(4) a track record for creating and transferring knowledge with respect to continuous manufacturing;

"(5) the potential to train a future workforce for research on and implementation of advanced manufacturing and continuous manufacturing; and

"(6) experience in participating in and leading a continuous manufacturing technology partnership with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other entities—

"(A) to support companies with continuous manufacturing in the United States;

"(B) to support Federal agencies with technical assistance, which may include regulatory and quality metric guidance as applicable, for advanced manufacturing and continuous manufacturing;

"(C) with respect to continuous manufacturing, to organize and conduct research and development activities needed to create new and more effective technology, capture and disseminate expertise, create intellectual property, and maintain technological leadership;

"(D) to develop best practices for designing continuous manufacturing; and

"(E) to assess and respond to the workforce needs for continuous manufacturing, including the development of training programs if needed.

"(d) TERMINATION OF DESIGNATION.—The Secretary may terminate the designation of any National Center of Excellence designated under this section if the Secretary determines such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later than 60 days before the effective date of such a termination, the Secretary shall provide written notice to the National Center of Excellence, including the rationale for such termination.

"(e) CONDITIONS FOR DESIGNATION.—As a condition of designation as a National Center of Excellence under this section, the Secretary shall require that an institution of higher education enter into an agreement with the Secretary under which the institution agrees—

"(1) to collaborate directly with the Food and Drug Administration to publish the reports required by subsection (g);

"(2) to share data with the Food and Drug Administration regarding best practices and research generated through the funding under subsection (f);

"(3) to develop, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers) and another institution or institutions designated under this section, if any, a roadmap for developing a continuous manufacturing workforce;

"(4) to develop, along with industry partners and other institutions designated under this section, a roadmap for strengthening existing, and developing new, relationships with other institutions; and

"(5) to provide an annual report to the Food and Drug Administration regarding the institution's activities under this section, including a description of how the institution continues to meet and make progress on the criteria listed in subsection (c).

"(f) FUNDING.—

"(1) IN GENERAL.—The Secretary shall award funding, through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated under this section for the purpose of studying and recommending improvements to continuous manufacturing, including such improvements as may enable the Centers—

"(A) to continue to meet the conditions specified in subsection (e); and

"(B) to expand capacity for research on, and development of, continuing manufacturing.

"(2) CONSISTENCY WITH FDA MISSION.—As a condition on receipt of funding under this subsection, a National Center of Excellence shall agree to consider any input from the Secretary regarding the use of funding that would—

"(A) help to further the advancement of continuous manufacturing through the National Center of Excellence; and

"(B) be relevant to the mission of the Food and Drug Administration.

"(3) AUTHORIZATION OF APPROPRIATIONS.—There is authorized to be appropriated to carry out this subsection $80,000,000 for the period of fiscal years 2021 through 2025.

"(4) RULE OF CONSTRUCTION.—Nothing in this section shall be construed as precluding a National Center for Excellence designated under this section from receiving funds under any other provision of this Act or any other Federal law.

"(g) ANNUAL REVIEW AND REPORTS.—

"(1) ANNUAL REPORT.—Beginning not later than one year after the date on which the first designation is made under subsection (a), and annually thereafter, the Secretary shall—

"(A) submit to Congress a report describing the activities, partnerships and collaborations, Federal policy recommendations, previous and continuing funding, and findings of, and any other applicable information from, the National Centers of Excellence designated under this section; and

"(B) make such report available to the public in an easily accessible electronic format on the website of the Food and Drug Administration.

"(2) REVIEW OF NATIONAL CENTERS OF EXCELLENCE AND POTENTIAL DESIGNEES.—The Secretary shall periodically review the National Centers of Excellence designated under this section to ensure that such National Centers of Excellence continue to meet the criteria for designation under this section.

"(3) REPORT ON LONG-TERM VISION OF FDA ROLE.—Not later than 2 years after the date on which the first designation is made under subsection (a), the Secretary, in consultation with the National Centers of Excellence designated under this section, shall submit a report to the Congress on the long-term vision of the Department of Health and Human Services on the role of the Food and Drug Administration in supporting continuous manufacturing, including—

"(A) a national framework of principles related to the implementation and regulation of continuous manufacturing;

"(B) a plan for the development of Federal regulations and guidance for how advanced manufacturing and continuous manufacturing can be incorporated into the development of pharmaceuticals and regulatory responsibilities of the Food and Drug Administration; and

"(C) appropriate feedback solicited from the public, which may include other institutions, large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers.

"(h) DEFINITIONS.—In this section:

"(1) ADVANCED MANUFACTURING.—The term 'advanced manufacturing' means an approach for the manufacturing of pharmaceuticals that incorporates novel

technology, or uses an established technique or technology in a new or innovative way (such as continuous manufacturing where the input materials are continuously transformed within the process by two or more unit operations) that enhances drug quality or improves the manufacturing process.

"(2) CONTINUOUS MANUFACTURING.—The term 'continuous manufacturing'—

"(A) means a process where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and

"(B) consists of an integrated process that consists of a series of two or more unit operations.

"(3) INSTITUTION OF HIGHER EDUCATION.—The term 'institution of higher education' has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).

"(4) SECRETARY.—The term 'Secretary' means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.".

(b) TRANSITION RULE.—Section 3016 of the 21st Century Cures Act (21 U.S.C. 399h), as in effect on the day before the date of the enactment of this section, shall apply with respect to grants awarded under such section before such date of enactment.

I. PURPOSE AND SUMMARY

H.R. 4866, the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2020", was introduced on October 28, 2019, by Committee Chairman Frank Pallone, Jr. (D–NJ) and Representative Brett Guthrie (R–KY) and the bill was referred to the Committee on Energy and Commerce. H.R. 4866 amends the 21st Century Cures Act to provide the Food and Drug Administration (FDA) with the authority to designate institutions of higher education that provide research, data, and leadership on continuous manufacturing for pharmaceuticals as National Centers of Excellence in Continuous Pharmaceutical Manufacturing. As defined by the bill, continuous manufacturing (CM) is a "process where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system" and "consists of an integrated process that consists of a series of two or more unit operations."

According to testimony before the Committee from Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research at FDA, advanced manufacturing, such as CM, "can be used to reduce the Nation's dependence on foreign sources of APIs [active pharmaceutical ingredients], increase the resilience of our domestic manufacturing base, and reduce quality issues that trigger drug shortages or recalls."[1] Within the last decade, the pharmaceutical industry has begun to move towards CM methods because it has been "shown to greatly reduce both the time and the cost of developing and manufacturing new medicines, while enabling significant improvements in the quality of the final product and the reliability of the manufacturing process."[2] However, despite this potential, CM has not yet been widely adopted by industry.

The legislation would support the advancement and development of CM by employing institutions of higher education to study and recommend improvements to CM, including a roadmap for developing a continuous manufacturing workforce, sharing data with

[1] House Committee on Energy and Commerce, Testimony of Janet Woodcock (Oct. 30, 2019) (energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/Testimony-Woodcock-API_103019).

[2] House Committee on Energy and Commerce, Testimony of Fernando J. Muzzio (Jan. 29, 2019) (docs.house.gov/meetings/IF/IF14/20200129/110423/HHRG-116-IF14-Wstate-MuzzioF-20200129.pdf).

FDA regarding best practices and research generated, and collaborating with FDA on a report to Congress regarding the role of FDA in supporting CM. This report should include a national framework of principles related to the implementation and regulation of CM and a plan for the development of regulations and guidance for how CM can be incorporated into drug development and FDA's regulatory responsibilities.

II. Background and Need for Legislation

Traditionally, pharmaceutical drugs are manufactured using "batch manufacturing." Batch manufacturing requires raw materials to be loaded into equipment and then undergo a series of lengthy steps, with quality testing of samples occurring after each step in the process.[3] CM, on the other hand, moves raw materials through a single system that incorporates monitoring and controls throughout the process.[4] According to FDA, which regulates drug development, CM "provides a quicker, more reliable way to make pharmaceuticals."[5] This is due to shorter processing times, real-time product quality assurance, and the removal of manual handling.[6] Shorter processing times with real-time quality assurance allows manufacturers to respond quickly to emergencies, address shortages, or defective products.[7]

CM also relies on smaller equipment, which reduces capital and inventory costs and allows for a smaller footprint.[8] Because of this, as well as the ability to achieve higher yields and rely on less direct labor than traditional pharmaceutical manufacturing, CM can directly affect the cost of drugs.[9] As the Committee heard at a hearing in March 2020 from Dr. Fernando Muzzio, distinguished professor of chemical and biochemical engineering and Director of the NSF Engineering Research Center on Structured Organic Particulate Systems at Rutgers University, because CM products and their manufacturing processes can be developed faster than batch manufacturing, these products can also reach the market faster, which could increase competition in the pharmaceutical industry and "contribute to lower drug prices to the U.S. consumer."[10] Further, in testimony before the Committee, Dr. Woodcock noted advanced manufacturing technologies, such as CM, "could enable U.S.-based pharmaceutical manufacturing to regain its competitiveness with China and other foreign countries, and potentially ensure a stable supply of drugs critical to the health of U.S. patients."[11]

Because of these potential benefits, the Committee has supported increased Federal investment into advanced manufacturing and CM. In the 21st Century Cures Act (P.L. 114–255), the Committee

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[3] U.S. Food and Drug Administration, *Modernizing the Way Drugs Are Made: A Transition to Continuous Manufacturing* (May 17, 2017) (www.fda.gov/drugs/news-events-human-drugs/modernizing-way-drugs-are-made-transition-continuous-manufacturing).

[4] U.S. Food and Drug Administration, Emergency Preparedness and Response, Counterterrorism and Emerging Threats, Medical Countermeasures Initiative (MCMi), MCM Issues, Advanced Manufacturing (www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing).

[5] *Id.*

[6] U.S. Food and Drug Administration, *FDA Perspective on Continuous Manufacturing* (Jan. 2012) (www.fda.gov/media/85366/download).

[7] *See* note 2.

[8] *See* note 6.

[9] *See* note 2.

[10] *Id.*

[11] *See* note 1.

authorized a grant program through the FDA to study and make recommendations for improvements to the process of CM of drugs and biological products, as well as similar innovative monitoring and control techniques.[12] Grants were to be awarded to institutions of higher education and non-profits, and since enactment, FDA has made eight such awards.[13] However, as of July 2020, only nine drug applications have been approved by FDA using advanced manufacturing technologies, with eight drugs relying on CM, and one utilizing 3-D printing.[14] Slow adoption of advanced manufacturing and CM is one reason why additional Federal support is necessary.

H.R. 4866, the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2020", would amend the 21st Century Cures Act to establish a program designating institutions of higher education as National Centers of Excellence in Continuous Pharmaceutical Manufacturing. Within one year of enactment of H.R. 4866, the FDA shall solicit and receive designation requests from institutions of higher education. To request a designation, institutions must meet the following criteria at the time of designation: (1) physical and technical capacity for research and development of CM; (2) manufacturing knowledge-sharing networks with other institutions of higher education, manufacturers, and other entities; (3) proven capacity to design and demonstrate new, highly effective technology for use in CM; (4) a track record for creating and transferring knowledge with respect to CM; (5) the potential to train a future workforce for research on and implementation of advanced manufacturing and CM; and (6) experience in participating in and leading a CM technology partnership with other institutions of higher education, manufacturers (large, small, generic, nonprescription, and contract), and other entities to support companies with CM in the United States: to support Federal agencies with technical assistance, which may include regulatory and quality metric guidance, as applicable, for advanced manufacturing and CM; with respect to CM, to organize and conduct research and development activities needed to create new and more effective technology, capture and disseminate expertise, create intellectual property, and maintain technology leadership; to develop best practices for designing CM; and to assess and respond to the workforce needs for CM, including the development of training programs if needed. FDA is granted authority to terminate the designation if it is determined that an institution no longer meets the criteria above following written notice to the institution and a rationale for such termination.

As a condition of designation, FDA shall require that an institution of higher education enter into an agreement under which the institution agrees to collaborate with FDA to publish the reports required under H.R. 4866, share data with FDA regarding best practices and research generated through funding of the Center, develop a roadmap for developing a CM workforce and for strengthening existing and new relationships with other institutions, and

[12] Pub. L. No. 114–255, Sec. 3016 (2016) (www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf).
[13] *See* note 4.
[14] Email from Staff, U.S. Food and Drug Administration, to Majority Staff, House Committee on Energy and Commerce (July 27, 2020).

provide an annual report to FDA regarding the institution's activities. FDA shall award funding through grants, contracts, or cooperative agreements, and is authorized $80 million for the period of fiscal years (FY) 2021 through 2025. As a condition of receipt of funding, a designated institution shall agree to input from FDA to ensure such funding help furthers the advancement of CM and is relevant to the mission of FDA.

No later than one year after the first designation of a Center of Excellence for Continuous Pharmaceutical Manufacturing, FDA shall submit to Congress an annual report describing the activities, partnerships, collaborations, policy recommendations, previous and continued funding, and findings of the Centers. Such report shall be made publicly available. FDA is also required to periodically review designated Centers to ensure that such Centers continue to meet the criteria for designation. Within two years of the first designation, the Secretary of the Department of Health and Human Services (HHS), in consultation with the National Centers of Excellence, shall submit to Congress a report on the long-term vision of HHS on the role of the FDA in supporting CM, including a national framework of principles related to the implementation and regulation of CM, a plan for the development of Federal regulations and guidance for how advanced manufacturing and CM can be incorporated into the development of drugs and regulatory responsibilities of FDA, and appropriate public feedback.

III. COMMITTEE HEARINGS

For the purposes of section 103(i) of H. Res. 6 of the 116th Congress, the following hearing was used to develop or consider H.R. 4866:

The Subcommittee on Health held a legislative hearing on January 29, 2020, entitled "Improving Safety and Transparency in America's Food and Drugs" to consider H.R. 4866, the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2019", among other legislation. The Subcommittee received testimony from the following witnesses:

Panel I:

- Jeff Allen, Ph.D, President and CEO, Friends of Cancer Research;
- Richard Kaeser, Vice President, Global Brand Protection, Johnson & Johnson;
- Fernando Muzzio, Ph.D., Distinguished Professor, Chemical and Biochemical Engineering, Rutgers, the State University of New Jersey; and
- Kao-Ping Chua, M.D., Ph.D., Assistant Professor, Department of Pediatrics University of Michigan Medical School.

Panel II:

- Melanie Benesh, Legislative Attorney, Environmental Working Group;
- Tom Balmer, Executive Vice President, National Milk Producers Federation;
- J. David Carlin, Senior Vice President of Legislative Affairs and Economic Policy, International Dairy Foods Association;
- Douglas Corey, D.V.M., Past President, American Association of Equine Practitioners;

- Talia Day, Patient Advocate;
- Paul C. DeLeo, Ph.D., Principal, Integral Consulting, Inc.;
- Mardi Mountford, President, Infant Nutrition Council of America;
- Nancy Perry, Senior Vice President, Government Relations, American Society for the Prevention of Cruelty to Animals; and
- Sara Sorscher, Deputy Director of Regulatory Affairs, Center for Science in the Public Interest.

IV. COMMITTEE CONSIDERATION

Representatives Pallone (D–NJ) and Guthrie (R–KY) introduced H.R. 4866, the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2019", on October 28, 2019, and the bill was referred to the Committee on Energy and Commerce. Subsequently, H.R. 4866 was referred to the Subcommittee on Health on October 29, 2019. A legislative hearing was held on the bill on January 29, 2020.

On March 11, 2020, the Subcommittee on Health met in open markup session, pursuant to notice, to consider H.R. 4866. During consideration of the bill, a manager's amendment offered by Mr. Pallone was agreed to by a voice vote. Subsequently, the Subcommittee on Health agreed by a voice vote to a motion by Ms. Eshoo, Chairwoman of the subcommittee, to forward favorably H.R. 4866, amended, to the full Committee on Energy and Commerce.

On July 15, 2020, the full Committee met in virtual open markup session, pursuant to notice, to consider a committee print of the bill H.R. 4866, as amended by the Subcommittee on Health on March 11, 2020. There were no amendments offered to the committee print of H.R. 4866. Upon conclusion of consideration of the bill, the full Committee agreed to a motion on final passage by Mr. Pallone, Chairman of the committee, to order H.R. 4866 reported favorably to the House, as amended, by a voice vote, a quorum being present.

V. COMMITTEE VOTES

Clause 3(b) of rule XIII of the Rules of the House of Representatives requires the Committee to list each record vote on the motion to report legislation and amendments thereto. The Committee advises that there were no record votes taken on H.R. 4866, including the motion for final passage of the bill.

VI. OVERSIGHT FINDINGS

Pursuant to clause 3(c)(1) of rule XIII and clause 2(b)(1) of rule X of the Rules of the House of Representatives, the oversight findings and recommendations of the Committee are reflected in the descriptive portion of the report.

VII. NEW BUDGET AUTHORITY, ENTITLEMENT AUTHORITY, AND TAX EXPENDITURES

Pursuant to 3(c)(2) of rule XIII of the Rules of the House of Representatives, the Committee adopts as its own the estimate of new budget authority, entitlement authority, or tax expenditures or rev-

enues contained in the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

The Committee has requested but not received from the Director of the Congressional Budget Office a statement as to whether this bill contains any new budget authority, spending authority, credit authority, or an increase or decrease in revenues or tax expenditures.

VIII. Federal Mandates Statement

The Committee adopts as its own the estimate of Federal mandates prepared by the Director of the Congressional Budget Office pursuant to section 423 of the Unfunded Mandates Reform Act.

IX. Statement of General Performance Goals and Objectives

Pursuant to clause 3(c)(4) of rule XIII, the general performance goal or objective of this legislation is to support the advancement and development of continuous manufacturing through the designation of institutions of higher education as National Centers of Excellence in Pharmaceutical Manufacturing, which will provide research, data, and leadership on continuous manufacturing.

X. Duplication of Federal Programs

Pursuant to clause 3(c)(5) of rule XIII, no provision of H.R. 4866 is known to be duplicative of another Federal program, including any program that was included in a report to Congress pursuant to section 21 of Public Law 111–139 or the most recent Catalog of Federal Domestic Assistance.

XI. Committee Cost Estimate

Pursuant to clause 3(d)(1) of rule XIII, the Committee adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

XII. Earmarks, Limited Tax Benefits, and Limited Tariff Benefits

Pursuant to clause 9(e), 9(f), and 9(g) of rule XXI, the Committee finds that H.R. 4866 contains no earmarks, limited tax benefits, or limited tariff benefits.

XIII. Advisory Committee Statement

No advisory committee within the meaning of section 5(b) of the Federal Advisory Committee Act was created by this legislation.

XIV. Applicability to Legislative Branch

The Committee finds that the legislation does not relate to the terms and conditions of employment or access to public services or accommodations within the meaning of section 102(b)(3) of the Congressional Accountability Act.

XV. SECTION BY SECTION ANALYSIS OF THE LEGISLATION

Section 1. Short title

Section 1 designates that the short title may be cited as the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2020".

Sec. 2. National Centers of Excellence in Continuous Pharmaceutical Manufacturing

Section 2 amends section 3016 of the 21st Century Cures Act to establish the National Centers of Excellence in Continuous Pharmaceutical Manufacturing program. Subsection (a) of the amended section 3016 requires within one year of enactment that the Secretary of HHS, acting through the Commissioner of Food and Drugs, solicit and receive requests from institutions of higher education to be designated as a National Center of Excellence in Continuous Pharmaceutical Manufacturing (referred to as a 'National Center of Excellence') to support the advancement and development of continuous manufacturing (CM). FDA shall designate any institution of higher education that requests such designation and meets the criteria identified.

Subsection (b) of the amended section 3016 requires designation requests to be made at such time, in such manner, and containing such information as FDA may require. Any request shall include a description of how the institution of higher education meets or plans to meet each of the criteria identified.

Subsection (c) of the amended section 3016 describes the criteria that an institution of higher education should have at the date of submission of a designation request. This shall include: (1) physical and technical capacity for research and development of CM; (2) manufacturing knowledge-sharing networks with other institutions of higher education, manufacturers (large, small, generic, nonprescription, and contract), and other entities; (3) proven capacity to design and demonstrate new, highly effective technology for use in CM; (4) a track record for creating and transferring knowledge with respect to CM; (5) the potential to train a future workforce for research on and implementation of advanced manufacturing and CM; and (6) experience in participating in and leading a CM technology partnership with other institutions of higher education, manufacturers (large, small, generic, nonprescription, and contract), and other entities to support companies with CM in the United States: to support Federal agencies with technical assistance, which may include regulatory and quality metric guidance, as applicable, for advanced manufacturing and CM; with respect to CM, to organize and conduct research and development activities needed to create new and more effective technology, capture and disseminate expertise, create intellectual property, and maintain technology leadership; to develop best practices for designing CM; and to assess and respond to the workforce needs for CM, including the development of training programs if needed.

Subsection (d) of the amended section 3016 grants FDA the authority to terminate the designation of any National Center of Excellence designated if it is determined that such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later than 60 days before the effective date of such termi-

nation, FDA shall provide written notice to the institution and a rationale for such termination.

Subsection (e) of the amended section 3016 specifies that as a condition of designation, FDA shall require that an institution of higher education enter into an agreement under which the institution agrees to collaborate with FDA to publish the reports required under subsection (g), share data with FDA regarding best practices and research generated through funding under subsection (f), develop a roadmap, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers) and other designated institutions for developing a CM workforce, to develop, along with industry partners and other designated institutions, a roadmap for strengthening existing and new relationships with other institutions, and to provide an annual report to FDA regarding the institution's activities, including how the institution continues to meet and make progress on the criteria listed in subsection (c).

Subsection (f) of the amended section 3016 requires FDA to award funding through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated for the purpose of studying and recommending improvements to CM, including such improvements as may enable the Centers to continue to meet the conditions specified in subsection (e) and to expand capacity for research on, and development of, CM. As a condition of receipt of funding, a designated institution shall agree to consider any input from FDA to ensure such funding help further the advancement of CM through the National Center of Excellence and is relevant to the mission of FDA. There is authorized to be appropriated to carry out the activities $80 million for the period of fiscal years 2021 through 2025. Nothing in this section shall be construed as precluding a designated National Center of Excellence from receiving funds under any other provision of H.R. 4866 or any other Federal law.

Subsection (g) of the amended section 3016 requires that not later than one year after the first designation of a National Center of Excellence, FDA shall submit to Congress an annual report describing the activities, partnerships, collaborations, Federal policy recommendations, previous and continued funding, and findings of, and any other applicable information from, the designated National Centers of Excellence. Such report shall be made publicly available on the website of the FDA. FDA is also required to periodically review designated National Centers of Excellence to ensure that such centers continue to meet the criteria for designation. Within two years of the first designation, the Secretary of HHS, in consultation with the National Centers of Excellence, shall submit to Congress a report on the long-term vision of HHS on the role of the FDA in supporting CM, including a national framework of principles related to the implementation and regulation of CM, a plan for the development of Federal regulations and guidance for how advanced manufacturing and CM can be incorporated into the development of drugs and regulatory responsibilities of FDA, and appropriate feedback solicited from the public, which may include other institutions and manufacturers (large, small, generic, nonprescription, and contract).

Subsection (h) of the amended section 3016 defines relevant terms in H.R. 4866 including "advanced manufacturing", "continuous manufacturing", "institution of higher education", and "Secretary". As defined in H.R. 4866, the term "advanced manufacturing" means an approach for the manufacturing of pharmaceuticals that incorporates novel technology, or uses an established technique or technology in a new or innovative way (such as continuous manufacturing where the input materials are continuously transformed within the process by two or more unit operations) that enhances drug quality or improves the manufacturing process. The term "continuous manufacturing", as defined in H.R. 4866, means a process where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and consists of an integrated process that consists of a series of two or more unit operations. The term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)). The term "Secretary", as defined in H.R. 4866, means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.

Section 2 also clarifies that section 3016 of the 21st Century Cures Act, as in effect on the day before the date of the enactment of this section, shall apply with respect to grants awarded under this section before such date of enactment.

XVI. CHANGES IN EXISTING LAW MADE BY THE BILL, AS REPORTED

In compliance with clause 3(e) of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italics, and existing law in which no change is proposed is shown in roman):

21ST CENTURY CURES ACT

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DIVISION A—21ST CENTURY CURES

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TITLE III—DEVELOPMENT

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Subtitle B—Advancing New Drug Therapies

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[SEC. 3016. GRANTS FOR STUDYING CONTINUOUS DRUG MANUFACTURING.

[(a) IN GENERAL.—The Secretary of Health and Human Services may award grants to institutions of higher education and nonprofit

organizations for the purpose of studying and recommending improvements to the process of continuous manufacturing of drugs and biological products and similar innovative monitoring and control techniques.

[(b) DEFINITIONS.—In this section—

[(1) the term "drug" has the meaning given such term in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321);

[(2) the term "biological product" has the meaning given such term in section 351(i) of the Public Health Service Act (42 U.S.C. 262(i)); and

[(3) the term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).]

SEC. 3016. NATIONAL CENTERS OF EXCELLENCE IN CONTINUOUS PHARMACEUTICAL MANUFACTURING.

(a) IN GENERAL.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs—

(1) shall solicit and, beginning not later than one year after the date of enactment of the National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2019, receive requests from institutions of higher education to be designated as a National Center of Excellence in Continuous Pharmaceutical Manufacturing (in this section referred to as a "National Center of Excellence") to support the advancement and development of continuous manufacturing; and

(2) shall so designate any institution of higher education that—

(A) requests such designation; and

(B) meets the criteria specified in subsection (c).

(b) REQUEST FOR DESIGNATION.—A request for designation under subsection (a) shall be made to the Secretary at such time, in such manner, and containing such information as the Secretary may require. Any such request shall include a description of how the institution of higher education meets or plans to meet each of the criteria specified in subsection (c).

(c) CRITERIA FOR DESIGNATION DESCRIBED.—The criteria specified in this subsection with respect to an institution of higher education are that the institution has, as of the date of the submission of a request under subsection (a) by such institution—

(1) physical and technical capacity for research and development of continuous manufacturing;

(2) manufacturing knowledge-sharing networks with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other entities;

(3) proven capacity to design and demonstrate new, highly effective technology for use in continuous manufacturing;

(4) a track record for creating and transferring knowledge with respect to continuous manufacturing;

(5) the potential to train a future workforce for research on and implementation of advanced manufacturing and continuous manufacturing; and

(6) experience in participating in and leading a continuous manufacturing technology partnership with other institutions of

higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other entities—

(A) to support companies with continuous manufacturing in the United States;

(B) to support Federal agencies with technical assistance, which may include regulatory and quality metric guidance as applicable, for advanced manufacturing and continuous manufacturing;

(C) with respect to continuous manufacturing, to organize and conduct research and development activities needed to create new and more effective technology, capture and disseminate expertise, create intellectual property, and maintain technological leadership;

(D) to develop best practices for designing continuous manufacturing; and

(E) to assess and respond to the workforce needs for continuous manufacturing, including the development of training programs if needed.

(d) TERMINATION OF DESIGNATION.—The Secretary may terminate the designation of any National Center of Excellence designated under this section if the Secretary determines such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later than 60 days before the effective date of such a termination, the Secretary shall provide written notice to the National Center of Excellence, including the rationale for such termination.

(e) CONDITIONS FOR DESIGNATION.—As a condition of designation as a National Center of Excellence under this section, the Secretary shall require that an institution of higher education enter into an agreement with the Secretary under which the institution agrees—

(1) to collaborate directly with the Food and Drug Administration to publish the reports required by subsection (g);

(2) to share data with the Food and Drug Administration regarding best practices and research generated through the funding under subsection (f);

(3) to develop, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers) and another institution or institutions designated under this section, if any, a roadmap for developing a continuous manufacturing workforce;

(4) to develop, along with industry partners and other institutions designated under this section, a roadmap for strengthening existing, and developing new, relationships with other institutions; and

(5) to provide an annual report to the Food and Drug Administration regarding the institution's activities under this section, including a description of how the institution continues to meet and make progress on the criteria listed in subsection (c).

(f) FUNDING.—

(1) IN GENERAL.—The Secretary shall award funding, through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated under this section for the purpose of studying and recommending improvements to

continuous manufacturing, including such improvements as may enable the Centers—

(A) to continue to meet the conditions specified in subsection (e); and

(B) to expand capacity for research on, and development of, continuing manufacturing.

(2) CONSISTENCY WITH FDA MISSION.—As a condition on receipt of funding under this subsection, a National Center of Excellence shall agree to consider any input from the Secretary regarding the use of funding that would—

(A) help to further the advancement of continuous manufacturing through the National Center of Excellence; and

(B) be relevant to the mission of the Food and Drug Administration.

(3) AUTHORIZATION OF APPROPRIATIONS.—There is authorized to be appropriated to carry out this subsection $80,000,000 for the period of fiscal years 2021 through 2025.

(4) RULE OF CONSTRUCTION.—Nothing in this section shall be construed as precluding a National Center for Excellence designated under this section from receiving funds under any other provision of this Act or any other Federal law.

(g) ANNUAL REVIEW AND REPORTS.—

(1) ANNUAL REPORT.—Beginning not later than one year after the date on which the first designation is made under subsection (a), and annually thereafter, the Secretary shall—

(A) submit to Congress a report describing the activities, partnerships and collaborations, Federal policy recommendations, previous and continuing funding, and findings of, and any other applicable information from, the National Centers of Excellence designated under this section; and

(B) make such report available to the public in an easily accessible electronic format on the website of the Food and Drug Administration.

(2) REVIEW OF NATIONAL CENTERS OF EXCELLENCE AND POTENTIAL DESIGNEES.—The Secretary shall periodically review the National Centers of Excellence designated under this section to ensure that such National Centers of Excellence continue to meet the criteria for designation under this section.

(3) REPORT ON LONG-TERM VISION OF FDA ROLE.—Not later than 2 years after the date on which the first designation is made under subsection (a), the Secretary, in consultation with the National Centers of Excellence designated under this section, shall submit a report to the Congress on the long-term vision of the Department of Health and Human Services on the role of the Food and Drug Administration in supporting continuous manufacturing, including—

(A) a national framework of principles related to the implementation and regulation of continuous manufacturing;

(B) a plan for the development of Federal regulations and guidance for how advanced manufacturing and continuous manufacturing can be incorporated into the development of pharmaceuticals and regulatory responsibilities of the Food and Drug Administration; and

(C) appropriate feedback solicited from the public, which may include other institutions, large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers.

(h) DEFINITIONS.—In this section:

(1) ADVANCED MANUFACTURING.—The term "advanced manufacturing" means an approach for the manufacturing of pharmaceuticals that incorporates novel technology, or uses an established technique or technology in a new or innovative way (such as continuous manufacturing where the input materials are continuously transformed within the process by two or more unit operations) that enhances drug quality or improves the manufacturing process.

(2) CONTINUOUS MANUFACTURING.—The term "continuous manufacturing"—

(A) means a process where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and

(B) consists of an integrated process that consists of a series of two or more unit operations.

(3) INSTITUTION OF HIGHER EDUCATION.—The term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).

(4) SECRETARY.—The term "Secretary" means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.

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