

114TH CONGRESS
1ST SESSION

S. 1391

To increase research, education, and treatment for cerebral cavernous malformations.

IN THE SENATE OF THE UNITED STATES

MAY 20, 2015

Mr. UDALL (for himself and Mr. HEINRICH) introduced the following bill;
which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

A BILL

To increase research, education, and treatment for cerebral cavernous malformations.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Cerebral Cavernous
5 Malformations Clinical Awareness, Research, and Edu-
6 cation Act of 2015” or the “CCM–CARE Act”.

7 **SEC. 2. FINDINGS.**

8 Congress finds as follows:

9 (1) Cerebral cavernous malformations (referred
10 to in this section as “CCM”), also known as cav-

1 ernous angioma, or cavernoma, is a devastating
2 blood vessel disease characterized by vascular lesions
3 that develop and grow within the brain and spinal
4 cord.

5 (2) Detection of CCM lesions is achieved
6 through costly and specialized medical imaging tech-
7 niques, often not accessible or convenient to patients
8 who need them.

9 (3) While CCM is a common type of vascular
10 anomaly, many individuals are not aware they have
11 the disease until the onset of serious clinical symp-
12 toms. CCM is often inherited unknowingly.

13 (4) CCM affects an estimated 1,500,000 people
14 in the United States.

15 (5) Individuals diagnosed with CCM may expe-
16 rience neurological deficits, seizure, stroke, or sud-
17 den death.

18 (6) Due to limited research, there is currently
19 no treatment for CCM other than brain and spinal
20 surgery, and only for certain patients. There is also
21 a shortage of trained physicians to provide skilled
22 and timely diagnosis and appropriate treatment for
23 CCM.

24 (7) While the hereditary form of CCM may
25 occur among any ethnicity, the presence of a muta-

1 tion called the “common Hispanic mutation”, has
 2 passed through 17 or more generations of American
 3 descendants from the original Spanish settlers of the
 4 Southwest in the 1590s. New Mexico has the highest
 5 population density of CCM in the world; Texas, Ari-
 6 zona, and Colorado also have high rates of CCM due
 7 to the common Hispanic mutation.

8 **SEC. 3. EXPANSION AND COORDINATION OF ACTIVITIES OF**
 9 **NATIONAL INSTITUTES OF HEALTH WITH RE-**
 10 **SPECT TO CEREBRAL CAVERNOUS MAL-**
 11 **FORMATIONS RESEARCH.**

12 Part B of title IV of the Public Health Service Act
 13 (42 U.S.C. 284 et seq.) is amended by adding at the end
 14 the following:

15 **“SEC. 409K. CEREBRAL CAVERNOUS MALFORMATIONS RE-**
 16 **SEARCH ACTIVITIES.**

17 “(a) EXPANSION AND COORDINATION OF ACTIVI-
 18 TIES.—The Director of NIH, in coordination with the di-
 19 rectors of the National Institute of Neurological Disorders
 20 and Stroke, the National Center for Advancing
 21 Translational Sciences, the National Heart, Lung, and
 22 Blood Institute, and other national research institutes, as
 23 appropriate, for the purpose of conducting research and
 24 related activities concerning cerebral cavernous malforma-
 25 tions (referred to in this section as ‘CCM’)—

1 “(1) shall strengthen and coordinate efforts of
2 the National Institutes of Health; and

3 “(2) may award grants and cooperative agree-
4 ments to public or nonprofit private entities (includ-
5 ing State health departments, political subdivisions
6 of States, universities, and other medical or edu-
7 cational entities).

8 “(b) ACTIVITIES.—The research and related activi-
9 ties described in subsection (a) shall include the following:

10 “(1) BASIC, TRANSLATIONAL, AND CLINICAL
11 RESEARCH.—The Director of NIH shall conduct or
12 support, through funding opportunity announce-
13 ments, grants, or cooperative agreements, basic, clin-
14 ical, and translational research on CCM, including
15 research on—

16 “(A) proteomic, pharmacological, and cell
17 biological analysis of CCM molecules;

18 “(B) continued development and expansion
19 of novel animal models for preclinical research
20 relating to CCM;

21 “(C) early detection, diagnosis, and treat-
22 ment of CCM;

23 “(D) biological mechanisms for lesion gen-
24 esis, development, and maturation;

1 “(E) biological mechanisms for lesion
2 bleeding and symptomology;

3 “(F) novel biomedical and pharmacological
4 interventions designed to inhibit new lesion de-
5 velopment, lesion growth, and lesion bleeding;

6 “(G) pre-clinical and clinical research re-
7 lated to repurposing currently approved drugs
8 for treatment of CCM;

9 “(H) contributions of genetic variation to
10 clinical presentation as targets for therapy;

11 “(I) identification and development of bio-
12 markers to measure phenotypic variation;

13 “(J) research related to improving the
14 quality of life for individuals with CCM and
15 their families; and

16 “(K) clinical training programs aimed at
17 increasing the number of scientists and clini-
18 cians who are trained to treat patients and
19 carry out the research described in this para-
20 graph.

21 “(2) FACILITATION OF RESEARCH RESOURCES;
22 CLINICAL TRIAL PREPAREDNESS.—

23 “(A) IN GENERAL.—The Director of NIH
24 shall award grants and contracts to public or
25 nonprofit private entities to fund all or part of

1 the cost of planning, establishing, and providing
2 basic operating support for a network of CCM
3 Clinical Research Centers, including Coordinating and Participating centers regarding re-
4 search on various forms of CCM.
5

6 “(B) CLINICAL AND RESEARCH COORDINA-
7 TION CENTERS.—

8 “(i) IN GENERAL.—The Director of
9 NIH shall identify and support the devel-
10 opment of 3 geographically distributed na-
11 tional clinical and research coordinating
12 centers with unique clinical expertise and
13 the potential for coordinating multi-site
14 clinical drug trials with respect to CCM.

15 “(ii) DUTIES.—The coordinating cen-
16 ters identified under clause (i) shall pro-
17 vide a model for the participation centers
18 described in paragraph (3), facilitate med-
19 ical research to develop a cure for CCM,
20 and enhance the medical care of individ-
21 uals with CCM nationwide, including by—

22 “(I) maintaining an institutional
23 infrastructure capable of hosting clin-
24 ical trials and facilitating translational

1 research projects and collaborations
2 for clinical trials;

3 “(II) implementing the programs
4 dedicated to patient education, patient
5 outreach, and awareness developed by
6 the Cerebral Cavernous Malformations
7 Consortium under subsection
8 (c)(3)(B);

9 “(III) developing the capacity to
10 establish and maintain communication
11 with other major CCM research and
12 care institutions internationally for in-
13 formation sharing and coordination of
14 research activities;

15 “(IV) demonstrating clinical ex-
16 pertise in the management of CCM
17 and appointing a director and support
18 staff, including a trainee and patient
19 representative, for CCM research pro-
20 gramming;

21 “(V) treating a sufficient number
22 of eligible patients for participation
23 with particular focus on unique sub-
24 populations, such as patients with the
25 common Hispanic mutation, Ash-

1 kenazi Jewish mutation, or CCM3
2 gene mutation carriers; and

3 “(VI) maintaining a telehealth
4 infrastructure to support and provide
5 clinical consultation for remote and
6 underserved communities.

7 “(3) PARTICIPATION CENTERS.—

8 “(A) IN GENERAL.—The Director of NIH
9 shall identify and support the development of 6
10 to 10 clinical and research participation centers
11 to facilitate medical research to develop a cure
12 for CCM and enhance the medical care of indi-
13 viduals with CCM, in partnership with the co-
14 ordinating centers under paragraph (2) and
15 other national and international entities, as ap-
16 propriate.

17 “(B) ELIGIBILITY.—To qualify for selec-
18 tion as a participation center under subpara-
19 graph (A), an entity shall—

20 “(i) at the time of selection—

21 “(I) be affiliated with an estab-
22 lished research network of the Na-
23 tional Institutes of Health; and

1 “(II) have the potential to par-
2 ticipate in a multisite clinical drug
3 trial with respect to CCM;

4 “(ii) demonstrate—

5 “(I) an institutional infrastruc-
6 ture capable of hosting a clinical trial
7 site and facilitating translational
8 projects and collaborations for clinical
9 trials;

10 “(II) the capacity to maintain
11 communication with other major CCM
12 research and care institutions inter-
13 nationally for information sharing and
14 coordination of research activities, es-
15 pecially through health information
16 technology; and

17 “(III) clinical expertise in CCM
18 management or complete the CCM
19 clinical training program under sub-
20 section (c)(4); and

21 “(iii) have a sufficient number of eli-
22 gible patients with CCM.

23 “(C) DURATION OF SUPPORT.—The Direc-
24 tor of NIH may provide support for participa-
25 tion centers under this section for a period not

1 to exceed 5 years. The Director of NIH may ex-
 2 tend the period of support for a center for 1 or
 3 more additional periods, not to exceed an addi-
 4 tional 5 years, if the operations of such center
 5 have been reviewed by an appropriate technical
 6 and scientific peer review group established by
 7 the Director of NIH and if such group has rec-
 8 ommended to the Director that such period
 9 should be extended.

10 “(c) CEREBRAL CAVERNOUS MALFORMATIONS CON-
 11 SORTIUM.—

12 “(1) IN GENERAL.—The Director of NIH shall
 13 convene a Cerebral Cavernous Malformations Re-
 14 search Consortium (referred to in this section as the
 15 ‘consortium’).

16 “(2) MEMBERSHIP.—The consortium—

17 “(A) shall include representatives of—

18 “(i) the coordinating centers selected
 19 under subsection (b)(2); and

20 “(ii) at least 1 national CCM patient
 21 advocacy organization, which may be an
 22 entity that receives a grant or contract
 23 under subsection (b)(2)(A); and

24 “(B) may include representatives of the
 25 National Institutes of Health or the Food and

1 Drug Administration, in an advisory or ex offi-
2 cio role.

3 “(3) RESPONSIBILITIES.—Through a consensus
4 based decisionmaking model, the consortium shall
5 divide assignments and be responsible for—

6 “(A) developing and implementing training
7 programs for clinicians and scientists in accord-
8 ance with paragraph (4);

9 “(B) developing patient education, out-
10 reach, and awareness programs and materials,
11 which may be tailored for specific regional
12 needs at coordinating centers, including—

13 “(i) a regional multimedia public
14 awareness campaign;

15 “(ii) patient education materials for
16 distribution by regional physician and sur-
17 geon offices;

18 “(iii) an education program for ele-
19 mentary and secondary school nurses to fa-
20 cilitate early detection and diagnosis of
21 CCM in areas in which there is a high den-
22 sity of cases of CCM;

23 “(iv) regular regional patient and
24 family-oriented educational conferences;
25 and

1 “(v) nationally relevant electronic
2 health teaching and communication tools
3 and a network of professional capacity and
4 patient and family support; and

5 “(C) preparing a biannual report to Con-
6 gress, in accordance with paragraph (5).

7 “(4) TRAINING PROGRAM FOR CLINICIANS AND
8 SCIENTISTS.—

9 “(A) IN GENERAL.—The consortium, in
10 cooperation with the coordinating centers, shall
11 establish or expand a physician training pro-
12 gram, including information and education on
13 advances in the diagnosis and treatment of
14 CCM, and training and continuing education
15 through programs for scientists, physicians,
16 medical students, and other health professionals
17 and care coordinators who provide care for pa-
18 tients with CCM, telehealth, and research rel-
19 evant to CCM, for the purpose of supporting
20 the development of new participation centers
21 through educational programming to gain the
22 expertise needed to become clinical and research
23 participation centers with the potential to par-
24 ticipate in clinical drug trials.

1 “(B) STIPENDS.—The Director of NIH
2 may provide stipends for health professionals
3 who are enrolled in the training programs de-
4 scribed in subparagraph (A).

5 “(C) ELIGIBILITY.—To be eligible to par-
6 ticipate in the training program, an individual
7 shall be affiliated with an entity that is in an
8 existing clinical research network of the Na-
9 tional Institutes of Health.

10 “(5) REPORT TO CONGRESS.—The consortium
11 shall biennially submit to the Committee on Health,
12 Education, Labor, and Pensions of the Senate and
13 the Committee on Energy and Commerce of the
14 House of Representatives a report that describes the
15 research, education, and other activities on CCM
16 conducted or supported through the Department of
17 Health and Human Services. Each such report shall
18 include—

19 “(A) a research plan;

20 “(B) provisions specifying the amounts ex-
21 pended by the Department of Health and
22 Human Services with respect to various forms
23 of CCM, including those affected by the com-
24 mon Hispanic Mutation, Ashkenazi Jewish mu-
25 tation, CCM3 gene mutations, and other famil-

ial and sporadic forms of cerebral cavernous malformation; and

“(C) recommendations for particular projects or types of projects that the national research institutes or other entities in the field of research should conduct on inherited or non-inherited forms of CCM.”.

SEC. 4. CENTERS FOR DISEASE CONTROL AND PREVENTION CEREBRAL CAVERNOUS MALFORMATIONS SURVEILLANCE AND RESEARCH PROGRAMS.

Part B of title III of the Public Health Service Act (42 U.S.C. 243 et seq.) is amended by inserting after section 317T the following:

“SEC. 317U. CEREBRAL CAVERNOUS MALFORMATIONS SURVEILLANCE AND RESEARCH PROGRAMS.

“(a) IN GENERAL.—The Secretary, acting through the Director of the Centers for Disease Control and Prevention, may award grants in such sums as may be necessary and cooperative agreements to public or nonprofit private entities (including State health departments, political subdivisions of States, universities, and other medical or educational entities) for the collection, analysis, and reporting of data on cerebral cavernous malformations (referred to in this section as ‘CCM’).

1 “(b) NATIONAL CEREBRAL CAVERNOUS MALFORMA-
 2 TIONS EPIDEMIOLOGY PROGRAM.—The Secretary of
 3 Health and Human Services shall award grants and coop-
 4 erative agreements, including technical assistance, to pub-
 5 lic or nonprofit private entities for—

6 “(1) the collection, analysis, and reporting of
 7 data on CCM; and

8 “(2) epidemiological activities, including col-
 9 lecting and analyzing information on the number, in-
 10 cidence, correlates, and symptoms of cases and the
 11 clinical utility of specific practice patterns.

12 “(c) NATIONAL SURVEILLANCE PROGRAM.—The
 13 Secretary shall—

14 “(1) provide for a national surveillance program
 15 for the purpose of carrying out epidemiological ac-
 16 tivities regarding CCM, including collecting and ana-
 17 lyzing information on the number, incidence, cor-
 18 relates, and symptoms of cases of CCM and the clin-
 19 ical utility (including costs and benefits) of specific
 20 practice patterns; and

21 “(2) wherever possible, ensure that the surveil-
 22 lance program is coordinated with the data and sam-
 23 ple collection activities of the National Institutes of
 24 Health under section 409K.

1 “(d) TECHNICAL ASSISTANCE.—In making awards
2 under this section, the Secretary may provide direct tech-
3 nical assistance, including personnel support.

4 “(e) COORDINATION WITH CLINICAL CENTERS.—
5 The Secretary shall ensure that epidemiological informa-
6 tion is made available to clinical centers as supported by
7 the Director of the National Institutes of Health under
8 section 409K.

9 “(f) AUTHORIZATION OF APPROPRIATIONS.—There
10 are authorized to be appropriated such sums as may be
11 necessary to carry out this section.”.

12 **SEC. 5. FOOD AND DRUG ADMINISTRATION CEREBRAL CAV-**
13 **ERNOUS MALFORMATIONS CLINICAL TRIAL**
14 **PREPAREDNESS AND SUPPORT PROGRAM.**

15 (a) INVESTIGATIONAL NEW DRUG APPLICATION.—
16 The Secretary of Health and Human Services, acting
17 through the Commissioner of Food and Drugs, shall co-
18 ordinate with clinical centers, investigators, and advocates
19 to support appropriate investigational new drug applica-
20 tions under section 505(i) of the Federal Food, Drug, and
21 Cosmetic Act (21 U.S.C. 355(i)) in an effort to hasten
22 the pace of clinical trials for cerebral cavernous malforma-
23 tion.

24 (b) ORPHAN PRODUCT DEVELOPMENT.—Where ap-
25 plicable in rare subpopulations of cerebral cavernous mal-

1 formation requiring unique pharmacological intervention,
2 including subpopulations with the common Hispanic mu-
3 tation or CCM3 gene mutations, the Commissioner of
4 Food and Drugs shall support appropriate requests for
5 designations of drugs as orphan drugs under section 526
6 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C.
7 360bb).

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