FDA's views on the Diagnostic Accuracy and Innovation Act (DAIA)

These comments are intended only to provide technical assistance and are by no means to be interpreted as any kind of approval or endorsement of the legislation by the Department of Health and Human Services and its agencies or the Administration.

The FDA supports the goal of legislation to create a predictable path to market for all in vitro clinical tests (IVCTs) that is a risk-based approach consistent with the least burdensome principle for regulation and assuring necessary safeguards for consumers.

Patients and health care providers need accurate, reliable, and clinically valid tests to make good health care decisions. Inaccurate or false test results, or accurate measurements with an invalid claim regarding the test results' relationship to a disease, can lead to patient harm. While excessive oversight can discourage innovation, inadequate and inconsistent oversight in which different test developers are treated differently can also discourage innovation by making it difficult for high-quality test developers to compete with poorer performing counterparts.

To achieve this goal, FDA believes it is necessary to create pathways that are efficient and achieve reasonable assurance of analytical and clinical validity, without imposing unnecessary burdens.

SECTION. 1. SHORT TITLE;

TABLE OF CONTENTS

(a) This Act may be cited as the _____.
(b) Table of Contents. — The table of contents of this Act is as follows:

SEC. 2. DEFINITION.

(a) Section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 321) is amended—

(1) by adding at the end the following:

"(ss)

"(1) The term 'in vitro clinical test' means—

"(A) a test intended to be used in the collection, preparation, analysis, or in vitro clinical examination of specimens taken or derived from the human body for the purpose of

"(i) identifying, diagnosing, screening, measuring, detecting, predicting, prognosing, analyzing, or monitoring a disease or condition, including a determination of the state of health; or

"(ii) selecting, monitoring, or informing therapy or treatment for a disease or condition;

"(B) a test protocol for a use described in subparagraph (A);

"(C) a test platform for use in or with a test described in subparagraph (A);

"(D) an article for taking or deriving specimens from the human body for a purpose described in subparagraph (A);

"(E) software for a purpose described in subparagraph (A), excluding software specified under section 520(o) as not within the definition a device under this Act; or

"(F) subject to paragraph (2), a component, part, or accessory of a test described in this paragraph, whether alone or in combination, including but not limited to reagents, calibrators, and controls.

"(2) Notwithstanding paragraph (1), the following articles, if intended to be used as components, parts, or accessories of an in vitro clinical test, are not in vitro clinical tests:

"(A) Blood, blood components, and human cells or tissues, from the time of donation or recovery of such article, including determination of donor eligibility, as applicable, until such time as the article is released into interstate commerce as a component, part, or accessory of an in vitro clinical test by the establishment that collected such article;

"(B) Articles used for invasive sampling;

"(C) General purpose laboratory equipment; and

"(D) Articles used solely for personal protection during the administering, conducting, or otherwise performing test activities.

(2) by adding at the end of subsection (g) the following:

"(3) The term 'drug' does not include an in vitro clinical test as defined in this section."; and

(3) in subsection (h), by striking "section 520520(o)" and inserting the following:

"section 520(o) or an in vitro clinical test as defined in subsection(ss).".

(b) Section 351 of the Public Health Service Act (42 U.S.C. § 262) is amended by adding at the end of subsection (i)(1) the following:

"The term 'biological product' does not include an in vitro clinical test as defined in section 201(ss) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 321(ss))."

SEC. 3. REGULATION OF IN VITRO CLINICAL TESTS.

The Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301 et seq.) is amended—

(a) by amending the title of Chapter V to read as follows "Drugs, Devices, and In Vitro Clinical Tests"; and

(b) by adding at the end of Chapter V the following:

"Subchapter J—In Vitro Clinical Tests

"SEC. 587. DEFINITIONS.

"In this part—

"(1) ANALYTICAL VALIDITY The term 'analytical validity' means, the ability of an in vitro clinical test to adequately identify, measure or detect a target analyte or substance that such test is intended to identify, measure, or detect. For articles for taking or deriving specimens from the human body under section 201(ss)(1)(DD) of this Act, analytical validity means a reasonable assurance that such article performs as intended and, will support the analytical validity of tests with which it is used.,.

"(2) CLINICAL USE. The term 'clinical use' means the operation, application, or functioning of an in vitro clinical test in connection with human specimens, including

patient, consumer, and donor specimens, for the purposes specified in section 201(ss)(1)(A).

"(3) CLINICAL VALIDITY. The term 'clinical validity' means the ability of an in vitro clinical test to adequately achieve the purpose for which it is intended as described under section 201(ss)(1)(A).

"(4) COMPREHENSIVE TEST INFORMATION SYSTEM. The term 'comprehensive test information system' means an on-line database that the Secretary may use to store and provide information about in vitro clinical tests to developers and the general public, as described in section [CTIS].

"(5) CROSS-REFERENCED TEST. The term 'cross-referenced test' means an in vitro clinical test that –

> "(A) references in its labeling the trade name or intended use of another medical product that is not an in vitro clinical test; or
>
> "(B)is referenced by trade name or intended use in the labeling of another medical product that is not an in vitro clinical test.

"(6) DEVELOPER. The term 'developer' means a person who—

> "(A) develops an in vitro clinical test, including by designing, validating, producing, manufacturing, remanufacturing, propagating, or assembling the kit of an in vitro clinical test,
>
> "(B) imports an in vitro clinical test, or
>
> "(C) modifies an in vitro clinical test initially developed by a different person in a manner that changes any of the notification elements specified in paragraph (12) that define a test group, performance claims, or, as applicable, safety of such in vitro clinical test, or adversely affects performance of the in vitro clinical test.

"(7) HIGH RISK. The term 'high-risk', with respect to an in vitro clinical test or category of in vitro clinical tests, means that—

> "(A)subject to subparagraph (B), an undetected inaccurate result from such in vitro clinical test, or such category of in vitro clinical tests----
>
> > "(i) when used as intended, would likely cause serious or irreversible harm or death to a patient or patients, or would otherwise cause serious harm to the public health; and
> >
> > "(ii) the likelihood of adverse patient impact or adverse public health impact caused by such an inaccurate result is not remote.
>
> "(B) An in vitro clinical test is not a high risk in vitro clinical test if mitigating measures are established and applied to sufficiently mitigate the risk of inaccurate results as described in subparagraph (A), taking into account—

"(i) the degree to which the technology for the intended use of the in vitro clinical test is well characterized, and the criteria for performance are well established to be sufficient for the intended use; and

"(ii) the clinical circumstances (including clinical presentation) under which the in vitro clinical test is used, and the availability of other tests (such as confirmatory or adjunctive tests) or relevant material standards.

"(8) IN VITRO CLINICAL TEST. The term "in vitro clinical test' has the meaning set forth in section 201(ss).

"(9) LOW-RISK. The term 'low-risk', with respect to an in vitro clinical test or category of in vitro clinical tests, means that an undetected inaccurate result from such in vitro clinical test, or such category of in vitro clinical tests, when used as intended—

"(A) would cause minimal or no harm or disability, or immediately reversible harm, or would lead to only a remote risk of adverse patient impact or adverse public health impact; or

"(B) (i) could cause non-life threatening injury or injury that is medically reversible, or delay necessary treatment; and

"(ii) mitigating measures are sufficient to prevent such inaccurate result, detect such inaccurate result prior to any adverse patient impact or adverse public health impact, or otherwise sufficiently mitigate the risk associated with such inaccurate result.

"(10) MITIGATING MEASURES. The term 'mitigating measures' ---

"(A) means requirements that the Secretary determines, based on available evidence, are necessary ---

"(i) for an in vitro clinical test, or a category of in vitro clinical tests, to meet the relevant standard for its intended use as defined in paragraph (11), or

"(ii) to mitigate the risk of harm ensuing from a false result or misinterpretation of any result; and

"(B) includes applicable requirements regarding labeling, advertising, website posting of information, testing, clinical studies, postmarket surveillance, user comprehension studies, training, conformance to standards, and performance criteria.

(11**)** RELEVANT STANDARD. The term 'relevant standard', with respect to an in vitro clinical test, means a reasonable assurance of analytical and clinical validity, except that such term —

"(A)with respect to provisional approval under [Section X], means a reasonable assurance of analytical validity and probable clinical validity;

"(B)with respect to test platforms as defined in [Section X], means a reasonable assurance of analytical validity; and

"(C)with respect to articles for taking or deriving specimens from the human body for purposes described in section 201(ss)(1)(A)(i) or (ii) as defined by [Section

X], means a reasonable assurance of analytical validity and, where applicable, safety.

"(12) TEST GROUP. The term 'test group' means one or more tests that have the following notification elements in common—

"(A) substance or substances measured by the in vitro clinical test, such as analyte, protein, or pathogen;

"(B) type or types of specimen or sample;

"(C) test method;

"(D) test purpose, as described in section 201(ss)(1)(A), such as screening, predicting, or monitoring;

"(E) disease or condition for which the in vitro clinical test is intended for use;

"(F) intended patient population; and

"(G) context of use, such as in a clinical laboratory, in a health care facility, prescription home use, over-the-counter use, or direct-to-consumer testing.

"(13) TEST PLATFORM. The term 'test platform' means hardware, including software used to effectuate the hardware's functionality, intended to be used with other in vitro clinical tests in the generation of a test result.

"(14) VALID SCIENTIFIC EVIDENCE. The term 'valid scientific evidence' means evidence from which it can fairly and responsibly be concluded by qualified experts that the relevant standard has been met for an in vitro clinical test for its intended use, including (depending on the characteristics of the in vitro clinical test, its intended use, the existence and adequacy of warnings and other restrictions, and the extent and nature of clinical experience relevant to its use) ---.

"(A) clinical studies;

"(B) evidence or data from peer-reviewed literature;

"(C) reports of significant human experience with an in vitro clinical test;

"(D) bench studies, well-documented case studies or case histories conducted by qualified experts;

"(E) clinical data, data registries, or postmarket data;

"(F) data collected in countries other than the United States if such data are demonstrated to be adequate for the purpose of making a regulatory determination under the relevant standard in the United States; and

"(G) where appropriate, clinical practice guidelines, consensus standards and reference standards.

"(15) FIRST-OF-A-KIND. The term 'first-of-a-kind' means an in vitro clinical test that has a combination of the notification elements under paragraph (12) that makes up a test group that differs from the combination in any legally available test group.

"(16) WELL-CHARACTERIZED. The term 'well-characterized' means well-established and well-recognized by the scientific or clinical community, if adequately evidenced by one or more of the following:

"(A) Literature;

"(B) Practice guidelines;

"(C) Consensus standards;

"(D) Recognized standards of care;

"(E) Technology in use for many years;

"(F) Scientific publication by multiple sites;

"(G) Wide recognition or adoption by the scientific or clinical community; and

"(H) Real world data."

"SEC. 587A. APPLICABILITY.

"(a) IN GENERAL. —

"(1) SCOPE. An in vitro clinical test –

"(A) shall be subject to the requirements of this subchapter, except as set forth in this section;

"(B) that is offered for clinical use is deemed to be introduced into interstate commerce for purposes of enforcing the requirements of this Act; and

"(C) subject to any exemption or exclusion in this section, shall not be subject to any provision or requirement of this Act other than this subchapter unless such other provision or requirement—

"(i) applies expressly to in vitro clinical tests; or

"(ii) applies with respect to –

"(I) all articles regulated by the Secretary through the Food and Drug Administration;

"(II) a subset of such articles that includes in vitro clinical tests; or

"(iii) describes the authority of the Secretary when regulating such articles or subset of articles.

"(2) LABORATORIES AND BLOOD AND TISSUE ESTABLISHMENTS.

"(A) Nothing in this subchapter shall be construed to change or modify the authority of the Secretary with respect to laboratories or clinical laboratories under section 353 of the Public Health Service Act, or any regulations promulgated thereunder.

"(B) In implementing this subchapter, the Secretary shall, to the greatest extent possible, unless necessary to protect public health, avoid undertaking programmatic regulatory functions separately being undertaken by the Secretary under section 353 of the Public Health Service Act, or any regulations promulgated thereunder.

"(C) Nothing in this subchapter shall be construed to change or modify the authority of the Secretary with respect to laboratories, establishments or other facilities engaged in the propagation, manufacture, or preparation, including but not limited to filling, testing, labelling, packaging, and storage, of blood, blood components, human cells, tissues or tissue products under this Act or Section 351 of the Public Health Service Act.

"(3) PRACTICE OF MEDICINE. —

"(A) Nothing in this subchapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed in vitro clinical test for any condition or disease within a legitimate health care practitioner-patient relationship.

"(B) This paragraph shall not limit any authority of the Secretary to establish and enforce restrictions on the sale or distribution, or in the labeling, of an in vitro clinical test that are part of a determination of precertification, established as a condition of approval, or promulgated through regulations or otherwise.

"(C) This section shall not be construed to alter any prohibition on the promotion of unapproved uses of legally marketed in vitro clinical tests.

"(4) SPECIAL RULE. —

"(A) Notwithstanding the exemptions from premarket review set forth in subsections (b), (c), (d), (e), (f), (g), (h), and (k) of this section, an in vitro clinical test shall be subject to the requirements of section [premarket review] if the Secretary determines, in accordance with subparagraph (B), that—

"(i) there is insufficient valid scientific evidence that an article for taking or deriving specimens from the human body for the purposes specified in section 201(ss) performs as intended, will support the analytical validity of tests with which it is used, or, where applicable, is safe for use

"(ii)there is insufficient valid scientific evidence to support the analytical validity or the clinical validity of such in vitro clinical test;

"(iii)such in vitro clinical test is being offered by its developer with materially deceptive or fraudulent analytical or clinical claims; or

"(iv)there is a reasonable potential that such in vitro clinical test will cause death or serious adverse health consequences, including by causing the absence, delay, or discontinuation of appropriate medical treatment.

"(B) PROCESS. —

"(i) If the Secretary has reason to believe that one or more of the criteria set forth in subparagraph (A) apply to an in vitro clinical test, the Secretary may request the developer to submit information pertaining to such criteria and to establishing the basis for any claimed exemption from premarket review.

"(ii) Upon receiving a request for information under subparagraph (B)(i), the developer shall submit the information within 30 days of the request.

"(iii) The Secretary shall review the information submitted within 30 days of its receipt. If the Secretary makes one or more of the findings specified in subparagraph (A), the developer shall promptly submit an application for premarket review, which submission shall be made no later than 90 days from such finding.

"(iv) If an application for premarket review is pending in accordance with clause (iii), the in vitro clinical test may continue to be marketed for clinical use while the application is pending, unless the Secretary issues an order to the developer to immediately cease distribution of the test in the best interest of the public health, which order may also direct the developer to immediately notify health professionals and other user facilities to cease use of such in vitro clinical test.

"(v) If the developer fails to submit an application for premarket review of a test as required under clause (iii), or if the Secretary determines not to approve an application submitted under this paragraph, the Secretary may issue an order as described in clause (vi).

"(vi) If the Secretary makes one of the findings specified in subparagraph (A) with respect to an in vitro clinical test, the Secretary may issue an order requiring the developer of such in vitro clinical test, and any other appropriate person (including a distributor or retailer of the in vitro clinical test)—

> "(I) to immediately cease distribution of such in vitro clinical test pending approval of an application under section [587B - premarket review]; and
>
> "(II) to immediately notify health professionals and other user facilities of the order and to instruct such professionals and facilities to cease use of such in vitro clinical test.
>
> Such order shall provide the person subject to the order with an opportunity for an informal hearing, to be held not later than 10 days after the date of the issuance of the order, on the actions required by the order and on whether the order should be amended to require a recall of such in vitro clinical test. If, after providing an opportunity for such a hearing, the Secretary determines that inadequate grounds exist to support the actions required by the order, the Secretary shall vacate the order.

"(vii) If the Secretary determines that an order issued under clause (vi) should be amended to include a recall of the in vitro clinical test with respect to which the order was issued, the Secretary shall amend the order to require a recall. The Secretary shall specify a timetable in which the in vitro clinical test

recall will occur and shall require periodic reports to the Secretary describing the progress of the recall.

"(viii) Any order issued under this paragraph with respect to an in vitro clinical test shall cease to be in effect if such test is granted approval under sections [premarket review, provisional approval], provided that the in vitro clinical test is developed and offered for clinical use in accordance with such approval.

"(5) EMERGENCY USE.–

"(A) IN GENERAL.—The exemptions set forth in this section shall not apply to any in vitro clinical test that is eligible for an emergency use authorization under section 564.

"(B) TESTS OFFERED FOR CLINICAL USE UNDER AN EXEMPTION PRIOR TO A DECLARATION.—

"(i) (I) Subject to subclause (II), an in vitro clinical test that would be eligible for an emergency use authorization under section 564 that is offered for clinical use under an exemption in [APPLICABILITY SECTION] prior to a declaration under section 564(b) affecting such test may continue to be offered for clinical use after such declaration only after it has been approved under section [premarket review] or granted an emergency use authorization under section 564.

"(II) However, if an application for approval is submitted under section [premarket review, (b)] or a request for emergency use authorization is submitted under section 564 not later than [5] days after a declaration, such test described in subclause (I) may be offered for clinical use until the application or request is denied.

"(ii) The Secretary, in collaboration with the developer and other affected entities, as appropriate, shall take necessary actions to ensure such tests are no longer distributed or offered for clinical use until they receive the required approval or authorization.

"(b) COMPONENTS, PARTS, AND ACCESSORIES. —

"(1) EXEMPTION. —

"(A) Subject to paragraph (b), an in vitro clinical test that is a component, part, or accessory within the meaning of section 201(ss)(1)(E), is exempt from the requirements of this subchapter and this Act, subject to the limitation described in subparagraph (B), if it is intended for further development under paragraph (2). Test platforms, articles for taking or deriving specimens from the human body, and software, as defined by subparagraphs (B) through (D) of section 201(ss)(1) are not considered to be components, parts, or accessories and are not eligible for this exemption.

"(B) Notwithstanding subparagraph (A), an in vitro clinical test that uses a component, part, or accessory described in such subparagraph shall be subject to

the requirements of this subchapter and this Act, including requirements relating to the establishment and use of supplier controls, unless such in vitro clinical test is otherwise exempted under this section.

"(2) FURTHER DEVELOPMENT. — An in vitro clinical test that is a component, part, or accessory as described in paragraph (1) intended for further development if—

"(A) it is intended solely for use in the development of another in vitro clinical test and

"(B) if introduced or delivered for introduction into interstate commerce after the date of enactment of this [subchapter/bill name], the labeling of such in vitro clinical test bears the following statement: "This product is intended solely for further development of an in vitro clinical test and is exempt from FDA regulation. This product must be evaluated by the in vitro clinical test developer in accordance with supplier controls if it is used with or in the development of an in vitro clinical test."

"(c) GRANDFATHERED TESTS. —

"(1) EXEMPTION. — An in vitro clinical test that meets the criteria set forth in paragraph (2) is exempt from premarket review under section [x], the labeling requirements under section [x], and the quality system requirements under section [x], and may be lawfully marketed subject to the other requirements of this subchapter and other applicable requirements of this Act, if—

"(A) Each test report template under section [LABELING] bears a statement of adequate prominence that reads as follows "This in vitro clinical test was developed and first introduced prior to [90 days prior to date of bill enactment] and has not been reviewed by the Food and Drug Administration"; and

"(B) The developer of such in vitro clinical test maintains documentation demonstrating that such test meets and continues to meet the criteria set forth in paragraph (2), which documentation shall be available to the Secretary upon request.

"(2) CRITERIA FOR EXEMPTION. — An in vitro clinical test is exempt as specified in paragraph (1) if it–

"(A) was developed by a laboratory certified by the Secretary under section 263a of title 42 that meets the requirements for performing high-complexity testing for use only within that certified laboratory and was first offered for clinical use or otherwise introduced or delivered for introduction into interstate commerce by that laboratory 90 days or more before the date of enactment of [subchapter/bill];]

"(B) does not have an approval under section 515, a clearance under section 510(k), an authorization under 513(f)(2), or an approval under 520(m);

"(C) is not modified on or after the date that is 90 days before the date of enactment of this [bill/subchapter] by its initial developer (or another person) in a manner such that it is a new in vitro clinical test according to [section l(1) (Modified Tests)]."(3) (A) When a person modifies its own or another person's in vitro clinical test that is exempt under

this subsection and makes a determination that it is not a new in vitro clinical test according to section l(1) [(Modified Tests)],section l(1) [(Modified Tests)], the person must document the modification(s) and basis for such determination and provide it to the Secretary upon request or inspection.

"(d) TESTS EXEMPT FROM 510(k) [PRIOR TO ENACTMENT OF [SUBCHAPTER/BILLNAME] —

"(1) EXEMPTION. — An in vitro clinical test is exempt from the requirements of section [premarket review], and may be lawfully marketed subject to the other requirements of this subchapter and other applicable requirements of this Act, if it meets the criteria for exemption described in paragraph 2.

"(2) CRITERIA FOR EXEMPTION. — An in vitro clinical test is exempt from the requirements of section [premarket review] if—

"(A) such test was offered for clinical use prior to the effective date of this [subchapter/bill], and was exempt from submission of a report under section 510(k) of the Act [21 U.S.C. 360(k)] pursuant to [the FDCA] (including class II 510(k)-exempt devices and excluding class I reserved devices); or

"(B) such test was not offered for clinical use prior to the effective date of this [subchapter/bill name] and—

"(i) is not a test platform as defined in [DEFINITIONS]; and

"(ii) falls within a category of tests that was exempt from submission of a report under section 510(k) [21 U.S.C. 360(k)] prior to the effective date of this [subchapter/bill name] (including class II 510(k)-exempt devices and excluding class I reserved devices).

"(3) EFFECT ON SPECIAL CONTROLS.—For any in vitro clinical test, or category of in vitro clinical tests, that is exempted from premarket review based on the criteria in paragraph (2), any special control that applied to a device within a predecessor category immediately prior to the date of enactment of this subsection shall be deemed a mitigating measure applicable to an in vitro clinical test within the successor category, , except to the extent such mitigating measure is withdrawn or changed in accordance with section [mitigating measures].

"(e) LOW-RISK TESTS. —

"(1) EXEMPTION. — An in vitro clinical test is exempt from the requirements of section [premarket review], and may be lawfully marketed subject to the other requirements of this subchapter and other applicable requirements of this Act, if such test is listed, or falls within a category of tests that is listed, as a low-risk test in the list that the Secretary maintains on the website of the Food and Drug Administration pursuant to paragraph (2).

"(2) LIST OF LOW-RISK TESTS.

"(A) The Secretary shall maintain, on the website of the Food and Drug Administration, a list of in vitro clinical tests, or categories of in vitro clinical tests, that have been designated as low-risk in accordance with this paragraph.

"(B) The list required under this paragraph shall include all tests or categories of tests that meet the criteria under subsection (d) for tests exempt from section 510(k) (including class II exempt devices and excluding class I reserved devices).

"(C) Notwithstanding subchapter II of chapter 5 of title 5, the Secretary may designate an additional in vitro clinical test, or category of in vitro clinical tests, as low-risk by adding it to the list required under this paragraph upon the initiative of the Secretary or in response to a request by any person. In determining whether an additional in vitro clinical test, or category of in vitro clinical tests, should be designated as low-risk, the Secretary shall consider—

"(i) whether such test, or category of tests, meets the definition of 'low-risk' set forth in section [x]; and

"(ii) such other factors as the Secretary may deem relevant.

"(f) MANUAL TESTS. —

"(1) EXEMPTION. — An in vitro clinical test that is designed, manufactured, and used within a single laboratory certified by the Secretary under section 263a of title 42 that meets the requirements for performing high-complexity testing is exempt from the requirements of this subchapter and this Act, if

"(A) it meets the criteria for exemption described in paragraph (2); and

"(B) it is not intended—

"(i)for detecting HIV, or for measuring an analyte that serves as a surrogate marker for screening, diagnosis, or monitoring or monitoring therapy for acquired immune deficiency syndrome (AIDS);

"(ii) for testing donors, donations, and recipients of blood, blood components, human cells, tissues, cellular-based products, or tissue-based products; or

"(iii)for testing maternal or fetal specimens in determining hemolytic disease of the fetus and newborn.]

"(2) CRITERIA FOR EXEMPTION. — An in vitro clinical test is exempt as specified in paragraph (1) if its output is the result of manual interpretation (meaning direct observation) by a qualified laboratory professional, without the use of automated instrumentation or software for intermediate or final interpretation, and is either

"(A) not a high-risk test; or

"(B) a high-risk test that the Secretary determines through issuance of a notice in the Federal Register is appropriate to be exempted and that meets one of the following conditions—

"(i) no component, part, or accessory of such test, including any reagent, is introduced into interstate commerce under the exemption for tests intended for further development under subsection (b)(1), and the article for taking or deriving specimens from the human body complies with the requirements of this Act; or

"(ii) the test has been developed in accordance with Section 587I [QS, supplier controls].

"(g) TESTS FOR RARE DISEASES. —

"(1) EXEMPTION — An in vitro clinical test is exempt from premarket review under section [x], and may be lawfully marketed subject to the other requirements of this subchapter and other applicable requirements of this Act, if—

"(A) it meets the criteria for exemption under paragraph (2); and

"(B) The developer maintains documentation demonstrating that such test meets and continues to meet the criteria set forth in paragraph (2), which documentation—

"(i) shall be available to the Secretary upon request; and

"(ii) may include literature citations in specialized medical journals, textbooks, specialized medical society proceedings, governmental statistics publications, or, if no such studies or literature citations exist, credible conclusions from appropriate research or surveys.

"(2) CRITERION FOR EXEMPTION. The criteria for the exemption under this subsection from premarket review are—

"(A) fewer than 8,000 individuals per year in the United States would be subject to testing using such in vitro clinical test;

"(B) such in vitro clinical test is not cross-referenced; and

"(C) such in vitro clinical test is not for a communicable disease

"(h) CUSTOM TESTS AND LOW-VOLUME TESTS. —

"(1) EXEMPTION. — An in vitro clinical test is exempt from premarket review under section [x], the quality system requirements under section [x], and the notification requirement in section [x], and may be lawfully marketed subject to the other requirements of this subchapter and other applicable requirements of this Act, if –

"(A) The developer maintains documentation demonstrating that such test meets and continues to meet the applicable criteria set forth in paragraph (2), which documentation shall be available to the Secretary upon request; and

"(B) The developer informs the Secretary, on an annual basis, in a manner prescribed by the Secretary in Level 2 guidance, that such in vitro clinical test was introduced into interstate commerce.

"(2) CRITERIA FOR EXEMPTION. — An in vitro clinical test is exempt under paragraph (1) if—

"(A) It is not included in a test menu, template test report, or other promotional materials, and is not otherwise advertised;

"(B) It is developed or modified in order to comply with the order of an individual physician, dentist, or other health care professional (or any other specially qualified person designated under regulations promulgated by the Secretary); and

"(C) It is either

"(i) a custom test to diagnose a unique pathology or physical condition of a specific patient named in the order for which no other in vitro clinical test is commercially available in the United States, and is not used for other patients; or

"(ii) a low-volume test offered to no more than 5 patients per year.

"(i) PUBLIC HEALTH SURVEILLANCE. —

"(1) EXEMPTION. — An in vitro clinical test that is intended solely for use by a public health laboratory in public health surveillance, as described in paragraph (2), is exempt from the requirements of this subchapter and this Act.

"(2) CRITERIA FOR EXEMPTION. — An in vitro clinical test is intended solely for use in public health surveillance under paragraph (1) if it is intended solely for use on systematically collected samples for analysis and interpretation of health data essential to the planning, implementation and evaluation of public health practice, where such practice is closely integrated with the dissemination of these data to public health officials and linked to the prevention or control of disease or other public health threat. An in vitro clinical test that is either intended for use in making clinical decisions for individual patients or other purposes not described in the preceding sentence or whose individually identifiable results may be reported back to an individual patient or the patient's healthcare provider, even if also intended for public health surveillance, is not intended solely for use in public health surveillance under paragraph (1).

"(j) LAW ENFORCEMENT. — An in vitro clinical test that is intended solely for use in forensic analysis or other law enforcement activity is exempt from the requirements of this subchapter and this Act. An in vitro clinical test that is intended for use in making clinical decisions for individual patients or other purposes not described in the preceding sentence, or whose individually identifiable results may be reported back to an individual patient or the patient's healthcare provider, even if also intended for law enforcement purposes, is not intended solely for use in law enforcement under this subsection.

"(k) PRECERTIFIED TESTS. — An in vitro clinical test that is precertified under section [precertification] is exempt from the requirements of section [premarket review].

"(l) MODIFIED TESTS.–

"(1) An in vitro clinical test that is modified, by the initial developer or a different person, is a new in vitro clinical test subject to all applicable provisions of sections XXX – XXX [IVCT sections of FDCA] if the modification—

"(A) changes any of the elements specified in section 587(12) that define a test group,

"(B) changes performance claims made with respect to such in vitro clinical test;

"(C) causes an in vitro clinical test to no longer comply with applicable mitigating measures or restrictions;

"(D) adversely affects performance of the in vitro clinical test; or

"(E) as applicable, affects the safety of an article for taking or deriving specimens from the human body for a purpose described in section 201(ss).

"(2) When a person modifies an in vitro clinical test that was developed by another person, such modified test is exempt from the requirements of this subchapter and this Act provided that such person shall document the modification that was made and the basis for determining that the modification, considering the changes individually and collectively, was not a type of modification described in paragraph (1) and shall provide such documentation to the Secretary upon request or inspection.

"(m) INVESTIGATIONAL USE.——An in vitro clinical test for investigational use is exempt from the requirements of this subchapter and this Act other than the requirements of and under section [investigational use], and may be lawfully marketed subject to such requirements.

"(n) GENERAL EXEMPTION AUTHORITY.——The Secretary may, by order published in the Federal Register following notice and an opportunity for comment, exempt a class of persons from any section under this subchapter upon a finding that such exemption is appropriate in light of public health and other relevant considerations.

"(o) REGULATIONS.- The Secretary is authorized to issue regulations to implement this subchapter.

"SEC. 587B. PREMARKET REVIEW

"(a) GENERAL REQUIREMENT. — No person shall introduce or deliver for introduction into interstate commerce any in vitro clinical test, unless an approval of an application filed pursuant to subsection (b), including an approval under section [587C – priority review/provisional approval] is effective with respect to such in vitro clinical test or such in vitro clinical test is exempt from the requirements of this section under section [587A – applicability].

"(b) APPLICATION FOR PREMARKET APPROVAL. —

"(1) Any person may file with the Secretary an application for premarket approval for an in vitro clinical test.

"(2) An application submitted under paragraph (1) shall include—

"(A) The information required in 21 CFR 814. 20(a), (b)(1), (2), (3)(iii), (iv), (v), (vi), (8), (10), (12), which shall be interpreted to apply to in vitro clinical tests, until such time as regulations requiring comparable information are in effect with respect to in vitro clinical tests, at which time an application submitted under paragraph (1) shall include the information required under such regulations;

"(B) General information regarding the test, including a description of its intended use; an explanation regarding how the test functions and significant performance characteristics; a risk assessment of the test; and a statement attesting to the truthfulness and accuracy of the information submitted in the application;

"(C) Except for test platforms, information regarding the methods used in, or the facilities or controls used for, the development of the test to demonstrate compliance with the applicable quality system requirements set forth in section [QS].

"(D) Information demonstrating compliance with any applicable standards established or recognized under section [standards], or established or recognized under section 514 [prior to the date of enactment of this [subchapter/bill name], and any applicable mitigating measures established under section [mitigating measures].

"(E) Valid scientific evidence from nonclinical laboratory studies involving the test, or in the case of a test platform or article for taking or deriving specimens from the human body, with a representative test or tests covering all intended test methodologies that include the test platform or collection article, to support analytical and clinical validity, which shall include—

"(i) summary information for all supporting validation studies performed and a statement that studies were conducted in compliance with applicable good laboratory practices under part 58 of title 21 of the Code of Federal Regulations which shall be interpreted to apply to in vitro clinical tests; and

"(ii) raw data for tests that are high-risk, cross-referenced, or first-of-a-kind, unless the Secretary determines otherwise; with raw data for all other tests available upon the Secretary's request;

"(F) For in vitro clinical tests for which clinical validity is included in the relevant standard, valid scientific evidence from clinical investigations with the test involving human subjects to support clinical validity, which shall include—

"(i) raw data for tests that are high-risk, cross-referenced, or first-of-a-kind, unless the Secretary determines otherwise; with raw data for all other tests available upon the Secretary's request;

"(ii) information on clinical investigations involving human subjects including statements that any clinical investigation involving human subjects was conducted in compliance with: (I) institutional review board regulations in 21 CFR part 56, which shall be interpreted to apply to in vitro clinical tests, (II) informed consent regulations in 21 CFR part 50, which shall be interpreted to apply to in vitro clinical tests, and (III) investigational use requirements in section [investigational use], as applicable;

"(G) To the extent the application seeks authorization to make modifications within the scope of the approval, a change protocol that includes validation procedures and acceptance criteria for specific types of anticipated modifications that could be made to the test under an approved application;

"(H) For an article for taking or deriving specimens from the human body, and for any in vitro clinical test that includes such article, safety information, as applicable, including but not limited to biocompatibility, sterility, human factors studies and user studies, and information regarding the types of tests that could be used with the article;

"(I) For a test platform, and for any in vitro clinical test that includes a test platform, data, as applicable, to support software validation, electromagnetic compatibility, and electrical safety, or information demonstrating compliance with applicable recognized standards addressing these areas;

"(J) Proposed labeling, in accordance with the requirements in section [labeling]; and

"(K) Such other information as the Secretary may require through guidance.

"(3) Upon receipt of an application meeting the requirements set forth in paragraph (2), the Secretary –

"(A) may on the Secretary's own initiative, or

"(B) may, upon the request of an applicant unless the Secretary finds that the information in the application which would be reviewed by a panel substantially duplicates information which has previously been reviewed by a panel appointed under section [513], "refer such application to the appropriate panel under section [513] for study and for submission (within such period as he may establish) of a report and recommendation respecting approval of the application, together with all underlying data and the reasons or basis for the recommendation.

"(4) If, after receipt of an application under this section, the Secretary determines that any portion of such application is deficient, the Secretary shall provide to the applicant a description of such deficiencies and identify the information required to correct such deficiencies.

"(c) AMENDMENTS TO AN APPLICATION. —

"(1) An applicant may amend an application or supplement to revise or provide additional information.

"(2) An applicant shall amend an application or supplement to provide additional information if such information could reasonably affect an evaluation of whether the relevant standard has been met, or could reasonably affect the statement of contraindications, warnings, precautions, and adverse reactions in the proposed labeling.

"(3) The Secretary may request that an applicant amend an application or supplement with any information necessary for the review of the application or supplement.

"(d) ACTION ON AN APPLICATION FOR PREMARKET APPROVAL. —

"(1) REVIEW. As promptly as possible, but in no event later than [X] days after an application is accepted for submission, unless an extension is necessary to review major amendments under subsection (c), the Secretary, after considering any applicable report and recommendation submitted under paragraph (b)(3), shall –

"(A) Issue an order approving the application if the Secretary finds that all of the grounds for approval in paragraph (2) are met; or

"(B) Deny approval of the application if he finds that one or more grounds for approval in paragraph (2) are not met.

"In making the determination whether to approve or deny the application, the Secretary shall rely on the intended use included in the proposed labeling, if such labeling is not false or misleading based on a fair evaluation of all material facts.

"(2) APPROVAL OR DENIAL OF AN APPLICATION. —

"(A) The Secretary shall approve an application under this section if the Secretary finds that there has been an adequate showing of the following—

"(i) The relevant standard is met;

"(ii) Compliance with applicable quality system requirements set forth in section [QS] or as otherwise specified in a condition of approval;

"(iii) The application does not contain a false statement of material fact;

"(iv) Based on a fair evaluation of all material facts, the proposed labeling is truthful and non-misleading and complies with the requirements in section [labeling];

"(v) The applicant permits authorized FDA employees or persons accredited under this [subchapter/bill name] an opportunity to inspect at a reasonable time and in a reasonable manner the facilities and all pertinent equipment, finished and unfinished materials, containers, and labeling therein, including all things (including records, files, papers, and controls) bearing on whether an in vitro clinical test is adulterated, misbranded, or otherwise in violation of this Act, and permits authorized FDA employees or persons accredited under this Act to view and to copy and verify all records pertinent to the application and the in vitro clinical test;

"(vi) The test conforms in all respects with any applicable performance standards established under section [standards] and complies with any applicable mitigating measures established under section [mitigating measures];

"(vii) All nonclinical laboratory studies that are described in the application and that are essential to show that the test is analytically and clinically valid, were conducted in compliance with the good laboratory practice regulations in 21 CFR part 58, which shall be interpreted to apply to in vitro clinical tests;

"(viii) All clinical investigations involving human subjects described in the application subject to the institutional review board regulations in 21 CFR part 56 and informed consent regulations in 21 CFR part 50, each of which shall be interpreted to apply to in vitro clinical tests, were conducted in compliance with those regulations such that the rights or safety of human subjects were adequately protected; and

"(ix) Such other showings as the Secretary may require.

"(B) An order approving an application may require conditions of approval for the in vitro clinical test, including conformance with performance standards established under section [standards] and compliance with restrictions established under section [restrictions].

"(C) For a first-of-a-kind test, an order approving an application may impose requirements for the test group, including conformance with performance standards established under section [standards], compliance with restrictions established under section [restrictions], and compliance with mitigating measures established under section [mitigating measures]. An approval order for a first-of-a-kind test shall indicate whether subsequent tests in that test group may meet an exemption set forth in section [applicability].

"(D) The Secretary shall publish the approval order on a website of the Food and Drug Administration and make publicly available a summary of the data used to make the decision, except for information restricted from disclosure pursuant to another statute.

"(3) REVIEW FOR DENIALS AND APPROVALS OF APPLICATION. An applicant whose application has been denied approval may, by petition filed on or before the [X] day after the date upon which he receives notice of such denial, obtain review in accordance with section [appeals], and any interested person may obtain review, in accordance with section [appeals], of an order of the Secretary approving an application.

"(e) PROVISIONAL APPROVAL. If the Secretary, after reviewing an application submitted under this section, determines that the applicant has not demonstrated a reasonable assurance of clinical validity, but that the application meets the requirements for provisional approval under section [387C(e)], the Secretary may grant the application provisional approval under section [387C(e)] without regard to whether the application has been designated for priority review under section [387C(c)]. The Secretary shall not grant provisional approval in accordance with this subsection without first notifying the applicant and obtaining authorization from the applicant to so act.

"(f) SUPPLEMENTS TO AN APPLICATION.—

"(1) RISK ANALYSIS. Prior to implementing any modification to an in vitro clinical test, the holder of such approved application shall perform a risk analysis in accordance with section [QS].

"(2) SUPPLEMENT REQUIREMENT.—

"(A) Except as provided in subparagraph (B), or otherwise specified by the Secretary, the holder of an approved application shall submit and receive approval of a supplement before implementing a modification to an approved test.

"(B) The holder of an approved application may implement the following modifications to a test without prior approval of a supplement, provided the holder does not add a manufacturing site, or change activities at an existing manufacturing site, and subject to the requirements of subparagraphs (C) and (D)—

"(i) Modifications included in and implemented in accordance with an approved change protocol;

"(ii) Modifications that

"(I) do not change any of the elements specified in section 587(12) that define a test group;

"(II) do not change performance claims for the in vitro clinical test; or,

"(III) do not change, as applicable, safety of the in vitro clinical test;

"(IV)) do not adversely affect performance of the in vitro clinical test; and

"(V)) do not cause an in vitro clinical test to no longer comply with applicable mitigating measures or restrictions; or

(iii) Labeling changes that are appropriate to address a safety concern.

"(C) A modification described in clause (i) and clause (ii) of subparagraph (B) shall be reported in the next annual report for the test under subsection (h) following the date on which an in vitro clinical test with such modification is introduced into interstate commerce. Such report shall include a description of the modification, and, as applicable, a summary of the analytical and clinical validity, and acceptance criteria.

"(D) A modification referenced in clause (iii) of subparagraph (B) shall be reported to the Secretary within 30 days of the date on which an in vitro clinical test with such modification is introduced into interstate commerce. Any such report shall include—

"(i) A summary of the relevant change or changes;

"(ii) The rationale for implementing such change or changes; and

"(iii) A description of how the change or changes were evaluated.

"Upon review of such report and a finding that the relevant modification is inconsistent with the standard specified under clause (iii) of subparagraph (B), the Secretary may require a supplement under subparagraph (A).

"(3) CONTENTS OF SUPPLEMENT. Unless otherwise specified by the Secretary, a supplement under this subsection shall include–

"(A) For modifications other than manufacturing site changes, a description of the modification, summary or raw data, as applicable, to demonstrate that the relevant standard is met, acceptance criteria, and any revised labeling.

"(B) For manufacturing site changes, the information required in subparagraph (A) and information regarding the methods used in, or the facilities or controls used for, the development of the test to demonstrate compliance with the applicable quality system requirements set forth in section [QS].

"(4) APPROVAL. The Secretary shall approve a supplement if—

"(A) the data, if applicable, demonstrate that the modified test meets the relevant standard; and

"(B) the holder of the approved application has demonstrated compliance with applicable quality system and inspection requirements, where appropriate.

"(5) ADDITIONAL DATA. The Secretary may require, when necessary, additional data to evaluate the modification of the test.

"(6) CONDITIONS OF APPROVAL. An order approving a supplement may require conditions of approval for the in vitro clinical test, including conformance with performance standards established under section [standards] and compliance with restrictions established under section [restrictions].

"(7) PUBLICATION. The Secretary shall publish notice of the supplemental approval order on FDA's website.

"(8) REVIEW OF DENIAL. An applicant whose supplement has been denied approval may, by petition filed on or before the [X] day after the date upon which he receives notice of such denial, obtain review in accordance with section [appeals], and any interested person may obtain review, in accordance with section [appeals], of an order of the Secretary approving a supplement.

"(g) WITHDRAWAL AND TEMPORARY SUSPENSION OF APPROVAL.

"(1) The Secretary may, after providing due notice and an opportunity for informal hearing to the holder of an approved application, issue an order withdrawing approval of the application of an in vitro clinical test if the Secretary finds that –

"(A) The grounds for approval in subsection (d)(2) are no longer met; or

"(B) There is a there is a reasonable likelihood that the in vitro clinical test would cause death or serious adverse health consequences, including by causing the absence, delay, or discontinuation of appropriate medical treatment.

"(2) An order withdrawing approval shall state each ground for withdrawal and shall notify the holder of such withdrawn approval.

"(3) The Secretary shall publish the withdrawal order on the website of the Food and Drug Administration.

"(4) If, after providing an opportunity for an informal hearing, the Secretary determines there is a reasonable likelihood that the in vitro clinical test would cause death or serious adverse health consequences, including by causing the absence, delay, or discontinuation of appropriate medical treatment, the Secretary shall by order temporarily suspend the approval of the application. If the Secretary issues such an order, the Secretary shall proceed expeditiously under paragraph (1) to withdraw such application.

"(h) ANNUAL REPORT.

"(1) Unless the Secretary specifies otherwise, the holder of an approved application shall submit an annual report each year at a time designated by the Secretary in the approval order. Such report shall—

"(A) identify all modifications that an approved application holder has made to any test, including any modification that requires a supplement under subsection (f); and

"(B) include any other information required by the Secretary.

"(2) This annual report requirement shall not apply to in vitro clinical tests that are deemed to have a premarket approval based on a prior clearance under section 510(k) or prior authorization under section 513(f).

"(i) SERVICE OF ORDERS. Orders of the Secretary under this section shall be served (1) in person by any officer or employee of the Department of Health and Human Services designated by the Secretary, or (2) by mailing the order by registered mail or certified mail or electronic equivalent addressed to the applicant at the last known address in the records of the Secretary.

"SEC. 587C. PRIORITY REVIEW

"(a) IN GENERAL.

"(1) An in vitro clinical test that is otherwise required to have approval under section [premarket review] may be designated by the Secretary for priority review in accordance with this section. An application for in vitro clinical test that has been so designated may be granted provisional approval under subsection (e) or approval under subsection (f), in accordance with the requirements of this section.

"(2) An in vitro clinical test for which provisional approval or approval has been granted under this section, and for which such approval is in effect, is exempt from the requirement to obtain premarket approval under section [premarket review].

"(b) ELIGIBILITY.-- An in vitro clinical test is eligible for designation, review, and provisional approval or approval under this section if—

"(1) The test provides or enables more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions compared to existing approved or precertified alternatives; and

"(2) It is a test -

"(A) that represents a breakthrough technology;

"(B) for which no approved or precertified alternative exists;

"(C) that offers a clinically meaningful advantage over existing approved or precertified alternatives, including the potential, compared to existing approved or precertified alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or

"(D) the availability of which is in the best interest of patients or public health.

"(c) DESIGNATION.

"(1) REQUEST. Except as provided in section [387(e) – provisional approval under premarket review], to receive provisional approval or approval under this section, an applicant must first request that the Secretary designate the in vitro clinical test for priority review. Such a request shall include information demonstrating that the test is eligible for designation under subsection (b).

"(2) DETERMINATION. Not later than 60 calendar days after the receipt of a request under paragraph (1), and prior to acceptance of an application for provisional approval or approval, the Secretary shall determine whether the in vitro clinical test that is the subject

of the request meets the criteria described in subsection (b). If the Secretary determines that the test meets the criteria, the Secretary shall designate the test for priority review.

"(3) REVIEW. Review of a request under paragraph (1) shall be undertaken by a team that is composed of experienced staff and senior managers of the Food and Drug Administration.

"(4) WITHDRAWAL.

"(A) The designation of an in vitro clinical test under this subsection is deemed to be withdrawn, and such in vitro clinical test shall no longer be eligible for review and approval under this section, if—

"(i) the test is deemed not approved under subsection (e)(10);

"(ii) provisional approval for the test is withdrawn under subsection (e)(8); or

"(iii) an application for approval under subsection (f) for the test is denied.

"(B) The Secretary may not withdraw a designation granted under this subsection based on the subsequent approval or precertification of another test that--

"(i) is designated under this section; or

"(ii) was given priority review under section 515C."

"(d) EXPEDITED DEVELOPMENT AND PRIORITY REVIEW.

"(1) For purposes of expediting the development and review of in vitro clinical tests under this section, the Secretary may take the actions and additional actions set forth in section 515B(e) when reviewing such tests under subsection (e) or (f).

"(2) Any reference or authorization in section 515B(e) with respect to a device shall be deemed a reference or authorization with respect to an in vitro clinical test for purposes of this section.

"(e) PROVISIONAL APPROVAL AND APPROVAL.

"(1) APPLICATION FOR PROVISIONAL APPROVAL. Unless otherwise specified by the Secretary, sections [premarket review; (b)(2)(A) – (F), (H)-(K), (b)(3)] apply to applications under this subsection for designated in vitro clinical tests.

"(2) AMENDMENTS. Unless otherwise specified by the Secretary, section [premarket review; (c)] applies to amendments to applications under this subsection.

"(3) ACTION. Unless otherwise specified by the Secretary, sections [premarket review; (d)(1) and (d)(2)(A), (D)] apply to the review, and approval or denial, of applications under this subsection.

"(4) SUPPLEMENTS. Unless otherwise specified by the Secretary, section [premarket review; (ff)] applies to supplements to applications under this subsection.

"(5) CONFIRMATORY POSTMARKET OBLIGATIONS. As set forth in the provisional approval order issued under paragraph (1), the applicant shall—

"(A) Submit within a specified timeframe to the Secretary, and receive approval for, a proposal regarding developing and completing required postmarket studies; and

"(B) Complete the required postmarket studies within the timeframe specified in the provisional approval order, which shall not exceed three years from the date of approval, unless an extension has been granted by the Secretary.

"(6) EXPIRATION. Provisional approval under paragraph (1) shall expire on—

"(A) the date that is specified in the provisional approval order, except that if an application for approval is submitted three months before this date in accordance with subparagraph (8)(B), on the date that the Secretary makes a decision on such application;

"(B) the date that is specified in an order issued by the Secretary that amends the provisional approval timeframe, except that if an application for approval is submitted three months before this date in accordance with subparagraph (8)(B), on the date the Secretary makes a decision on such application; "(C) the date on which provisional approval is withdrawn under paragraph (11) of this subsection.

"(7) LABELING. Any in vitro clinical test that is provisionally approved shall include in labeling a statement that the test is "provisionally approved with confirmatory postmarket obligations."

"(8) APPLICATION FOR APPROVAL.

"(A) Any holder of a provisional approval may submit an application for approval, which shall contain the information required under section [587B(b)]. Such application may incorporate by reference information from the application for provisional approval for that in vitro clinical test.

"(B) An application for approval under this paragraph shall be submitted at least three months before the date that provisional approval expires under subparagraph (A) or (B) of paragraph (6).

"(C) Applications for approval shall be reviewed in accordance with the procedures and requirements of section [premarket review – 387B(b)–(d), (f)], subject to any actions or additional actions taken by the Secretary under subsection (d). In reviewing such an application, the relevant standard shall be a reasonable assurance of analytical and clinical validity.

"(9) REVIEW FOR DENIALS AND APPROVALS OF APPLICATION. An applicant whose application has been denied provisional approval or approval under this subsection may, by petition filed on or before the [X] day after the date upon which he receives notice of such denial, obtain review in accordance with section [appeals], and any interested person may obtain review, in accordance with section [appeals], of an order of the Secretary approving an application.

"(10) TEST DEEMED NOT APPROVED. A test for which provisional approval has been granted under this subsection shall be deemed not approved on–

"(A) The date that provisional approval expires under paragraph (6), unless an application for approval under paragraph (8) has been approved prior to such date;

"(B) The date on which a denial of approval order is issued under paragraph (8)(C), if the applicant does not appeal the order under subsection (f)(4) and if such denial occurs prior to the date of expiration of provisional approval; or

"(C) The date on which the Director of the Center for Devices and Radiological Health or the Director of the Center for Biologics Evaluation and Research, whichever is appropriate, issues a decision on an appeal regarding an application for approval, if such decision occurs prior to the date of expiration of provisional approval.

"(11) WITHDRAWAL.

"(A) The Secretary may, based on new valid scientific evidence and after providing due notice and an opportunity for an informal hearing, issue an order withdrawing the provisional approval of an in vitro clinical test under this subsection if the Secretary determines that—

"(i) the test no longer meets the relevant standard; or

"(ii) the test presents an unreasonable risk to human health.

"(B) An order withdrawing approval shall state each ground for withdrawal and shall notify holders of such applications that they may, by petition filed on or before the [thirtieth] day after the date upon which he receives notice of such withdrawal, obtain review under section [appeals].

"(C) The Secretary shall provide notice of the withdrawal order on the website of the Food and Drug Administration.

"(f) ANNUAL REPORT. Unless otherwise specified by the Secretary, section [premarket approval; (g)] requiring annual reports applies to in vitro clinical tests provisionally approved or approved under this subsection.

"(g) SERVICE OF ORDERS. Orders of the Secretary under this section shall be served (1) in person by any officer or employee of the Department of Health and Human Services designated by the Secretary, or (2) by mailing the order by registered mail or certified mail or electronic equivalent addressed to the applicant at his last known address in the records of the Secretary.

"(h) STATUTORY CONSTRUCTION—The term "approval" when used throughout this title generally does not include provisional approval and does include approval under paragraph (8) of subsection (e).

"SEC. 587D. PRECERTIFICATION.

"(a) IN GENERAL. —

"(1) Any eligible person may seek precertification in accordance with this section.

"(2) An in vitro clinical test is exempt from premarket review under section 587A if its developer is precertified under this section and the in vitro clinical test—

"(A) is an eligible in vitro clinical test under subsection (b)(2); and

"(B) falls within the scope of a precertification order issued under this section, and such order is in effect.

"(b) ELIGIBILITY. —

"(1) ELIGIBLE PERSON. — As used in this section, the term 'eligible person' means an in vitro clinical test developer unless, at the time such person seeks or would seek precertification, the person—

"(A) has been found to have committed a significant violation of this Act or the Public Health Service Act, except that this subparagraph shall not apply if—

"(i) such violation occurred more than five years prior to the date on which such precertification is or would be sought;

"(ii) such violation has been resolved; or

"(iii) such violation is not pertinent to any in vitro clinical test within the scope of the precertification that such person seeks or would seek; or

"(B) has been disqualified by the Secretary on the basis of actions or omissions that raise serious questions regarding whether the eligibility of such person would be in the interest of public health, such as—

"(i) making false or misleading statements about matters relevant under this subchapter;

"(ii) failing to maintain required certifications under section 353 of the Public Health Service Act (42 U.S.C. 263a); or

"(iii) violating any requirement of this Act or the Public Health Service Act, where such violation exposes persons to serious risk of illness, injury, or death.

"(2) ELIGIBLE IN VITRO CLINICAL TEST.—An in vitro clinical test is eligible under subsection (a)(2) for exemption from premarket review under section 587A except as provided in this paragraph.

"(A) An in vitro clinical test is not eligible for an exemption from premarket review if it is—

"(i) a component, part, or accessory of an in vitro clinical test as described under section 201(ss)(1)(E);

"(ii) a test platform under section 201(ss)(1)(B);

"(iii) an article for taking or deriving specimens from the human body under section 201(ss)(1)(C);

"(iv) software under section 201(ss)(1)(D), unless such software itself identifies, diagnoses, screens, measures, detects, predicts, prognoses, analyzes, or monitors a disease or condition, including a determination of the state of health, or itself selects, monitors, or informs therapy or treatment for a disease or condition;

"(v) a first-of-a-kind in vitro clinical test;

"(vi) a test system for home use;

high risk in vitro clinical test; or

"(vii) an in vitro clinical test, including reagents used in such tests, intended for use—

"(I) in the collection, manufacture, or use of blood and blood components intended for transfusion or further manufacturing use or the recovery, manufacture, or use of human cells, tissues, and cellular and tissue-based products intended for implantation, transplantation, infusion, or transfer into a human recipient, including tests intended for use in determination of donor eligibility, donation suitability, and compatibility between donor and recipient;

"(II) in the diagnosis, monitoring, or treatment of hemolytic disease of the newborn, including tests intended for use in determination of compatibility between mother and newborn; or

"(III) in the diagnosis or monitoring of human retroviruses or human retrovirus infection.

"(B) For a cross-referenced in vitro clinical test or a direct-to-consumer in vitro clinical test, such test shall be eligible for precertification only upon a determination by the Secretary that eligibility is appropriate on the basis of the mitigating measures applicable to such test. Notwithstanding subchapter II of chapter 5 of title 5, any determination by the Secretary under this subparagraph—

"(i) shall take effect if it is published in the Federal Register with an accompanying rationale; and

"(ii) may be revoked if the Secretary publishes a proposed revocation in the Federal Register, provides an opportunity for comment, and publishes a final revocation after consideration of the comments.

"(c) APPLICATION FOR PRECERTIFICATION. —

"(1) IN GENERAL -- A person seeking precertification [ ][] shall submit an application under this subsection, which shall contain the information specified under paragraph (2).

"(2) CONTENTS OF APPLICATION -- An application for precertification shall contain—

"(A) A statement identifying the scope of the proposed precertification, which shall be no broader than a single technology (i.e., test method) and a single medical subspecialty (such as would be described by the combination of a test purpose and disease or condition), consistent with the procedures for analytical validation and clinical validation included in the application;

"(B) Information showing that the person seeking precertification is an eligible person under subsection (b)(1);

"(C) Information showing that the methods used in, and the facilities and controls used for, the development of all eligible in vitro clinical tests within the proposed scope of precertification conform to the quality system requirements of section [quality systems];

"(D) Procedures for analytical validation, including all procedures for validation, verification, and acceptance criteria, and an explanation as to how such procedures, when used, provide a reasonable assurance of analytical validity of all eligible in vitro clinical tests within the proposed scope of precertification;

"(E) Procedures for clinical validation, including all procedures for validation, verification, and acceptance criteria, and an explanation as to how such procedures, when used, provide a reasonable assurance of clinical validity of all eligible in vitro clinical tests within the proposed scope of precertification;

"(F) A notification under section [x] for each in vitro clinical test that would be precertified under the application for precertification and would be introduced or delivered for introduction into interstate commerce upon the issuance of the precertification order;

"(G) Information concerning one or more representative in vitro clinical tests, including—

"(i) The information specified in [premarket submission content requirements] for the representative in vitro clinical test or tests, except that raw data shall be provided for any such in vitro clinical test unless the Secretary determines otherwise;

"(ii) An explanation of how the representative in vitro clinical test or tests adequately represent the range of procedures included in the application under subparagraphs (C), (D), (E), and (F);

"(iii) A narrative description of how the procedures included in the application under subparagraphs (C), (D), (E), and (F) have been applied to the representative in vitro clinical test or tests; and

"(H) Such other information relevant to the subject matter of the application as the Secretary may require.

"(d) ACTION ON AN APPLICATION FOR PRECERTIFICATION. —

"(1) As promptly as possible, but in no event later than __ days after receipt of an application under subsection (c), the Secretary shall—

"(A) Issue a precertification order granting the application, which shall specify the scope of the precertification, if the Secretary finds that all of the grounds in paragraph (3) are met; or

"(B) Deny the application if the Secretary finds (and sets forth the basis of such finding as part of or accompanying such denial) that one or more grounds for granting the application specified in paragraph (3) are not met.

"(2) If, after receipt of an application under this section, the Secretary determines that any portion of such application is deficient, the Secretary shall provide to the applicant a

description of such deficiencies and identify the information required to correct such deficiencies.

"(3) The Secretary shall grant an application under this section if, on the basis of the information submitted to the Secretary as part of the application and any other information before him or her with respect to such applicant, the Secretary finds that—

"(A) There is a showing of reasonable assurance of analytical validity for all eligible in vitro clinical tests within the proposed scope of the precertification, as evidenced by the procedures for analytical validation;

"(B) There is a showing of reasonable assurance of clinical validity for all eligible in vitro clinical tests within the proposed scope of the precertification, as evidenced by the procedures for clinical validation;

"(C) The methods used in, or the facilities or controls used for, the development of all eligible in vitro clinical tests within the proposed scope of the precertification conform to the requirements of section [quality systems];

"(D) Based on a fair evaluation of all material facts, the applicant's labeling and advertising is not false or misleading in any particular;

"(E) The application does not contain a false statement of material fact;

"(F) There is a showing that the representative in vitro clinical test or tests—

"(i) meets the standard for approval under section [premarket review standard]; and

"(ii) adequately represent the range of procedures for analytical validation and clinical validation included in the application; and

"(G) The applicant permits authorized employees of the Food and Drug Administration or persons accredited under this Act an opportunity to inspect at a reasonable time and in a reasonable manner the facilities and all pertinent equipment, finished and unfinished materials, containers, and labeling therein, including all things (including records, files, papers, and controls) bearing on whether an in vitro clinical test is adulterated, misbranded, or otherwise in violation of this Act, and permits such authorized employees or persons accredited under this Act to view and to copy and verify all records pertinent to the application and the in vitro clinical test;

"(4) An applicant whose application has been denied may, by petition filed on or before the date that is 30 calendar days after the date upon which such applicant receives notice of such denial, obtain review thereof in accordance with section [appeals].

"(e) DURATION; SUBSEQUENT SUBMISSIONS. —

"(1) A precertification order under subsection (d)(1)(A) shall remain in effect until the earliest of—

"(A) the expiration of such precertification order under paragraph (2); or

"(B) the withdrawal of such precertification order under subsection (h).

"(2) A precertification order under subsection (d)(1)(A) shall expire on the date that is two years after the date that such order is issued, except that if an application for renewal under paragraph (3) has been received not later than __ days prior to the expiration of such order under this paragraph, such order shall expire on the date on which the Secretary has granted or denied the application for renewal.

"(3)(A) Any person with a precertification order in effect with respect to development of in vitro clinical tests may seek renewal of such order provided that –

"(i) such person is an eligible person under subsection (b)(1); and

"(ii) none of the information specified in subsection (c)(2) has changed.

"(B) An application for renewal under this paragraph shall include information concerning one or more representative in vitro clinical tests in accordance with subsection (c)(2)(G), except that such representative test or tests shall be different from the representative test or tests included in any prior application.

"(C) The Secretary's action on an application for renewal of precertification under this paragraph shall be conducted in accordance with subsection (d), and any order resulting from such application shall be treated as a precertification order for purposes of this subchapter.

"(4) SUPPLEMENTS; REPORTS. —

"(A) Except as provided in subparagraph (B), any person with a precertification order in effect may seek a supplement to such order upon a change or changes to the information provided in the application for precertification under subparagraphs (C), (D), and (E) of subsection (c)(2), provided that such person is an eligible person under subsection (b)(1) and that such change does not expand the scope of the precertification. A supplement may contain only information relevant to the change or changes. The Secretary's action on a supplement shall be in accordance with subsection (d), and any order resulting from such supplement shall be treated as an amendment to a precertification order that is in effect.

"(B) If a change or changes described in subparagraph (A) is made in order to address a potential risk to public health by adding a new specification or test method, the person may immediately implement such change or changes and shall report such changes or changes to the Secretary within 30 days.

"(i) Any report to the Secretary under this subparagraph shall include—

"(I) A summary of the relevant change or changes;

"(II) The rationale for implementing such change or changes; and

"(III) A description of how the change or changes were evaluated.

"(ii) Upon review of such report and a finding that the relevant change or changes are inconsistent with the standard specified under this subparagraph, the Secretary may require a supplement under subparagraph (A).

"(f) MAINTENANCE REQUIREMENTS. — For the duration of a precertification under subsection (e)(1), a holder of a precertification order shall—

"(1) use the procedures included in the relevant application, supplement, or report under subsections (b) and (e);

"(2) ensure compliance with any applicable mitigating measures;

"(3) maintain, and provide to the Secretary upon request, records related to any precertified in vitro clinical test that are pertinent to matters under this Act; and

"(4) Comply with the notification requirements under section [notification] for each precertified in vitro clinical test.

"(g) TEMPORARY HOLD. —

"(1) Upon one or more findings under paragraph (3), the Secretary may prohibit any holder of a precertification order from introducing into interstate commerce an in vitro clinical test that was not previously the subject of a notification under section [notification] (referred to in this subsection as a "temporary hold").

"(2) Such temporary hold shall be removed upon resolution of the relevant finding or findings under paragraph (3).

"(3) GROUNDS FOR TEMPORARY HOLD. — A temporary hold under this subsection may be instated upon a finding or findings that the holder of a precertification order—

"(A)is not in compliance with any maintenance requirements under subsection (f);

"(B)labels or advertises one or more in vitro clinical tests with false or misleading claims; or

"(C)is no longer an eligible person under subsection (b)(1).

"(h) WITHDRAWAL. — The Secretary may, after due notice and opportunity for informal hearing, issue an order withdrawing a precertification order if the Secretary finds that

"(1) the application, supplement, or report under subsections (b) or (e) contains false or misleading information or fails to reveal a material fact; or

"(2) such holder fails to correct false or misleading labeling or advertising upon the request of the Secretary;

"(3) in connection with a precertification, the holder provides false or misleading information to the Secretary; or

"(4) the holder of such precertification order fails to correct the grounds for temporary hold within a timeframe specified in the precertification order.

"SEC. 587E. MITIGATING MEASURES

"(a) DEFINITION. The term 'mitigating measures' shall have the meaning set forth in section [Definitions587(10)].

"(b) ESTABLISHMENT OF MITIGATING MEASURES--

"(1) ESTABLISHING, CHANGING, OR WITHDRAWING –

"(A) If the Secretary determines that the establishment of mitigating measures is necessary for any of the reasons identified in [definitions section] for any test group or test groups, the Secretary may require that tests in such group or groups comply with such mitigating measures.

"(B) The Secretary may establish, change, or withdraw mitigating measures by administrative order published in the Federal Register following publication of a proposed mitigating measure order and consideration of comments to a public docket, notwithstanding subchapter II of chapter 5 of title 5, United States Code.

"(2) In Vitro Clinical Tests Previously Regulated As Devices –

"(A) Any special controls or restrictions applicable to an in vitro clinical test or test group based on prior regulation as a device, including those established in the period from the enactment date to the effective date of this [subchapter/bill name], shall continue to apply to such test or test group after this[subchapter/bill name] takes effect. Such special controls or restrictions shall be deemed mitigating measures upon the effective date of this [subchapter/bill name].

"(B) The Secretary may establish, change, or withdraw mitigating measures for such test or test group using the procedures under paragraph (1).

"(c) DOCUMENTATION—

"(1) The developer of an in vitro clinical test subject to premarket review and to which mitigating measures apply must, in accordance with [section 587C(b)(2)(D) of premarket review] submit documentation to the Secretary as part of its premarket application demonstrating that such mitigating measures have been met. If such application is approved, such developer shall maintain documentation demonstrating that such mitigating measures continue to be met, and must make such documentation available to the Secretary upon request or inspection.

"(2) The developer of an in vitro clinical test that is marketed within the scope of a precertification or other exemption from premarket review and to which mitigating measures apply must –

"(A) maintain documentation in accordance with the quality systems requirements in [section QS] demonstrating that such mitigating measures have been met, and must make such documentation available to the Secretary upon request or inspection; and

"(B) include in the performance summary for such test a description of how such mitigating measures are met, if applicable.

[*Add adulteration/misbranding/prohibited act for failure to comply with mitigating measures*]

"SEC. 587F. RISK REDESIGNATION.

"(a) Based on new information, including the establishment of mitigating measures under [], and after considering all available evidence respecting a test group, the Secretary may, upon the initiative of the Secretary or upon petition of an interested person ---

"(1) change the risk designation of such test group;

"(2) revoke any exemption or requirement in effect with respect to such test group; or

"(3) determine that a test group or test groups subject to premarket review is eligible for precertification, consistent with section 587D(b)(2)(B), or other exemptions.

"(b) Any action under subsection (a) shall be made by publication of a notice of such proposed action in the Federal Register, consideration of comments to a public docket on such proposal, and publication of a final notice in the Federal Register, notwithstanding subchapter II of chapter 5 of title 5, United States Code.

"SEC. 587G. ADVISORY COMMITTEES [placeholder]

"SEC. 587H. REQUEST FOR INFORMAL FEEDBACK

PRESUBMISSION MEETINGS.—The Secretary shall establish a program for stakeholders to request meetings to discuss which regulatory pathway is appropriate for an in vitro clinical test, a future premarket application for an in vitro clinical test, or a precertification package for an in vitro clinical test.

"SEC. 587I. REGISTRATION AND NOTIFICATION.

"(a) REGISTRATION OF ESTABLISHMENTS FOR IN VITRO CLINICAL TESTS.

"(1) Each person who is an in vitro clinical test developer— or a contract manufacturer (including contract packaging), contract sterilizer, repackager, relabeler, distributor, or a person who introduces or proposes to begin the introduction or delivery for introduction into interstate commerce any in vitro clinical test—— shall –

"(A) During the period beginning on October 1 and ending on December 31 of each year, register with the Secretary the name of such person, places of business of such person, all establishments engaged in the activities specified under this paragraph, the unique facility identifier of each such establishment, and a point of contact for each such establishment, including an electronic point of contact; and

"(B) Submit an initial registration containing the information required under subparagraph (A) not later than—

"(i) the date of implementation of this section if such establishment is engaged in any activity described in this paragraph on the date of enactment of this section, unless the Secretary establishes by guidance a date later than such implementation date for all or a category of such establishments; or

” (ii) thirty days prior to engaging in any activity described in this paragraph after enactment of this section, if such establishment is not engaged in any activity described in this paragraph on the date of enactment of this section.

“(2) The Secretary may assign a registration number or unique facility identifier to any person or any establishment registered in accordance with this section. Registration information shall be made publicly available by publication on the website maintained by the Food and Drug Administration.

“(3) Every person or establishment that is required to be registered with the Secretary under this section shall be subject to inspection pursuant to section 704.

“(b) NOTIFICATION INFORMATION FOR IN VITRO CLINICAL TESTS.

“(1) Each developer of an in vitro clinical test shall submit a notification to the Secretary containing the information described in this subsection in accordance with the applicable schedule described under subsection (c). Such notification shall be prepared in such form and manner as the Secretary may specify in guidance. Notification information shall be submitted to the comprehensive test information system in accordance with section XX.

“(2) Each developer shall electronically submit to the comprehensive test information system the following information for each in vitro clinical test for which such person is a developer in the form and manner prescribed by the Secretary:

“(A) name of the establishment and its unique facility identifier;

“(B) contact information for the official correspondent for the notification;

“(C) name (common name and trade name, if applicable) of the in vitro clinical test; and its test notification number (when available).

“(D) CLIA certificate number for any laboratory certified by the Secretary under section 263a of title 42 that meets the requirements for performing high-complexity testing that is the developer of the in vitro clinical test, and CLIA certificate number for any laboratory under common ownership that is performing the test developed by such test developer;

“(E) the appropriate category under this subchapter under which the in vitro clinical test is offered, introduced or marketed, such as — precertification, low-risk exemption, premarket approval, grandfathering, or another specified category;

“(F) brief narrative description of the in vitro clinical test;

“(G) substance or substances measured by the in vitro clinical test, such as analyte, protein, or pathogen;

“(H) type or types of specimen or sample;

“(I) test method;

“(J) test purpose, as described in section 201(ss)(1)(A), such as screening, predicting, or monitoring;

“(K) disease or condition for which the in vitro clinical test is intended for use;

"(L) intended patient population;

"(M) context of use, such as in a clinical laboratory, in a health care facility, prescription home use, over-the-counter use, or direct-to-consumer testing.

"(N) summary of in vitro clinical test analytical performance and clinical performance, and as applicable lot release criteria;

"(O) statement describing conformance with applicable mitigating measures, restrictions, and standards;

"(P) representative labeling for the in vitro clinical test; and

"(Q) a certification that the information submitted is truthful and accurate.

"(3) The Secretary may assign a test notification number to each in vitro clinical test that is the subject of a notification under this section. The process for assigning test notification numbers may be established through guidance, and may include the recognition of standards, formats, or conventions developed by a third-party organization.

"(4) A person who is not a developer but is otherwise required to register pursuant to subsection (a) shall submit an abbreviated notification to the Secretary containing the information described in subparagraphs (A) through (C) of paragraph (2), the name of the developer, and any other information described in paragraph (2) as may be specified by the Secretary in guidance, as applicable to the activities of each class of persons required to register. The information shall be submitted in accordance with the applicable schedule described under subsection (c). Such abbreviated notification shall be prepared in such form and manner as the Secretary may specify in guidance. Notification information shall be submitted to the comprehensive test information system in accordance with section XX.

"(c) TIMELINES FOR SUBMISSION

"(1) For an in vitro clinical test that was listed as a device under section 510(j) prior to the date of enactment of this section, a person shall maintain a device listing under section 510 until such time as the system for submitting the notification information required under subsection (b) becomes available to in vitro clinical test developers, and thereafter shall submit the notification information no later than [X].

"(2) For an in vitro clinical test that is subject to the grandfathering provisions of section 587Xxx, a person shall submit the notification information required under subsection (b) no later than X months after the system for submitting the notification becomes available.

"(3) For an in vitro clinical test that is not subject to paragraph (1) or (2), a person shall submit the required notification information prior to offering, introducing, or marketing the in vitro clinical test as follows:

"(A)for an in vitro clinical test that is not exempt from premarket approval, a person shall submit the required notification information no later than ten business days after the date of approval of the premarket approval application;

"(B)for an in vitro clinical test that is exempt from premarket approval, a person shall submit the required notification information at least ten business days prior

to offering the in vitro test for clinical use or otherwise introducing the in vitro clinical test into interstate commerce.

"(4) Each person required to submit notification information under this section shall update such information within ten business days of any change that causes any previously notified information to be inaccurate or incomplete.

"(5) Each person required to submit notification information under this section shall update its information annually during the period beginning on October 1 and ending on December 31 of each year and certify that the information contained in such notification is truthful and accurate, and shall pay the annual notification fee prescribed in section XXX.

"(d) PUBLIC AVAILABILITY OF NOTIFICATION INFORMATION.

"(1) Notification information submitted pursuant to this section shall be made publicly available by publication on the website of the Food and Drug Administration after the in vitro clinical test developer has certified the information as truthful and accurate.

"(2) Notification information for an in vitro clinical test that is subject to premarket approval or precertification shall remain confidential until such date as the in vitro clinical test receives the applicable premarket approval or precertification.

"(3) The registration and notification information requirements described in subsections (a) and (b) shall not apply to the extent the Secretary determines that such information is restricted from disclosure pursuant to another statute, including information relating to national security or countermeasures.

"SEC. 587J.

QUALITY SYSTEM REQUIREMENTS

"(a) APPLICABILITY.

"(1) Each developer and each other person required to register undersection 587I(a)(1) shall establish and maintain a quality system in accordance with the applicable requirements set forth in subsection (b), except as provided in section [applicability].

"(2) A developer that operates its own clinical laboratory certified by the Secretary under section 263a of title 42 of the United States Code that meets the requirements for performing high-complexity testing and develops its own in vitro clinical test or tests or modifies another developer's in vitro clinical test in that certified laboratory in a manner described in [developer definition], where such in vitro clinical test or in vitro clinical tests are for use only within that certified laboratory, shall establish and maintain with respect to such test or tests a quality system that complies with the requirements set forth in subsection (b)(2). The applicable requirements set forth in subsection (b)(1) shall apply to any test platform, article for taking or deriving specimens from the human body, component, part or accessory that is developed for use by a clinical laboratory to which the first sentence of this paragraph applies.

"(3) A clinical laboratory certified by the Secretary under section 263a of title 42 of the United States Code that meets the requirements for performing high-complexity testing

must comply with the applicable quality system requirements under subsection (b) no later than the date of implementation of this subchapter.

"(4) As necessary, the Secretary shall amend part 820 of title 21 of the Code of Federal Regulations, or successor regulations, to implement the provisions of this [section]. In considering such amendment, the Secretary shall consider whether and to what extent international harmonization might be appropriate. Until such amendment takes effect, such regulations shall be interpreted to apply to in vitro clinical tests and developers.

"(5) The Secretary may establish such other regulations under this section as are necessary to assure the analytical and clinical validity of in vitro clinical tests, or the safety of articles for taking or deriving specimens from the human body.

"(b) QUALITY SYSTEM REQUIREMENTS.

"(1) IN GENERAL—-- For—-- For purposes of establishing quality system requirements under this [section], including applying or amending 21 CFR part 820 as provided in subsection (a)(4), the quality system requirements applicable to in vitro clinical tests shall include each of the following, subject to paragraphs (2) and (3):

"(A) management responsibility;

"(B) quality audit;

"(C) personnel;

"(D) design controls;

"(E) document controls;

"(F)purchasing controls, including supplier controls;

"(G) identification and Traceability;

"(H) production and process controls;

"(I) acceptance activities;

"(J) nonconforming product;

"(K) corrective and preventive action;

"(L) labeling and packaging controls;

"(M) handling, storage, distribution, and installation;

"(N) records;

"(O) servicing; and

"(P) statistical techniques.

"(2) QUALITY SYSTEM REQUIREMENTS FOR CERTAIN LABORATORIES.— With regard to establishing quality system requirements under this Act, including applying or amending 21 CFR part 820 as provided in subsection (a)(4), quality system requirements applicable to the in vitro clinical tests and developers described in subsection (a)(2) shall consist of the following:

"(A) design controls;

"(B) purchasing controls, including supplier controls;

(C) acceptance activities;

"(D) corrective and preventative action; and

"(E) records.

"(3) QUALITY SYSTEM REQUIREMENTS FOR CERTAIN LABORATORIES DISTRIBUTING PROTOCOLS.—

"(A) With regard to establishing quality system requirements under this Act, including applying or amending 21 CFR part 820 as provided in subsection (a)(4), quality system requirements applicable to the developer and in vitro clinical test distributed under subparagraph (B) shall consist of the following provided that the conditions of subparagraph (B) are met —

"(i) the requirements in paragraph (2),

"(ii) the labeling requirements in subparagraph (1)(L), and

"(iii) the requirement to maintain records of the laboratories to which the test protocol is distributed.

"(B) To be eligible for subparagraph (A), the following conditions must be met—

"(i) the laboratory distributing the protocol is certified by the Secretary under section 263a of title 42 of the United States Code and meets the requirements for performing high-complexity testing;

"(ii) the laboratory develops its own in vitro clinical test or modifies another developer's in vitro clinical test in a manner described in [Section 587(6)]; and

"(iii) the laboratory distributes the test protocol for such test only to another laboratory that—

(I) is certified by the Secretary under section 263a of title 42 of the United States Code and meets the requirements for performing high-complexity testing; and

"(II) is within the same corporate organization and having common ownership by the same parent corporation; or as applicable, is within the Laboratory Response Network of the Centers for Disease Control and Prevention.

"SEC. 587K. LABELING REQUIREMENTS.

"(a) IN GENERAL. An in vitro clinical test shall bear or be accompanied by labeling, and a label as applicable, that meet the requirements set forth in subsections (b) and (c), and any other requirements established by the Secretary by regulations, unless such test is exempt as specified in subsection (d) or (e).

"(b) LABELS. —

"(1) The label of an in vitro clinical test shall meet the requirements set forth in paragraph (2), except this requirement shall not apply to an in vitro clinical test that consists solely of a test protocol, or that is designed, manufactured, and used solely within a single laboratory certified by the Secretary under section 263a of title 42 that meets the requirements for performing high-complexity testing.

"(2) The label of an in vitro clinical test shall state the name and place of business of its developer and meet the requirements set forth in section 809.10(a) of title 21 of the Code of Federal Regulations, or any successor regulation. The Secretary shall amend such regulation, as necessary, to ensure its applicability to in vitro clinical tests. Until such amendment takes effect, such regulations shall be interpreted to apply to in vitro clinical tests.

"(c) LABELING. —

"(1) Labeling accompanying an in vitro clinical test, including labeling in the form of a package insert, standalone laboratory reference document, or other similar document except the labeling specified in paragraph (2), shall include adequate directions for use and shall meet the requirements set forth in section 809.10(b) and (g) of title 21 of the Code of Federal Regulations, or any successor regulation, except as provided in subsection (d). Labeling in the form of a package insert shall also include the information in subparagraphs (2)(A) through (C). The Secretary shall amend such regulation, as necessary, to ensure its applicability to in vitro clinical tests. Until such amendment takes effect, such regulation shall be interpreted to apply to in vitro clinical tests.

"(2) Labeling accompanying an in vitro clinical test that is in the form of a test report template or ordering information shall include

"(A) The test notification number that was provided to the developer at the time of notification;

"(B) Instructions for how and where to report an adverse event under section [Adverse Events], such as "Please report adverse events related to this test to the FDA at X."; and

"(C) Instructions for how and where to access the performance summary data displayed in the notification database for the test.

(D)The intended use of the in vitro clinical test;

(E) Any warnings,

(F) Contraindications, and

(G) Limitations.

"(3) Labeling for an in vitro clinical test [used for] immunohematology testing shall meet the following additional requirements set forth in part 660 of the Code of Federal Regulations (or any successor regulation), as they appear on the date of enactment of this subchapter if to the extent such test fell within the scope of such regulations immediately prior to such date of enactment:

(A) Section 660.28 (a)(1)(i); (a)(1)(ii)(A) and (F); (a)(2)(i) and (xiv); and (a)(4);

(B) Section 660.35 (a)(1)(ii); (a)(2) - (4); (a)(6) - (9); and

(C) Section 660.55 (a)(1)(i); (a)(1)(ii)(A) and (H).

The Secretary shall amend such regulations, as necessary, to ensure their applicability to in vitro clinical tests. Until such amendment takes effect, such regulations shall be interpreted to apply to in vitro clinical tests.

"(d) EXEMPTIONS AND ALTERNATIVE REQUIREMENTS.

"(1) For an in vitro clinical test that is designed, manufactured, and used solely within a single high complexity laboratory certified by the Secretary under section 353353 of the Public Health Service Act, and owned and operated by the developer of such in vitro clinical test, the requirement in section 809.10(b) of title 21 of the Code of Federal Regulations that the labeling "state in one place" all of the required information may be satisfied by the laboratory posting such required information on its website or in multiple documents, if such documents are maintained and accessible in one place.

"(2) The labeling for a test platform, when such platform is not committed to specific diagnostic procedures or systems, is not required to bear the information indicated in paragraphs (3), (4), (5), (7), (8), (9), (10), (11), (12), and (13) of section 809.10(b) of title 21 of the Code of Federal Regulations, as it appears on the date of enactment of this subchapter and amended thereafter.

"(3) For purposes of compliance with subsection (c)(1), the labeling for a reagent intended for use as a replacement in a diagnostic system may be limited to that information necessary to identify the reagent adequately and to describe its proper use in the system.

"(4) LAB RESEARCH OR INVESTIGATIONAL USE. A shipment or other delivery of an in vitro diagnostic test shall be exempt from the requirements of subsection (b) and (c)(1) and from any standard promulgated under part 861 of title 21 of the Code of Federal Regulations, or any successor regulation, provided that the conditions set forth in 809.10(c) of such title, as it appears on the date of enactment of this subchapter and amended thereafter are met. The Secretary shall amend such regulations, as necessary, to ensure their applicability to in vitro clinical tests. Until such amendment takes effect, such regulations shall be interpreted to apply to in vitro clinical tests.

"(5) GENERAL PURPOSE LABORATORY REAGENTS. The labeling of general purpose laboratory reagents, such as hydrochloric acid, whose uses are generally known by persons trained in their use need not bear the directions for use required by subsection (b) and subsection (c)(1).

"(6) ANALYTE SPECIFIC REAGENTS. The labeling of analyte specific reagents, such as monoclonal antibodies, deoxyribonucleic acid (DNA) probes, viral antigens, ligands and other similar items, shall bear the information set forth in 21 C.F.R. 809.10(e)(1) through (2) as it appears on the date of enactment of this subchapter and amended thereafter and shall bear the following statement - "This product is intended solely for further

development of an in vitro clinical test and is exempt from most FDA regulation. This product must be evaluated by the in vitro clinical test developer in accordance with supplier controls if it is used with or in the development of an in vitro clinical test.". If the labeling of an analyte specific reagent bears the information set forth in this paragraph, it need not bear the information required by subsection (c)(1).

"(7) The labeling for over-the-counter (OTC) test sample collection systems for drugs of abuse testing shall bear the name and place of business of the developer and the information specified in 21 C.F.R. 809.10(f) as it appears on the date of enactment of this subchapter and amended thereafter, in language appropriate for the intended users. If the labeling of such OTC test sample collection system bears the information set forth in this paragraph (4)(G), it need not bear the information required by subsection (c)(1).

"(8) The labeling for an in vitro clinical test approved under [subsection (d) of priority review/provisional approval section], until approved under [subsection (e) of that section], or approved under [subsection (e) of premarket review], until approved under that section, shall bear a statement that the test is "provisionally approved with confirmatory postmarket obligations."

"(e) TESTS IN THE STRATEGIC NATIONAL STOCKPILE.

"(1) The Secretary may grant an exception or alternative to any provision listed in this section, unless explicitly required by a statutory provision outside this section, for specified lots, batches, or other units of an in vitro clinical test, if the Secretary determines that compliance with such labeling requirement could adversely affect the safety, effectiveness, or availability of such products that are or will be included in the Strategic National Stockpile.

"(2) The Secretary may issue regulations amending section 809.11 of title 21 of the Code of Federal Regulations or any successor regulation to apply in full or in part to in vitro clinical tests and in vitro clinical test developers.

"(f) The Secretary may, in collaboration with developers, issue guidance on standardized, general content and format for in vitro clinical test labeling to help ensure compliance with applicable requirements in this subsection."

"SEC. 587L. ADVERSE EVENT REPORTING.

"(a) APPLICABILITY.

"(1) Each in vitro clinical test developer shall establish, maintain, and implement a system for reporting adverse events in accordance with subsection (b), except as provided in section [applicability].

"(2) The Secretary shall amend part 803 of Title 21 of the Code of Federal Regulations (or any successor regulations) to apply to in vitro clinical tests. Until such amendment takes effect, such part shall be interpreted to apply to in vitro clinical tests.

"(3) The Secretary may by regulation require reporting of such other adverse event experiences as determined by the Secretary to be necessary to be reported to assure the analytical and clinical validity of in vitro clinical tests, and in addition, the safety of articles for taking or deriving specimens from the human body.

"(b) ADVERSE EVENT REPORTING REQUIREMENTS.

"(1) Each in vitro clinical test developer shall report to the Secretary whenever the developer receives or otherwise becomes aware of information that reasonably suggests that one of its in vitro clinical tests–

"(A) may have caused or contributed to a death or serious injury, or

"(B) has malfunctioned and the in vitro clinical test, or a similar in vitro clinical test developed or marketed by the in vitro clinical test developer, would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, and

"(C) such adverse event cannot be directly attributed to laboratory error.

"(2) For purposes of this section, the term "serious injury" shall mean—

"(A) a critical delay in diagnosis or causing the absence, delay, or discontinuation of appropriate medical treatment; or

"(B) an injury that—

"(i) is life threatening,

"(ii) results in permanent impairment of a body function or permanent damage to a body structure, or

"(iii) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

"(3) Reports required under this section shall be submitted as follows:

"(A) An individual adverse event reports shall be submitted for the following events not later than—

"(i) 5 calendar days after an in vitro clinical test developer receives or otherwise becomes aware of information that reasonably suggests the adverse event involves a patient death; or

"(ii) 5 calendar days after an in vitro clinical test developer receives or otherwise becomes aware of information that reasonably suggests the event presents an imminent threat to public health.

"(B) Quarterly reports shall be submitted for all other adverse events and no later than the end of the quarter following the quarter in which the adverse event information was received by the in vitro clinical test developer.

[ ]**“SEC.587M. CORRECTIONS AND REMOVALS**

“(a) APPLICABILITY.

“(1) The Secretary shall amend part 806 of Title 21 of the Code of Federal Regulations (or any successor regulations) to apply to in vitro clinical tests. Until such amendment takes effect, such part shall be interpreted to apply to in vitro clinical tests.

“(2) The Secretary may by regulation require reporting of such corrections and removals as determined by the Secretary to be necessary to be reported to assure the analytical and clinical validity of in vitro clinical tests, and in addition, the safety of articles for taking or deriving specimens from the human body.

“(b) Reports of Removals and Corrections

(1) Each in vitro clinical test developer or importer shall report to the Secretary any correction or removal of an in vitro clinical test undertaken by such developer or importer if the removal or correction was undertaken –

(A) To reduce the risk to health posed by the in vitro clinical test, or

(B) To remedy a violation of this Act caused by the in vitro clinical test which may present a risk to health.

(2) The developer or importer shall submit any report required under this subsection to the Secretary within 10 business days of initiating such correction or removal.

(3) A developer or importer of an in vitro clinical test who undertakes a correction or removal of an IVCT which is not required to be reported under this subsection shall keep a record of such correction or removal.

(4) For purposes of this section, the terms “correction” and “removal” do not include routine servicing.

“SEC. 587N. RESTRICTED IN VITRO CLINICAL TESTS.

“(a) APPLICABILITY.

“(1) IN GENERAL - The Secretary, in issuing an approval, provisional approval, or precertification under sections [587_, _, or _] of an in vitro clinical test of a category described in paragraph (3) may require that such test be restricted to sale, distribution, or use upon such conditions as the Secretary may prescribe under paragraph (2).

“(2) CONDITIONS PRESCRIBED BY THE SECRETARY – The conditions prescribed by the Secretary under this paragraph, with respect to an in vitro clinical test described in paragraph (3), are those conditions which the Secretary determines due to the potentiality for harmful effect of such test (including any resulting absence, delay, or discontinuation of appropriate medical treatment), are necessary to assure the analytical or clinical validity of the test, or the safety of an article for taking or deriving specimens from the human body.

"(3) IN VITRO CLINICAL TESTS SUBJECT TO RESTRICTIONS - The restrictions authorized under this section may be applied by the Secretary to any high-risk in vitro clinical test, prescription home-use in vitro clinical test, direct-to-consumer in vitro clinical test, or over-the-counter in vitro clinical test.

"(4) PROMULGATION OF REGULATIONS.—In addition to imposing restrictions under paragraph (1), the Secretary may promulgate regulations restricting the sale, distribution, or use of any in vitro clinical test described in paragraph (3), based on such conditions as may be prescribed by the Secretary under paragraph (2) with respect to such test.

"(b) LABELING AND ADVERTISING OF A RESTRICTED IN VITRO CLINICAL TEST.

"(1) The label, labeling, and advertising of an= in vitro clinical test to which restrictions apply under subsection (a) shall bear such appropriate statements of the restrictions as the Secretary may prescribe in the approval, provisional approval, precertification, or regulation, as applicable.

"(2) Except in extraordinary circumstances, the Secretary shall not require prior approval of the content of any advertisement, and no advertisement of a restricted in vitro clinical test, published after the effective date of this section shall, with respect to the matters specified in this section 587[ ] or in orders or regulations issued hereunder, be subject to the provisions of sections 12 through 15 of the Federal Trade Commission Act (15 U.S.C. §§52-55). This subparagraph shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 201(m).

"(c) An in vitro clinical test that was offered, sold, or distributed as a restricted device prior to the enactment date of this [subchapter/bill name] shall continue to comply with the applicable restrictions imposed under section 515 or section 520(e) until the effective date of restrictions issued under subsection (a).

"SEC. 587O. APPEALS. [*placeholder*]

"SEC. 587P. ACCREDITED PERSONS.

"(a) IN GENERAL.

"(1) REVIEW OF APPLICATIONS.

"(A) The Secretary may accredit persons for the purpose of reviewing applications for precertification and applications for premarket approval of an in vitro clinical test, and making recommendations to the Secretary with respect to such applications, subject to the requirements of this section.

"(B) The Secretary shall issue guidance on the factors that the Secretary will use in determining whether a test group or a scope of precertification is eligible for review by an accredited person.

"(C) In making a recommendation to the Secretary under this paragraph, an accredited person shall notify the Secretary in writing of the reasons for the recommendation concerning the application.

"(D) Not later than 90 days after the date on which the Secretary is notified of a recommendation under subparagraph (C) by an accredited person with respect to an application, the Secretary shall make a determination with respect to such application.

"(2) INSPECTIONS.

"(A) The Secretary may accredit persons for the purpose of conducting inspections under section 704 of in vitro clinical test developers and other persons required to register pursuant to section xxx, subject to the requirements of this section.

"(B) The Secretary shall issue guidance on the factors that the Secretary will use in determining whether an in vitro clinical test developer or other registered person is eligible for inspection by an accredited person.

"(C) Persons accredited to conduct inspections, when conducting such inspections, shall record in writing their specific observations and shall present their observations to the establishment's designated representative. Additionally, such accredited person shall prepare and submit to the Secretary an inspection report in a form and manner designated by the Secretary for conducting inspections, taking into consideration the goals of international harmonization of quality systems standards. Any official classification of the inspection shall be determined by the Secretary.

"(D) Any statement or representation made by an employee or agent of an establishment to a person accredited to conduct inspections shall be subject to section 1001 of title 18, United States Code.

"(E) Nothing in this section affects the authority of the Secretary to inspect any in vitro clinical test developer or other person registered under section XXX ..

"(b) ACCREDITATION.

"(1) ACCREDITATION PROGRAM.

"(A) The Secretary may provide for accreditation of persons to perform the duties specified under subsection (a) for some or all eligible in vitro clinical tests through programs administered by the Food and Drug Administration, by other non-Federal government agencies, or by qualified nongovernment organizations.

"(B) The Secretary shall issue guidance on the criteria that the Secretary will use to accredit or deny accreditation to a person who requests to perform any of the duties specified under subsection (a).

"(C) The Secretary shall not accredit or maintain accreditation for a person unless such person meets the minimum qualifications required under subsection (c).

"(D) The Secretary shall publish on the website of the Food and Drug Administration a list of persons who are accredited under this section. Such list shall be updated on at least a monthly basis. The list shall specify the particular activity or activities under this section for which the person is accredited.

"(2) ACCREDITATION PROCESS.

"(A) The Secretary shall issue guidance specifying the process for submitting a request for accreditation and reaccreditation under this section, including the form and content of information to be submitted in such a request.

"(B) The Secretary shall respond to a request for accreditation or reaccreditation within 90 days of the receipt of the request. The Secretary's response may be to accredit or reaccredit the person, to deny accreditation, or to request additional information in support of the request.

"(C) The accreditation of a person shall specify the particular activity or activities under subsection (a) for which such person is accredited, including if the activity is limited to certain eligible in vitro clinical tests.

"(D) The Secretary may audit the performance of persons accredited under this section for purposes of assuring that they continue to meet the published criteria for accreditation, and may modify the scope or particular activities for which a person is accredited if the Secretary determines that such person fails to meet one or more criteria for accreditation.

"(E) The Secretary may suspend or withdraw accreditation of any person accredited under this section, after providing notice and an opportunity for an informal hearing, when such person is substantially not in compliance with the requirements of this section or the published criteria for accreditation, or poses a threat to public health, or fails to act in a manner that is consistent with the purposes of this section.

(F) Accredited persons must be reaccredited at least every 2 years.

"(c) QUALIFICATIONS OF ACCREDITED PERSONS.

(1) An accredited person shall, at a minimum, meet the following requirements:

"(A) Such person may not be an employee of the Federal Government;

"(B) Such person shall not engage in the development of in vitro clinical tests and shall not be a person required to register under section XXX;

"(C) Such person shall not be owned or controlled by, and shall have no organizational, material or financial affiliation with, an in vitro clinical test developer or other person required to register under section XXX;

"(D) Such person shall be a legally constituted entity permitted to conduct the activities for which it seeks accreditation;

"(E) The operations of such person shall be in accordance with generally accepted professional and ethical business practices; and

"(F) Such person shall include in its request for accreditation a commitment to, at the time of accreditation and at any time it is performing activities pursuant to this section—

"(i) certify that the information reported to the Secretary accurately reflects the data or operations reviewed;

"(ii) limit work to that for which competence and capacity are available;

"(iii) treat information received or learned, records, reports, and recommendations as proprietary information of the person submitting such information; and

"(iv) in conducting the activities for which the person is accredited in respect to a particular in vitro clinical test, protect against the use of any employee or consultant who has a financial conflict of interest regarding that in vitro clinical test.

"(2) The Secretary may waive any requirements in subparagraphs (1)(A), (1)(B), or (1)(C) upon making a determination that such person has implemented other appropriate controls sufficient to ensure a competent and impartial review."

"(d) COMPENSATION OF ACCREDITED PERSONS.

"(1) Compensation of an accredited person who reviews an application for precertification or an application for premarket approval shall be determined by agreement between the accredited person and the person who engages the services of the accredited person, and shall be paid by the person who engages such services.

"(2) Compensation of an accredited person who is conducting an inspection under section 704 shall be determined by agreement between the accredited person and the person who engages the services of the accredited person, and shall be paid by the person who engages such services.

"(e) COOPERATIVE AGREEMENTS. The Secretary is authorized to enter into cooperative arrangements with officials of foreign countries to ensure that adequate and effective means are available for purposes of determining, from time to time, whether in vitro clinical tests intended for use in the United States by a person whose facility is located outside the United States shall be refused admission on any of the grounds set forth in section 801(a).

"SEC. 587Q. STANDARDS. [*placeholder*]

[placeholder for section authorizing FDA utilization of certain standards developed by non-governmental organizations in the review process]

"SEC. 587R. INVESTIGATIONAL USE

"(a) IN GENERAL. — Except as provided in subsection (c), an in vitro clinical test for investigational use shall be exempt from the requirements of this subchapter other than [sections

on appeals, preemption and applicability of FD&C Act].

"(b) The Secretary shall amend part 812 of Title 21 of the Code of Federal Regulations, or successor regulations, to apply as the Secretary deems appropriate to in vitro clinical tests and to implement the requirements in subsection (c). The Secretary shall amend parts 50, 54, and 56of Title 21 of the Code of Federal Regulations, or successor regulations, to apply as the Secretary deems appropriate to in vitro clinical tests. Until each such amendment takes effect, each such regulation shall be interpreted to apply to in vitro clinical tests.

"(c) APPLICATION FOR AN EXEMPTION.—

"(1) IN GENERAL.—

"(A)In the case of an in vitro clinical test the investigational use of which poses a significant risk, a sponsor of an investigation of such a test seeking an investigational use exemption shall submit to the Secretary an investigational use application with respect to the test in accordance with paragraphs (2) and (3). For purposes of this subparagraph, the term 'significant risk' means that the investigational use of the test—

"(i) is for a use of substantial importance in performing the activities described in section (ss)(1)(A) or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of an in vitro clinical test subject; or

"(ii) otherwise presents a potential for serious risk to the health, safety or welfare of a human subject of the in vitro clinical test.

"(B) In the case of an in vitro clinical test, the investigational use of which does not pose a significant risk—

"(i) the sponsor of such investigation shall comply with—

"(I) the requirements specified in paragraphs (3)(A), (3)(B), and (5)(A)(iii); and

"(II) such other requirements as the Secretary may determine to be necessary for the protection of the public health and safety, including the monitoring of investigations conducted with such test, the establishment and maintenance of records, or the submission to the Secretary of reports of data obtained as a result of the investigational use of the in vitro clinical test during the period covered by the exemption; and

"(ii) the sponsor may rely on any exception or exemption identified in paragraph (5)(B) or as established by the Secretary in regulations issued under subsection (b).b

"(2) APPLICATION CONTENTS.— An investigational use application shall be submitted in such time and manner and contain such information as the Secretary may require in regulation, and shall include assurances to the satisfaction of the Secretary that the sponsor involved shall, with respect to the in vitro clinical test that is the subject of the application—

"(A) establish and maintain any records relevant to such in vitro clinical test; and

"(B) submit to the Secretary reports of data obtained as a result of the investigational use of the in vitro clinical test during the period covered by the exemption that the Secretary reasonably determines will enable the Secretary—

"(i) to ensure compliance with the conditions for approval specified in paragraph (3);

"(ii) to review the progress of the investigation involved; and

"(iii) to evaluate the analytical validity and clinical validity of such test.

"(3) CONDITIONS OF APPROVAL.—An investigational use application with respect to an in vitro clinical test shall only be approved if each of the following conditions is met—

"(A) The Secretary finds that the risks to the subjects of the in vitro clinical test are outweighed by the anticipated benefits to the subjects and the importance of the knowledge to be gained, informed consent is adequate or waived, the investigation is scientifically sound, and there is no reason to believe that the in vitro clinical test as used is ineffective;

"(B) The proposed labeling for the in vitro clinical test involved clearly and conspicuously states 'For investigational use'; and

"(C) the sponsor submitting such application complies with the requirements of this section and such other requirements as the Secretary determines to be necessary for the protection of the public health and safety and requires in regulation.

"(4) COORDINATION WITH INVESTIGATIONAL NEW DRUG APPLICATIONS.—Any requirement for the submission of a report to the Secretary pursuant to an investigational new drug application involving an in vitro clinical test shall supersede the reporting requirement in paragraph (2)(B), but only to the extent the requirement with respect to the investigational new drug application is duplicative of the reporting requirement under such paragraph.

"(5) INVESTIGATION PLAN REQUIREMENTS.—

"(A) IN GENERAL.—With respect to a plan submitted under paragraph (3)(B), the sponsor submitting such plan shall—

"(i) in the case of such a plan submitted to an institutional review committee, promptly notify the Secretary of the approval or the suspension or termination of the approval of such plan by an institutional review committee;

"(ii) in the case of an in vitro clinical test to be distributed or otherwise made available to investigators for clinical testing, obtain, and submit to the Secretary, signed agreements from each of the individuals carrying out the investigation that is the subject of such plan that—

"(I) any testing under such plan involving human subjects will be under the supervision of such individual;

"(II) any testing under such plan will be conducted in compliance with the investigational plan and applicable regulations;

"(III) the individual will ensure that informed consent is obtained from each such human subject, except in cases specifically exempted pursuant to this section; and

"(IV) the individual will comply with additional investigator obligations as set forth in the final rule issued pursuant to subsection (b); and

"(iii) submit an assurance to the Secretary that informed consent will be obtained from each human subject (or the representative of such subject) of proposed clinical testing involving such in vitro clinical test, except in the following cases, for which informed consent is not required, subject to such other conditions as the Secretary may prescribe—

"(I) the proposed clinical testing poses no more than minimal risk to the human subject and includes appropriate safeguards to protect the rights, safety, and welfare of the human subject; or

"(II) the investigator conducting or supervising the proposed clinical testing determines (subject to subparagraph (B)(ii), with the concurrence of a licensed physician who is not involved in the testing of the human subject) in writing that—

"(aa) there exists a life-threatening situation involving the human subject of such testing which necessitates the use of such in vitro clinical test;

"(bb) it is not feasible to obtain informed consent from the subject; and

"(cc) there is not sufficient time to obtain such consent from a representative of such subject.

"(B) EXCEPTIONS.—

"(i) SIGNED AGREEMENTS NOT REQUIRED.—Subparagraph (A)(iii) shall not apply to the distribution of or other arrangements by a sponsor to make available an in vitro clinical test to an investigator that is employed by the sponsor.

"(ii) CONCURRENCE OF PHYSICIAN NOT REQUIRED.—The requirement to obtain the concurrence of a licensed physician or informed consent from the human subject's representative with respect to a determination under subparagraph (A)(iii)(II) shall not apply if—

"(I) immediate use of the in vitro clinical test in the investigation involved is required to save the life of the human subject; and

"(II) there is not sufficient time to obtain such concurrence.

"(iii) INFORMED CONSENT NOT REQUIRED WITH RESPECT TO CERTAIN SPECIMENS.— Notwithstanding subparagraph (A)(iii)(II), the informed consent of human subjects shall not be required with respect to clinical testing conducted as part of an investigation, if—

"(I) the clinical testing uses remnants of specimens collected for routine clinical care or analysis that would have been discarded, leftover specimens

that were previously collected for other research purposes, or specimens obtained from specimen repositories;

"(II) the identity of the subject of the specimen is not known to, and may not readily be ascertained by, the investigator or any other individual associated with the investigation, including the sponsor;

"(III) any clinical information that accompanies the specimens does not make the specimen source identifiable to the investigator or any other individual associated with the investigation, including the sponsor;

"(IV) the individuals caring for the human subjects as patients are different from, and do not share information about the patient with, the individuals conducting the investigation; and

"(V) the specimens are provided to the investigators without personally identifiable information and the supplier of the specimens has established policies and procedures to prevent the release of personally identifiable information.

"(6) VARIATION.—The requirements imposed under this subsection with respect to an investigational use application may vary based on—

"(A) the scope and duration of clinical testing to be conducted under investigation that is the subject of such application;

"(B) the number of human subjects that are to be involved in such testing;

"(C) the need to permit changes to be made in the in vitro clinical test involved during testing conducted in accordance with a plan required under paragraph (3)(B); or

"(D) whether the clinical testing of such in vitro clinical test is for the purpose of developing data to obtain approval to offer such test.

"(d) REVIEW OF APPLICATIONS.—

"(1) IN GENERAL.—The Secretary may issue an order approving an investigation as proposed, approving it with conditions or modifications, or disapproving it.

"(2) FAILURE TO ACT.—Unless the Secretary, not later than the date that is 30 calendar days after the date of the submission of an investigational use application that meets the requirements of subsection (c)(2), issues an order under subsection (d)(1) and notifies the sponsor submitting the application, the application shall be treated as approved as of such date without further action by the Secretary.

"(3) DISAPPROVAL.—The Secretary may disapprove an investigational use application submitted under this subsection if the Secretary determines that the investigation with respect to which the application is submitted does not conform to the requirements of subsection (c)(3). A notification of such disapproval submitted to the sponsor with respect to such an application shall contain the order of disapproval and a complete statement of the reasons for the Secretary's disapproval of the application.

"(e) WITHDRAWAL OF APPROVAL.—

"(1) IN GENERAL.—The Secretary may, by administrative order, withdraw the approval of an exemption granted under this subsection with respect to an in vitro clinical test, including an exemption granted based on the Secretary's failure to act pursuant to subsection (d)(2), if the Secretary determines that the test does not meet the applicable conditions under subsection (c)(3) for such approval.

"(2) OPPORTUNITY TO BE HEARD.—

"(A) IN GENERAL.—Subject to subparagraph (B), an order withdrawing the approval of an exemption granted under this subsection may be issued only after the Secretary provides the applicant or sponsor of the test with an opportunity for an informal hearing.

"(B) EXCEPTION.—An order referred to in subparagraph (A) with respect to an exemption granted under this subsection may be issued on a preliminary basis before the provision of an opportunity for an informal hearing if the Secretary determines that the continuation of testing under the exemption will result in an unreasonable risk to the public health. The Secretary will provide an opportunity for an informal hearing promptly following any preliminary action under this subparagraph.

"(f) CHANGES.—

"(1) IN GENERAL.—The amended regulations under subsection (b) shall provide, with respect to an in vitro clinical test for which an exemption under this subsection is in effect, procedures and conditions under which the changes to the test are allowed without the additional approval of an application for an exemption or the approval of a supplement to such an application. Such regulations shall provide that such a change may be made if—

"(A) the sponsor or applicant determines, on the basis of credible information (as defined by the Secretary) that the change meets the conditions specified in paragraph (2); and

"(B) the sponsor or applicant submits to the Secretary, not later than 5 calendar days after making the change, a notice of the change.

"(2) CONDITIONS.—The conditions specified in this paragraph are that—

"(A) in the case of developmental changes to an in vitro clinical test (including manufacturing changes), the changes—

"(i) do not constitute a significant change in design or in basic principles of operation;

"(ii) do not affect the rights, safety, or welfare of the human subjects (if any) involved in the investigation; and

"(iii) are made in response to information gathered during the course of an investigation; and

"(B) in the case of changes to clinical protocols applicable to the test, the changes do not affect—

"(i) the validity of data or information resulting from the completion of an

approved clinical protocol;

"(ii) the scientific soundness of a plan submitted under subsection (cc)(3)(B); or

"(iii) the rights, safety, or welfare of the human subjects (if any) involved in the investigation.

"(g) CLINICAL HOLD.—

"(1) IN GENERAL.—At any time, the Secretary may impose a clinical hold with respect to an investigation of an in vitro clinical test if the Secretary makes a determination described in paragraph (2). The Secretary shall, in imposing such clinical hold, specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing. The applicant or sponsor may immediately appeal any such determination pursuant to [section XX appeals].

"(2) DETERMINATION.—For purposes of paragraph (1), a determination described in this subparagraph with respect to a clinical hold is a determination that—

(A) the in vitro clinical test involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the in vitro clinical test, the design of the clinical investigation, the condition for which the in vitro clinical test is to be investigated, and the health status of the subjects involved; or

(B) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish.

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

"SEC. 587S. EMERGENCY USE AUTHORIZATION.

"An in vitro clinical test may be authorized for use in emergency, and used, held, and developed for such use, pursuant to Sections 564, 564A, 564B, and 564C.

"SEC. 587T. COLLABORATIVE COMMUNITIES FOR IN VITRO CLINICAL TESTS

"(a) IN GENERAL.--

"(1) The Secretary may initiate, establish and participate in collaborative communities of public and private participants that may provide recommendations

and other advice to the Secretary on the development and regulation of in vitro clinical tests.

"(2) A collaborative community under this section shall have broad representation of interested private and public-sector stakeholder communities and may include patients, care partners, academics, healthcare professionals, healthcare systems, payers, federal and state agencies, international regulatory bodies, industry, or other interested entities or communities.

"(b) RECOMMENDATIONS.— A collaborative community may make recommendations to the Secretary on matters including—

"(1) Mitigating measures for in vitro clinical tests;

"(2) Standards development activities and performance standards for in vitro clinical tests;

"(3) Scientific and clinical evidence to support new claims for in vitro clinical tests;

"(4) New technologies and methodologies for in vitro clinical tests;

"(5) Stakeholder engagement;

"(6) New approaches and solutions to multifaceted problems involving diverse stakeholders; and

"(7) Development of effective policies and processes.

"(c) USE BY SECRETARY.-- The Secretary may adopt one or more recommendations made under subsection (b), or otherwise incorporate the feedback from collaborative communities, in its application of its authorities under this [subchapter/bill name] to one or more in vitro clinical tests or a group of in vitro clinical tests, as appropriate.

"(d) TRANSPARENCY - The Secretary shall:

"(1) Publish on the internet website of the Food and Drug Administration matters for which it is seeking comments or recommendations;

"(2) Maintain a list of Collaborative Communities recognized by the Secretary and make this list available on the internet website of the Food and Drug Administration; and

"(3) Post on the internet website of the Food and Drug Administration at least once every year a report on the recommendations it has adopted from Collaborative Communities.

"(e) The Federal Advisory Committee Act in the appendix to title 5 shall not apply to collaborative communities established and used in accordance with this section.

"SEC. 587U. CTIS. [*placeholder*]

"SEC. 587V. PREEMPTION. [*placeholder*]

"SEC. 587W. USER FEES. [*placeholder*]

"SEC. 4. TRANSITION.

(a) FUNDING. – For the purposes of carrying out this Act, there is authorized to be appropriated [$X MILLION] for fiscal year X.

(b) IMPLEMENTATION — The amendments made by this Act shall take effect on DATE X, except that the Secretary is authorized to take such actions, and expend such funds, as the Secretary deems necessary to prepare for this Act to take effect and to ensure an orderly transition.

(c) APPLICATION OF DEVICE AUTHORITIES TO IN VITRO CLINICAL TESTS UNTIL AND AFTER EFFECTIVE DATE OF THIS ACT. — Except as provided in subsection (d), for any product or test that is within the definition of in vitro clinical test as established under the amendments by this Act, the following authorities shall apply:

(1) Any such product or test that was offered, sold, or distributed prior to the enactment date of this Act, except for those addressed in paragraph (d), shall continue to comply with the applicable device provisions of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act until the effective date of this Act.

(2) Before any such product or test is first offered, sold, or distributed after the enactment date but prior to the effective date of this Act, such product or test shall comply with the applicable device provisions of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, except that a product or test which is the same type of product or test referenced in subsection (d) shall likewise be subject to the provisions of that subsection.

(3) For any such product or test that has a submission for marketing authorization under section 515, clearance under section 510(k), authorization under 513(f)(2), approval under section 520(m), or emergency use authorization under section 564 of the Federal Food, Drug, and Cosmetic Act or approval under the Public Health Service Act pending on the effective date of this Act, the Secretary is authorized to review and take action on such submission after the effective date of this Act according to the statutory provision under which such submission for marketing authorization was submitted.

(d) APPLICATION OF AUTHORITIES TO GRANDFATHERED AND TRANSITIONAL IN VITRO CLINICAL TESTS.–

(1) For purposes of this subsection, a Transitional In Vitro Clinical Test is an in vitro clinical test that was developed by a laboratory certified by the Secretary under section 263a of title 42 of the United States Code that meets the requirements for performing high-complexity testing for use only within that certified laboratory and that does not have an approval under section 515, a clearance under section 510(k), an authorization under 513(f)(2), an approval under section 520(m), or an emergency use authorization under section 564 of the Federal Food, Drug, and Cosmetic Act or an approved application under the Public Health Service Act, and is first offered for clinical use in the

period that is within the 90 days preceding the enactment date and up to the effective date of this Act.

(2) An in vitro clinical test that was first offered for clinical use prior to the enactment date of this Act and that meets the criteria for a grandfathered test as set forth in section 587A(c)(2) of the Federal Food, Drug, and Cosmetic Act as added by this Act may continue to be offered for clinical use until the effective date of this Act, except that the Secretary of Health and Human Services retains authority to enforce the device provisions of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act for any specific product or test or any type of product or test as the Secretary determines necessary to protect the public from a serious risk to health. Such in vitro clinical test shall be subject to the applicable provisions of this Act as of the effective date of this Act.

(3) A transitional in vitro clinical test may continue to be offered for clinical use until the effective date of this Act, except that the Secretary of Health and Human Services retains authority to enforce the device provisions of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act for any specific product or test or any type of product or test as the Secretary determines necessary to protect the public from a serious risk to health. Such in vitro clinical test shall be subject to the provisions of this Act as of the effective date of this Act.

(4) A transitional in vitro clinical test under paragraph (1) that is the subject of an application for premarket review or precertification that is submitted on the effective date or within [ ] days of the effective date of this Act may continue to be offered, sold, or distributed until completion of the Secretary's review of the premarket application or precertification application.

(e) CONVERSION.–

(1) Any in vitro clinical test as defined by [definitions section] with a premarket approval, a clearance under section 510(k), an authorized de novo under section 513(f), or a BLA under the Public Health Service Act is deemed to have an approved application under section [premarket review] after the effective date of this Act.

(2) Any in vitro clinical test that has an approved investigational device exemption under section 520(g) is deemed to have an approved investigational use under section 587Q after the effective date of this Act.

(f) PLATFORMS.– A test platform that was purchased prior to the enactment date of this Act and was not cleared, authorized, or approved by the Food and Drug Administration at the time of purchase may continue to be used by the purchaser to develop and introduce into interstate commerce an in vitro clinical test during the period up to five years after the enactment date of this Act. Beginning five years after the enactment date of this Act, any new in vitro clinical test that is developed and introduced into interstate commerce in accordance must be based on a test platform that complies with the requirements of this Act.

(g) These transition provisions apply notwithstanding the provisions of Section 587A(a)(1)(C).

“SEC. 5. GENERAL APPLICABILITY. The Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301 et seq.) is amended—

[Placeholder for provision which includes IVCTs in all the necessary violative, adulteration, misbranding and other relevant sections of the FDCA and PHSA (e.g., section 319F-3, etc.), or new language for these sections where necessary].

“SEC. 6. ANTIMICROBIAL SUSCEPTIBILITY TESTS.

“(a) Section 511A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 360a-2) is amended—

(1) by inserting in subparagraph (a)(1)(C) after the words “section 515” the words “clear, approve, or exempt under [Subchapter J ref. 587A sections] and before “antimicrobial susceptibility…” and
(2) By replacing “testing devices” with “tests.”
(3) by inserting “or in vitro clinical test” after “device” in both instances in (c)(5)
(4) by inserting “in vitro clinical tests” after “susceptibility” in (e)
(5) by striking “and” in (e), inserting “and” after “515” and then inserting [reference to in vitro clinical test IPA approval provision]
(6) by replacing “device” with “in vitro clinical test” in each occurrence in (e)
(7) by striking (e)(2)(C) and replacing with “(C) The antimicrobial susceptibility test in vitro clinical test meets all other requirements to be approved under [insert ref. to in vitro clinical test IPA provision] or exempted from premarket review under [add ref to applicable precert provision] of this title.”
(8) by striking (f)(1) and replacing it with “The term “antimicrobial susceptibility test in vitro clinical test” means an in vitro clinical test that utilizes susceptibility test interpretive criteria to determine and report the in vitro susceptibility of certain microorganisms to a drug (or drugs).”
(9) by striking (g)(2) and replacing it with “with respect to approving in vitro clinical tests under section [add ref. to in vitro clinical test IPA approval provision] or exempting in vitro clinical tests from premarket review under [add ref to applicable precert section] of this title — “
(10) by replacing “device” with “in vitro clinical test” and “antimicrobial susceptibility testing device” with “antimicrobial susceptibility in vitro clinical test” in (g)(2)(A).

“SEC. 7. COMBINATION PRODUCTS.

(a) Section 503(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(g)) is amended—

(1) in subparagraph (1)(A) by inserting “except for a combination product constituted of a device and an in vitro clinical test,” after “agency center,” and by inserting “in vitro clinical test” before “or biological product.”
(2) in subparagraph (1)(D) by inserting “except for a combination product constituted of a device and an in vitro clinical test. For other combination products,” before “if the Secretary…”
(3) in subparagraph (1)(D)(ii) by inserting “or in vitro clinical test” after “device” and “and

in vitro clinical tests" before "shall"

(4) in subparagraph (3) by adding [reference to the relevant standard for in vitro clinical tests] before "for the approved constituent part…"

(5) in subparagraphs (4)(A), 4(B), and 5(A), by adding "[cites to in vitro clinical test IPA provision]" to the list of [sections]

(6) in subparagraph (7) by adding "[reference to the relevant standard for in vitro clinical tests]" after "substantial equivalence"

(7) in subparagraph (8) by adding "This paragraph shall not apply to a combination product constituted of a device and an in vitro clinical test"

(8) in subparagraph (9)(C)(i) by striking "or" before "520(g) and adding "or [cite to IPA approval provision]" at the end

(9) in subparagraph (9)(D) by striking "or" before "520" and adding "or [cite to in vitro clinical test IPA provision]" before "of this Act…"

(b) Section 563 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb-2) is amended --

(1) in subsection (a) by inserting "in vitro clinical test," after "device," and by inserting ", except for a combination product constituted of a device and an in vitro clinical test," before "respecting the component…"

(2) in subsection (b) by inserting "except for a combination product constituted of a device and an in vitro clinical test" before "the component of the…"

(3) in subsection (c) by inserting "except for a combination product constituted of a device and an in vitro clinical test" before "the component of the…"

"SEC. 8. LIST OF ADULTERATION, MISBRANDING, AND PROHIBITED ACTS/GENERAL ENFORCEMENT PROVISIONS [*placeholder*]