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IDSA
Infectious Diseases Society of America

April 1, 2020

The Honorable Michael Bennet
United States Senate
261 Russell Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
United States Senate
217 Russell Senate Office Building
Washington, DC 20510

The Honorable Larry Bucshon, MD
United States House of Representatives
1005 Longworth House Office Building
Washington, DC 20515

The Honorable Diana DeGette
United States House of Representatives
2111 Rayburn House Office Building
Washington, DC 20515

The Infectious Diseases Society of America (IDSA) appreciates the opportunity to offer feedback on the Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2020, which builds upon previous efforts to establish a modern framework for the regulation of *in vitro* diagnostic tests (IVDs) and laboratory-developed tests (LDTs). The current COVID-19 pandemic underscores the need for multiple high-quality testing options, including rapid point-of-care testing and those developed by academic clinical laboratories, to ensure sufficient testing capacity. We look forward to sharing our perspective on the important role of infectious disease (ID) LDTs in clinical care and public health and the potential impacts of the proposed regulations on innovation and patient access to testing.

IDSA appreciates the improvements to the bill that the sponsors have made and their willingness to continue working with IDSA and physician and academic clinical laboratory stakeholders. In particular, we are pleased to see specimen changes removed from modification requirements to allow for necessary flexibility and the expansion of public health surveillance provisions to include tests that are intended for use in making clinical decisions for individual patients. We believe this will greatly increase innovation and accessibility for tests that fall under these provisions. However, we have concerns that many other provisions in the bill will hamper access to testing in numerous areas of infectious disease. The COVID-19 pandemic has rapidly taught us the limitations of not having rapidly available adequate testing in managing infectious diseases, and these limitations lead to loss of life when infection mitigation is underinformed.

IDSA recognizes that Congress and the Food and Drug Administration (FDA) are committed to protecting patients, and we look forward to continuing to work together to craft appropriate policies to spur advancement and protect patient access to high-quality diagnostic testing. **We therefore urge Congress not to advance the VALID Act, which would upend the oversight system for diagnostics in the U.S., until immediate public health challenges are addressed and the economic and patient care impacts have been thoroughly assessed.**

Use of LDTs in Infectious Diseases

Unlike commercial *in vitro* diagnostic devices, which are currently regulated through FDA pathways, LDTs for infectious diseases are intended for testing in accredited

clinical laboratories and are vigorously validated under a system of regulations by the Clinical Laboratory Improvement Amendments (CLIA). The validation data collected by these laboratories are subject to ongoing peer review. In many cases, LDTs have become the standard of infectious disease patient care.

LDTs with well-documented data and peer-reviewed literature have been successfully used to diagnose infections for decades, including:

- BKV, a polyoma virus that can affect transplant patients, requires serial surveillance but has no FDA-cleared tests. All transplant centers need access to accurate, rapid results and only LDTs exist to provide longitudinal monitoring for viral reactivation.
- Spinal fluid testing for Herpes Simplex Virus Encephalitis, a serious brain infection that often causes permanent damage if not diagnosed and treated quickly. These tests are as effective, less invasive, and lower risk than the previous method of brain biopsies. Well-validated LDTs were used routinely for several years before tests became widely available commercially.
- During the 2009 H1N1 influenza outbreak, many local hospitals relied on LDTs to diagnose and guide treatment of patients. Similarly, the ability to develop and validate tests for the ongoing COVID-19 outbreak as outlined in the March 16, 2020 FDA guidance will increase testing capacity and slow community transmission.

Unlike other areas of medicine where a single test may determine the course of treatment (e.g. oncology), ID diagnostics are one piece of a complex clinical decision-making puzzle that relies on complementary data and medical expertise. ID LDTs are used in conjunction with other diagnostics and frequently represent the most rapid testing option available at many institutions, particularly when sending specimens to an external reference laboratory is the only alternative. In some cases (e.g., antimicrobial susceptibility testing for novel antimicrobials), there are no reference laboratories that can perform testing. For infectious diseases, a delay of even a few hours can have a devastating impact on patients (e.g., increased mortality) and public health. In-house testing is especially important at major medical centers that specialize in transplantation and the management of complex, critically ill patients, where physician and clinical laboratory scientists regularly develop and validate LDTs to keep pace with newly emerging diseases and offer diagnosis for less common pathogens that do not have FDA-approved commercial testing. Lastly, these tests are vital for guiding successful antimicrobial stewardship that limits the emergence of drug resistance and enhances hospital infection prevention. With new ID threats emerging, and a growing population of immunocompromised patients at high risk for infections, maintaining patient access to high-quality testing is critical to preventing transmissions and containing outbreaks. Optimal clinical outcomes of infectious diseases rely on accurate, rapid diagnosis.

An additional limitation of commercial tests is cost. LDTs are often specifically designed for high-level and accurate performance on consolidated and standardized instrumentation in an individual laboratory. In contrast, commercial tests often require laboratory investment in new instruments from multiple companies. Such investment will not be feasible for many hospital laboratories or, if made, may result in increased costs to the patient.

IDSA is extremely concerned that the proposed regulations will impede patient access to existing high-quality diagnostic testing and threaten the innovation needed to keep pace with constantly changing and emerging pathogens. As written, the VALID Act's impact on IVD manufacturers will be minimal due to the decades-long alignment between VALID and existing medical device statutory and regulatory requirements. Conversely, it will have a significant negative impact on clinical laboratories without the personnel, funding, regulatory and legal expertise or capacity to comply with the extensive development/design control, premarket analytical and clinical studies, application fees, and postmarket regulatory and surveillance requirements.

VALID Act 2020 and COVID-19

ID diagnostics protect public health when used to identify outbreaks and prevent the transmission of infectious diseases. To that end, there are lessons to be learned from the 2020 COVID-19 outbreak about how diagnostic regulation should balance patient access and safety going forward.

The current outbreak illustrates the need to respond to public health threats with a cohesive, multisectoral response. To do so successfully requires an acknowledgement of the ways academic and not-for-profit laboratories differ from public health and large reference laboratories, and the roles each group plays within the diagnostic landscape. These roles require unique considerations and do not fit under the umbrella of a single regulatory pathway.

We are seeing firsthand the impact that delayed testing has on transmission, reporting, resource utilization, and management, and above all, patient and public health. Beyond its public health provisions, the VALID Act introduces new and duplicative regulatory hurdles for laboratories developing tests for numerous conditions that are critical in everyday patient care.

VALID Act provisions and clinical laboratory impacts

SEC. 587. Definitions

High-risk tests

The definition for "high-risk" tests outlines mitigating measures that are defined by the degrees to which "the intended use of the IVCT is well-characterized, and the criteria for performance of the test are well-established to be sufficient for the intended use" (pp. 9-10). It is unclear how Congress or FDA intend to define "well-characterized" intended use and performance. IDSA recommends that these definitions be clearly outlined and align with existing Clinical Laboratory Improvement Amendments (CLIA) standards to avoid duplicative requirements and reduce burden on accredited developers. Given the ways in which they are developed and used, we believe that most tests for infectious diseases should not fall into a high-risk category.

Sec. 587A. Applicability

Modifications

The 2020 VALID Act requires oversight for test modifications that change any of the elements defining indications for use. IDSA appreciates that the VALID Act's revised modification protocols have been updated to focus on oversight for test elements that primarily impact analytical validity and clinical utility. This will allow for increased flexibility for elements such as specimen type that do not alter the validity of a test. However, we strongly recommend exempting changes in well-established test components that do not affect intended use (e.g., changing nucleic acid extraction platforms or PCR thermocycler instruments). The inability to modify these elements without triggering additional oversight was one of the major impediments to implementation of the CDC SARS-COV2 assay in the early days of the COVID-19 pandemic, as any parts of the testing protocol that differed from those used in the CDC validation were considered outside the Emergency Use Authorization. Many different instruments capable of performing the universal aspects of a test are in routine clinical use and have established efficacy.

IDSA is also concerned that from an antimicrobial susceptibility testing (AST) perspective, the current framework would require a laboratory to submit a modification application for every new drug tested, which may cause a substantial delay in adoption of testing for new agents (i.e., prior to disk availability). FDA has held multiple workshops in recent years to foster coordinated development of antimicrobial drugs and ASTs, which will be adversely impacted by these requirements.

Grandfathered Tests

While we appreciate the inclusion of grandfathering provisions to protect existing tests, continued innovation will be essential to keep pace with emerging infectious disease threats and evolving strains. We thus request clarification as to the eligibility of Gram and other laboratory developed stains (e.g., calcofluor, AFB), as

additional regulatory requirements for these tests would pose issues for CLIA-waived and moderate complexity laboratories.

IDSA recommends that eligibility for grandfathered tests aligns with a laboratory's CLIA complexity grade. This approach will ensure that tests are developed and conducted in appropriate settings without restricting critical access to high complexity labs. We urge Congress not to place regulatory burden on well-validated tests currently performed in laboratories and to clarify the testing scope of this provision.

Near-Patient Testing

IDSA recommends additional clarifications and provisions in this section to most effectively target the bad actors that the VALID Act is partially intended to address. As few (if any) LDTs are performed at the point of care, which generally requires low or moderate complexity in order to be performed by clinical staff, this exemption appears to apply mainly to commercial tests. We encourage Congress to tailor this provision to address laboratories marketing faulty tests directly to consumers and non-ID physicians (e.g., whole genome sequencing tests that utilize direct-from-urine or direct-from-sinus swabs). Increased vigilance in this area will increase protections for patients while maintaining access to well-developed, well-validated, non-commercial tests.

Humanitarian Test Exemption

IDSA has continued to express substantial concern over the VALID Act's humanitarian text exemption, previously known as the "tests for rare diseases" exemption in earlier drafts. Updates to the 2020 bill include a revision of the number of tests performed from 8,000 to 10,000 tests, and additional language to the communicable disease provision excluding tests for ID that are "highly likely to result in fatal or irreversibly debilitating outcome and for which prompt and accurate diagnosis offers the opportunity to mitigate a public health impact of the condition."

Notwithstanding that many infectious diseases can result in fatal or irreversibly debilitating outcomes without proper diagnosis, it is essential in cases of localized emerging outbreaks that may not necessarily meet the criteria for an Emergency Use Authorization that well-validated tests make their way to public health officials as expediently as possible. LDTs can often be developed quickly to help combat emerging outbreaks (e.g., COVID-19, H1N1 influenza) and support state reference laboratories by providing decreased test turn-around time. Bacterial strain typing can also help limit spread in outbreaks and local transmission cases, such as duodenoscope contamination. Further, these results are frequently critical in informing clinician decisions for patient care.

The VALID Act humanitarian test exemption fails to consider that the clinical signs and symptoms of many infectious diseases are indistinguishable. Therefore, physicians end up testing many more patients than actually turn out to have the rare disease. As illustrated by the 2020 COVID-19 outbreak, tens of thousands of tests are needed in order to isolate a small number of positives; those countries that were able to deploy a greater number of tests were more effective in their containment efforts. **There are also many infectious diseases with an incidence above 10,000 that are still sufficiently rare and for which no commercial testing options exist (e.g., BK virus, JC polyomavirus, adenovirus, pneumocystis pneumonia, malaria, carbapenem-resistant Enterobacteriaceae infections, human herpes virus-6).** For other rare diseases, such as herpes encephalitis, thousands of tests may need to be run to identify a very small number of cases. If the VALID Act restricts rare disease exemptions to total volume of testing for non-communicable diseases only, continuing to develop and run these tests will be prohibitive. Insufficient testing can delay diagnosis and appropriate treatment for sick patients who have few or no other options, and IDSA is extremely concerned that this provision will leave thousands of vulnerable patients without access to testing or care.

To address this issue, IDSA has previously suggested aligning the VALID framework with the 1983 Orphan Drug Act definition of rare diseases (those that affect fewer than 200,000 patients in the U.S. per year). Alternatively, the following revision to the bill text would achieve a similar effect:

"(A) is intended for use for a disease or condition for which no more than 10,000 individuals, unless otherwise determined by the Secretary, would be subject to ~~negative or~~ positive diagnosis by such test in the United States per year…"

The presumed rationale for excluding contagious diseases from the exemption is to ensure that these tests are well-validated due to the potential for false negatives, thus leading to increased transmission. However, this is not the case for a plurality of infectious diseases, such as HSV encephalitis. ID LDTs are already rigorously validated and, more importantly, **do not serve as the sole source of clinical decision-making**. The vast majority of ID LDTs are not used as stand-alone tests, and this reduces the inherent risks of erroneous or misleading results. A potentially imperfect ID test that relies on confirmatory methods and physician expertise is far preferable to no test at all.

Finally, this section does not account for the drivers of rare disease testing. These tests are most often developed because there is a void in the market for conditions that will never lend themselves to a profitable diagnostic product. There are no provisions in the bill to consider push and/or pull incentives that would increase the commercial development of tests that are clinically necessary but low profit, so there will necessarily continue to be a critical dearth in this area.

Custom and Low-Volume Tests

IDSA recommends the expansion of custom test exemption criteria to include tests that are developed and used to treat patients within one facility, a network of related facilities (such as a hospital system), public health laboratories, and possibly for reference laboratories that provide testing for both local hospitals and local physician practices. This expansion would reflect the appropriate, longstanding use of ID LDTs and maintain access to what is often the most rapid form of testing. Under such a scenario, analytic validation would still be required for these tests and could continue to be regulated by the Centers for Medicare & Medicaid Services (CMS) under 42 CFR 493.1253.

The low-volume testing limit of five patients per year also does not consider that some academic medical centers act as referral centers for many rare diseases.

Sec. 587B. Premarket Review

Breakthrough IVCTs

IDSA appreciates the various updates in this section, including the breakthrough designation for new technologies eligible for priority review. However, we recommend that the criteria for IVCTs eligible for priority review (Sec. 587C) be expanded to include up to two approved or certified alternatives to accommodate for clinical laboratory budget and space constraints while preserving patient access to care. Often there may be a single commercial IVD on the market for a lesser-known disease, but with only one option laboratories may be forced to purchase expensive equipment for a single test (or purchase equipment for high-throughput testing that may not be needed) if it is not performed on a platform they currently use. Further, some commercial tests (e.g., cerebrospinal fluid HSV) can have false negative rates of up to 15%, thus underscoring the importance of having access to confirmatory LDTs when only one commercial test is on the market.

> ***Clinical example: Herpes Simplex Virus.*** Disseminated herpes simplex virus (HSV) infection in newborns is a life-threatening disease, associated with high morbidity and mortality. Rapid diagnosis and treatment are critical in halting disease progression. Many clinical laboratories have developed and comprehensively validated PCR LDTs to test cerebrospinal fluid (CSF) and blood of these newborns for swift, local testing. Many must be tested to find the few who are diagnosed, and test volume exceeds the VALID Act's recommended threshold for the humanitarian testing exemption.
>
> Two FDA-cleared commercial tests for HSV CSF analysis are available but require purchase of an instrument for the sole use of this test. For one of the two assays, HSV is a component of a highly multiplexed test which is not appropriate in all clinical settings. There are also currently no FDA-

cleared assays to test blood. While this is a known example of a critical test developed in the absence of feasible FDA-approved alternatives, new and rare pathogens are constantly emerging for which we will need to develop tests. Clinical laboratories are unlikely to commit limited resources to purchasing the instrument due to the low frequency of rare disease, and cannot afford the user fees or staff resources required for technology certification and premarket review. This could create a significant loss of patient access to the local, rapid testing needed to combat neonatal HSV and other infections.

We also remain concerned that – regardless of eligibility – academic and not-for-profit laboratories will be unable to comply with premarket requirements for which commercial manufacturers have entire regulatory teams. For many laboratories, critical rapid diagnostics will have to be outsourced to reference labs or dropped from test menus entirely, resulting in extended turnaround times due to delays inherent in specimen transport. **IDSA strongly recommends that the VALID Act designate low-risk tests that are designed, manufactured, and used in a single high-complexity laboratory or laboratory system and not marketed for commercial use as exempt from premarket review.**

Sec. 587D. Technology Certification

IDSA agrees that a precertification pathway for groups of similar IVCTs may help ease the prohibitive burdens of premarket review for many developers, including academic medical centers and not-for-profit laboratories. However, we urge Congress to make the precertification process highly accessible for academic and non-profit laboratories. One possible pathway would be to allow laboratories that develop tests for in-house, non-commercial use to apply for developer precertification, as opposed to requiring various onerous precertification packages for multiple technologies.

We also request that Congress clarify the exclusion language for blood and tissue donors and recipients. As written, is unclear whether this exclusion is intended to apply to compatibility testing for these products and patients (as implied), or whether it extends to all IVCTs used on donors and transplant recipients (e.g., testing for transplant-associated viruses on immunocompromised patients).

Sec. 587X. Postmarket Surveillance

The requirement for post-market surveillance is unreasonably burdensome and outside the scope of what a clinical laboratory is equipped to do. The CAP Laboratory Accreditation Program, which the majority of clinical laboratories pursue, has been approved by the Centers for Medicare and Medicaid Services to implement the Individualized Quality Control Plan (IQCP) option. While IDSA recognizes that the CAP Laboratory Accreditation Program is not statutory and therefore cannot be included within the VALID Act framework, we urge Congress to allow compliance with CAP IQCP guidance as a mitigating measure for technology certification and risk assessment.

Beyond postmarket quality control, academic and not-for-profit laboratories will require a modified process to determine potential reportable (PRE) criteria for submitting notifications to the FDA, as well as the process for a "product recall" in the event of testing issues.

Sec. 9. Resources

It is both unprecedented and inappropriate to require user fees for not-for-profit entities that are not marketing a commercial product. While it is customary that for-profit manufacturers have dedicated regulatory affairs departments, clinical laboratories and academic medical centers typically lack these departments and the financial resources to create additional staff positions. **Moving to a manufacturer-based (vs. patient-centered) regulatory process, as the VALID Act proposes, will cause substantial delays in processing ordered patient tests and severely limit access to testing, lengthen hospital stays, increase healthcare costs, and worsen patient care.** Further, as evidenced by the multiple FDA Emergency Use Authorization policy updates needed to adequately scale up testing in the COVID-19 outbreak, we are concerned that the agency likely lacks the capacity and third-party reviewer infrastructure to enforce proposed legislation in a timely fashion.

IDSA strongly urges the exemption of laboratory tests not developed for commercial use from FDA user fees. Any proposed user fees would fall outside the budgets of even top-tier academic medical centers and prohibit the development and use of lifesaving ID diagnostics. We are further concerned that, unlike the 2018 discussion draft, the 2020 VALID Act does not provide language for congressionally appropriated funding. Without this, the expansive modernized framework for diagnostics regulation will rely entirely on user fees, which are untenable for the bulk of academic and non-profit LDT developers.

IDSA requests that an economic impact analysis of technology certification and premarket review applications be performed as legislation is being considered, both in order to gauge the costs of the bill and determine appropriate FDA resources for implementation.

Conclusion

IDSA continues to maintain that it is inappropriate to hold tests developed and used by not-for-profit clinical laboratories to the same requirements as tests developed and marketed commercially, given the very different ways in which the tests are developed and used. The fees and requirements associated with the FDA premarket approval processes would force academic medical centers and hospital laboratories to undertake an unaffordable and inappropriately burdensome process for which they could not recoup the costs, **particularly as they are not marketing a product for commercial use**. As a result, many of these tests would not be performed, or would be outsourced to reference laboratories, delaying results and negatively impacting patient care – often the difference between life and death in infectious disease treatment.

IDSA supports federal efforts to expand access to diagnostic testing during the COVID-19 outbreak and future public health emergencies. However, the current public health situation illustrates the life-threatening implications for patients when there is inadequate access to testing. Rapid diagnostics that facilitate early initiation of life-saving treatment are critical in ID patient care, where same-day results can significantly improve patient outcomes. For clinical laboratories that use their own ID LDTs within a single institution or hospital system, the unprecedented and inappropriate burden of FDA user fees would severely limit patient access to innovative and well-validated tests needed to save lives and guide optimal treatment.

ID LDTs are primarily developed to address unmet medical needs and to improve care for the patients in local and regional health systems. Commercial developers are not the best or only test innovators, and it is critical that academic medical centers and not-for-profit laboratories remain unencumbered by prohibitive regulatory pathways that favor industry manufacturers and the largest reference laboratories. The long-term consequences of LDT regulation as currently proposed could be an anticompetitive environment in which only national reference laboratories would be able to offer broad LDT test menus that are currently available in many medical centers. IDSA is also concerned that VALID will create the testing shortage we're seeing with COVID-19 in other areas of ID as well. **We therefore urge Congress not to advance the VALID Act until we address immediate challenges and thoroughly assess impacts on patient care.**

Our intent is to recommend provisions that provide appropriate rigor with regard to test validity and patient safety without imposing unnecessary burden upon not-for-profit laboratories. We appreciate your close attention to these important and complex issues, and we look forward to working together to craft appropriate policies to spur innovation and protect patient access to high-quality diagnostic testing.

Sincerely,

Thomas M. File, Jr., MD, MSc, FIDSA
President, IDSA

Attached: Summary table of IDSA VALID Act 2020 comments

Summary: IDSA VALID Act 2020 Comments

SECTION	TOPIC	IDSA RECOMMENDATIONS
587	Definitions: High-Risk Tests	It is unclear how Congress or FDA intend to define "well-characterized" intended use and performance. IDSA recommends that these definitions be clearly outlined and align with existing Clinical Laboratory Improvement Amendments (CLIA) standards to avoid duplicative requirements and reduce burden on accredited developers. Given the ways in which they are developed and used, we believe most tests for infectious diseases should not fall into a high-risk category.
587A	Applicability: Modifications	IDSA appreciates that the VALID Act's revised modification protocols have been updated to focus on oversight for test elements that primarily impact analytical validity and clinical utility. This will allow for increased flexibility for elements such as specimen type that do not alter the validity of a test. However, we strongly recommend exempting changes in well-established test components that do not affect intended use (e.g., changing nucleic acid extraction platforms or PCR thermocycler instruments). The inability to modify these elements without triggering additional oversight was one of the major impediments to implementation of the CDC SARS-COV2 assay in the early days of the COVID-19 pandemic, as any parts of the testing protocol that differed from those used in the CDC validation were considered outside the Emergency Use Authorization. Many different instruments capable of performing the universal aspects of a test are in routine clinical use and have established efficacy. We agree with the importance of documenting modifications but strongly recommend that these modified tests, if documented properly, remain exempt from additional regulatory requirements.
587A	Applicability: Grandfathered Tests	While we appreciate the inclusion of grandfathering provisions to protect existing tests, continued innovation will be essential to keep pace with emerging infectious disease threats and evolving strains. IDSA thus requests clarification as to the eligibility of Gram and other laboratory developed stains (e.g., calcofluor, AFB), as additional regulatory requirements for these tests would pose issues for CLIA-waived and moderate complexity laboratories.
587A	Applicability: Near-Patient Testing	IDSA recommends additional clarifications and provisions in this section to most effectively target the bad actors that the VALID Act is partially intended to address. As few (if any) LDTs are performed at the point of care, which generally requires low or moderate complexity in order to be performed by clinical staff, this exemption appears to apply mainly to commercial tests. We encourage Congress to tailor this provision to address laboratories marketing faulty tests directly to consumers and non-ID physicians (e.g., whole genome sequencing tests that utilize direct-from-urine or direct-from-sinus swabs). Increased vigilance in this area will increase protections for patients while maintaining access to well-developed, well-validated, non-commercial tests.
587A	Applicability: Humanitarian Test Exemption	The 10,000 test limit in this section fails to consider that the clinical signs and symptoms of many infectious diseases are indistinguishable. Therefore, physicians end up testing many more patients than actually turn out to have the rare disease. There are also many infectious diseases with an incidence above 10,000 that are still sufficiently rare and for which no commercial testing options exist (e.g., BK virus, JC polyomavirus, adenovirus, pneumocystis pneumonia, malaria, carbapenem-resistant Enterobacteriaceae infections, human herpes virus-6). For other rare diseases, such as herpes encephalitis, thousands of tests may need to be run to identify a very small number of cases. IDSA is extremely concerned that this provision will leave thousands of vulnerable patients who have few or no other options without access to testing or care and recommends the following revision to the VALID Act text: "(A) is intended for use for a disease or condition for which no more than 10,000 individuals, unless otherwise determined by the Secretary, would be subject to ~~negative or~~ positive diagnosis by such test in the United States per year…" This exemption does not account for the drivers of rare disease testing. These tests are most often developed because there is a void in the market for conditions that will never lend themselves to a profitable diagnostic product. There are no provisions in the bill to consider push and/or pull incentives that would increase the commercial development of tests that are clinically necessary but low profit, so there will necessarily continue to be a critical dearth in this area. It is essential in cases of localized emerging outbreaks that may not necessarily meet the criteria for an Emergency Use Authorization that well-validated tests make their way to public health officials as expediently as possible. LDTs can often be developed quickly to help combat emerging outbreaks (e.g., COVID-19, H1N1 influenza) and support state reference laboratories by providing decreased test turn-around time. Bacterial strain typing can also help limit spread in outbreaks and local transmission cases, such as duodenoscope contamination. Further, these results are frequently critical in informing clinician decisions for patient care.

587A	Custom and Low-Volume Tests	The low-volume testing limit of 5 patients per year does not take into account that some academic medical centers act as referral centers for many rare diseases, nor does it allow for appropriate care during outbreaks and other unforeseen events that may increase need for testing. IDSA recommends the expansion of custom test exemption criteria to include tests that are developed and used to treat patients within one facility, a network of related facilities (such as a hospital system), public health laboratories, and possibly for reference laboratories that provide testing for both local hospitals and local physician practices. This expansion would reflect the appropriate, longstanding use of ID LDTs and maintain access to what is often the most rapid form of testing. Under such a scenario, analytic validation would still be required for these tests and could continue to be regulated by the Centers for Medicare & Medicaid Services (CMS) under 42 CFR 493.1253.
587B	Premarket Review	IDSA remains concerned that – regardless of eligibility – academic and not-for-profit laboratories will be unable to comply with premarket requirements for which commercial manufacturers have entire regulatory teams. For many laboratories, critical rapid diagnostics will have to be outsourced to reference labs or dropped from test menus entirely, resulting in extended turnaround times due to delays inherent in specimen transport. **IDSA strongly recommends that the VALID Act designate low-risk tests that are designed, manufactured, and used in a single high-complexity laboratory or laboratory system and not marketed for commercial use as exempt from premarket review.**
587B	Premarket Review: Breakthrough IVCTs	IDSA recommends that the criteria for IVCTs eligible for priority review (Sec. 587C) be expanded to include up to two approved or certified alternatives to accommodate for clinical laboratory budget and space constraints while preserving patient access to care. Currently there are two FDA-approved tests on the market for herpes simplex virus (HSV) in cerebrospinal fluid: one requires a specific instrument that many labs may not be able to purchase, and one is a highly multiplexed test that is not appropriate for all patient populations. This is an example of a situation in which LDTs are critical. Limiting laboratories to use of a single manufacturer's test, when they may not have the platform or the budget/space to purchase it, will harm patient care.
587D	Technology Certification	**We urge Congress to make the precertification process highly accessible for academic and non-profit laboratories.** One possible pathway would be to allow laboratories that develop tests for in-house, non-commercial use to apply for developer precertification, as opposed to requiring various precertification packages for multiple technologies. IDSA would be happy to provide additional suggestions for framework and applicability. We also request that Congress clarify the exclusion language for blood and tissue donors and recipients. As written, it is unclear whether this exclusion is intended to apply to compatibility testing for these products and patients (as implied), or whether it extends to all IVCTs used on donors and transplant recipients (e.g., testing for transplant-associated viruses on immunocompromised patients).
587X	Postmarket Survillance	The requirement for post-market surveillance is unreasonably burdensome and outside the scope of what a clinical laboratory is equipped to do. Beyond postmarket quality control, academic and not-for-profit laboratories will require a modified process to determine potential reportable (PRE) criteria for submitting notifications to the FDA, as well as the process for a "product recall" in the event of testing issues.
9	Resources	It is unprecedented and inappropriate to require user fees for not-for-profit entities that are not marketing a commercial product. While it is customary that for-profit manufacturers have dedicated regulatory affairs departments, clinical laboratories and academic medical centers typically lack these departments and the financial resources to create additional staff positions. Moving to a manufacturer-based (vs. patient-centered) regulatory process, as the VALID Act proposes, will cause substantial delays in processing ordered patient tests and severely limit access to testing, lengthen hospital stays, increase healthcare costs, and worsen patient care. IDSA recommends that an economic impact analysis of technology certification and premarket review applications be performed as legislation is being considered. **We also strongly recommend that user fees be waived for academic and not-for-profit clinical laboratories that are developing tests for non-commercial use.**