December 7, 2017

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2017-N-5093: Review of Existing General Regulatory and Information Collection Requirements of the Food and Drug Administration

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments to the Review of Existing General Regulatory and Information Collection Requirements of the Food and Drug Administration.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products.

BIO is committed to promoting a regulatory environment that continues to support and incentivize the biopharmaceutical ecosystem. Minimizing the regulatory burden on this critical sector of the American economy will foster small business growth, create good, high-paying jobs, directly and indirectly expand the economy, and expedite the development and delivery of safe and effective therapies to patients in need.

To this end, BIO has developed a priority list of regulations and guidance documents that, if modified or eliminated, would significantly decrease regulatory costs, advance the fast and safe development and delivery of effective therapies, and drive investment in innovation by fostering an environment that recognizes the value these new medicines bring to patients and the overall healthcare system.

Our priority recommendations for regulatory reforms fall into three categories:

1. Accelerating Products to Market & Reducing Pre-Market Regulatory Costs
2. Lowering Post-Market Regulatory Compliance Costs
3. Removing Regulatory Barriers that Impede Value-Based Arrangements

We stand ready to work with the Agency to secure adoption and implementation of these reforms as quickly as practicable.

Accelerating Products to Market & Reducing Pre-Market Regulatory Costs

1. **Better Enable the Utilization of Novel Endpoints**
   FDA should revise guidance designed to improve the utilization of surrogates and novel endpoints (including digital health-related endpoints) for the purposes of approval and, if needed, how to most efficiently and effectively conduct any post-approval studies required.

2. **Streamline Requirements Regarding Cardiovascular Outcome Trials (CVOTs) for Diabetes Drugs**
   The current FDA requirement to conduct a pre-market CVOT for diabetes is hindering research and development of treatments for this disease, which is the fastest growing public health problem in the United States. The premise on which this requirement is based has been shown to be an inaccurate interpretation of the relevant data. CVOTs should be moved to post-approval to incentivize companies to gain CV benefit claims rather than preapproval. FDA should be able to utilize the Sentinel Network to enable more efficient post-market safety assessments in this area.

3. **Streamline Regulatory Processes for Medicines with Abuse Liability**
   Federal government processes, in particular at FDA, HHS, and DEA, are cumbersome and duplicative, and prevent timely access for U.S. patients to medicines with potential for abuse liability.

   Specifically, FDA should minimize the burden on sponsors by responding faster (*i.e.,* within 75 days) to abuse liability study proposals. Timely feedback will allow sponsors to move forward with key studies knowing they have considered FDA input on study design.

   HHS also should streamline its own regulations by delegating abuse liability recommendations to FDA, so that FDA can submit its recommendations directly to the Drug Enforcement Agency (DEA). This simplification would eliminate an unnecessary step that slows down the process. Furthermore, the DEA should be expected to act on FDA scheduling recommendations within 30 days of receipt.

4. **Streamline Regulations to Speed Hiring of Scientific Experts within FDA and on Its Advisory Committees**
   The Federal government processes and criteria evaluating conflicts of interest should be revised to make it faster and less cumbersome for FDA to hire scientific experts on its staff or for advisory committee/panel engagement. Policies should allow alternative methods of meeting the conflict of interest requirements to enable more timely hiring of these experts.

   Current FDA requirements make it difficult to hire experienced staff and top scientists, as rules requiring employees to divest all stock and patents in any FDA regulated industries also can include holdings of family members. Policies should be modified to allow recusals from participating in decisions that might impact their patents or holdings, rather than complete divestiture. In addition, FDA guidances such as the Guidance on Conflict of Interest for Advisory Committee Members, Consultants and Experts, can be overly burdensome and bar bona fide experts from providing advice to the FDA. All of these barriers to expert hiring and participation slow down the agency's drug evaluation processes.[1]

[1] 5 CFR 2635 Subparts D and E, 5 CFR 2640; FDA Guidance "FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees (August, 2008)

Lowering Post-Market Regulatory Compliance Costs

1. **Modernize and Streamline Post-Marketing Reporting of Adverse Drug Experiences**

   The current FDA regulation is outdated (*e.g.,* paper and telephone calls are no longer the primary source of adverse event data), which creates inefficiencies when using new data sources and business models such as social media, electronic health records (EHRs), and patient support programs. Furthermore, the current regulatory structure discourages the utilization of newer, potentially more powerful data sources that could provide insight on product safety profiles. This regulation needs to be withdrawn and re-written to incorporate current technology and to harmonize it with other regulatory authorities.[2]

   In addition, requiring adverse event reporting of public literature and claims in product liability studies is overly burdensome and does little to protect the public health. The FDA should identify types of public literature it does not consider necessary for expedited reporting.

   The agency also should exempt adverse event reporting based on information presented in lawsuits since this reporting does not contribute information that is significant to the safety profile of medicines. And, given that the relevant International Conference on Harmonization (ICH) guideline (E2C(R2)) does not require the inclusion of unpublished scientific papers in Periodic Safety Update Reports (PSURs), FDA should remove its requirement to list unpublished scientific papers to align with ICH.

   Furthermore, FDA should exclude reports arising from interventional studies, as most qualifying interventional reports identified in the literature would have been previously subject to reporting, whether expedited or periodic, during the clinical trial process.[3]

2. **Update Regulations Governing Supplements and Other Changes to an Approved NDA**

   FDA's current labeling regulations governing "Changes being effective" (CBEs) are outdated and impose unreasonable and unrealistic burdens on manufacturers. FDA should pre-approve all labeling changes in an efficient manner to ensure consistent labeling across products. This regulatory change would be consistent with current actual practices, since companies do not unilaterally file CBEs updating labeling with new safety information absent consultation and approval by FDA. In addition, FDA should revise these regulations in a manner that streamlines other operationally obsolete requirements as well.

   FDA's guidance on Chemistry, Manufacturing and Controls (CMC) changes also is outdated, as the user must refer to several other guidances to administer a single CMC change (*e.g.*, SUPAC Guidelines). Updating this guidance would reduce costs from having to comply with potentially discrepant requirements in other guidances, or having to address issues on an ad hoc, administrative basis (*i.e.,* scientific advice). FDA has begun to reform its approach to post-approval manufacturing changes for drugs, in line with its cGMP for the 21st Century – A Risk Based Approach Initiative. FDA should accelerate efforts to lower and remove barriers in current regulations that discourage the introduction of innovative process and product

[2] 21 CFR 314.80
[3] 21 CFR 314.80(b)

improvements. FDA also should eliminate CMC portions from the CBE regulation (and related guidance), as they are out-of-date with respect to modern regulatory science (*e.g.*, drug product sites transfers to CBE 30).[4]

3. **Standardize and Modernize Post-Marketing Study Requirements**
   A significant proportion of industry's R&D budget is dedicated to post-market trials and studies, which are typically agreed to at the time of FDA approval or mandated in the post-market under FFDCA Section 505(o)(3). There should be an opportunity to end the trial or to renegotiate trial design or timeliness if new scientific evidence indicates that the clinical trial or study would no longer provide useful scientific information, or if medical practice or the standard of care changes due to approvals of new drugs. FDA should modify this guidance accordingly.

4. **Modernize Paper Labeling Requirements for Drug and Device Product Directions for Use**
   FDA's paper labeling document and promotional material requirements are outdated. They demand a significant amount of time when updating all labeling in the supply chain and involve major costs associated with printing/destroying/reprinting. The FDA should modify physical labeling rules to allow paperless labeling, rely on the National Library of Medicine (NLM) labeling repository as the source of up-to-date information, and only require paper labeling to be printed as needed by patient or healthcare provider. The agency should allow sponsors to provide electronic labeling for all drug and device products, which currently is only allowed for prescription devices. This modernization could lead to significant cost savings and allow patients to access labeling in their native language, regardless of where they reside, as well as increase safe use of a product as new approved information can be disseminated much faster.[5]

Removing Regulatory Barriers that Impede Value-Based Arrangements

1. **Reform Rules Governing Manufacturer Product Communications with Healthcare Providers and Payors**
   Current FDA regulations state that manufacturer communications not supported by "substantial evidence" will be deemed false and misleading. Economic evidence and real-world outcomes that are not included in product labeling would be valuable endpoints for value-based arrangements (VBAs), but the inability of manufacturers to discuss this evidence limits the effectiveness of VBAs. Recently, FDA has taken up the pressing need to reform its approach to regulating manufacturer communications with healthcare providers and payors, formulary committees, and similar individuals and entities ("payors") (*i.e.,* Docket No. FDA-2016-N-1149; FDA 2016-D-1307; FDA 2016-D-2285). Yet the recently proposed guidances do not adequately capture many of these pressing communication needs. FDA must accommodate manufacturer communications regarding information not included in product labeling. We have submitted more comprehensive comments in response to the proposed regulations.[6][7]

   Similarly, requiring two adequate and well controlled studies to support a superiority or other comparative claim is not in the public interest. The ability to disseminate comparative data even without two head-to-head studies would result in companies generating even more comparative data about their products, and this additional data would benefit payors, providers, and patients. FDA should modify 21 CFR

[4] 21 CFR 314.70
[5] 21 CFR 201.100
[6] https://www.regulations.gov/document?D=FDA-2016-N-1149-0083
[7] 21 CFR 202.1

201.56 (a)(3) to clarify that it does not limit communication of comparative data that is truthful and non-misleading, and expressly permit the utilization of one robust single study to support a comparative claim in the label.[8]

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More detailed information on these and other regulatory changes that can modernize the current healthcare system to drive innovation, value, and competition are included in the attached table.

Again, BIO looks forward to working with the Agency on these and other ways to improve the regulatory environment for the biotechnology industry and the patients we serve.

Sincerely,

/S/

Sesquile Ramon, Ph.D.
Director, Science & Regulatory Affairs
Biotechnology Innovation Organization

[8] 21 CFR 201.1, 21 CFR 201.56

Summary Chart of BIO's Regulatory Reform Recommendations

The following chart provides detailed information on regulatory changes that can modernize the current healthcare system to drive innovation, value, and competition. To this end, the chart contains details for streamlining, modernizing, and harmonizing FDA regulations and guidances to reduce regulatory burdens, lower costs, and speed access to innovative medicines.

SECTION 1. Priority Regulations/Guidances Suggested for Streamlining or Elimination

SECTION 1.1. Priority Regulations Suggested for Streamlining or Elimination

SECTION 1.2. Priority Guidances Suggested for Streamlining or Elimination

SECTION 2. Priority Regulations/Guidances Suggested for Modification, Streamlining or Harmonization

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SECTION 4.1. Additional Regulations Suggested for Streamlining or Elimination

SECTION 4.2. Additional Guidances Suggested for Streamlining or Elimination

SECTION 4.3. Other Thematic Priorities

SECTION 1. Priority Regulations/Guidances Suggested for Streamlining or Elimination

SECTION 1.1. Priority Regulations Suggested for Streamlining or Elimination

Name of Regulation	§314.80 Postmarketing reporting of adverse drug experience
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Modernize and Harmonize Postmarketing reporting of adverse drug experience- 21 CFR 314.80
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The current regulation is based on legacy practices and expectations created over 30 years ago. Paper and telephone calls are no longer the primary source of AE data. Regulatory requirements based on antiquated communication modalities and systems create inefficiencies when trying to utilize new data sources and business models (e.g., social media, EHRs, patient support programs). Further, the current regulatory structure discourages the utilization of newer, potentially powerful data sources that could provide insight on product safety profiles.
Proposed solution	The regulations for postmarket reporting of adverse drug experiences needs to be withdrawn and re-written, to incorporate current technology and to harmonize with other regulatory authorities.
Name of Regulation	**§314.80 Postmarketing reporting of adverse drug experience**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Review of adverse drug experiences - 21 CFR 314.80 (b)

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	ICH E2C(R2) Guideline does not require the inclusion of unpublished scientific papers in Periodic Safety Update Reports (PSURs). Requiring adverse event reporting of public literature and claims in product liability studies is overly burdensome and does little to protect the public health. Reports arising from interventional studies should be excluded as most qualifying interventional reports identified in the literature would have been previously been subject to reporting, whether expedited or periodic, during the clinical trial.
Proposed solution	FDA should remove the requirement to list unpublished scientific papers to align with ICH E2C(Rs). FDA should identify types of public literature they do not consider valid for expedited reporting. FDA should exempt adverse event reporting based on information presented in lawsuits as they do not contribute information that is significant to the safety profile of medicines. FDA should exclude reports arising from interventional studies. FDA should also consider whether reports from social media should be excluded.
Name of Regulation	**§314.80 Postmarketing reporting of adverse drug experience**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Reporting requirements, Periodic adverse drug experience reports - 21CFR 314.80 (c)(2)

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA timelines do not align with EU timelines.
Proposed solution	Timing of AE reporting requirements should be written to align with requirements and timelines in the European Union References Dates calendar.
Name of Regulation	**§201 Labeling**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Streamline and Modernize Prescription drug labeling regulations - 21 CFR 201
Approved Information Collection and OMB Control Number (as applicable)	OMB No. for §§ 201.56, 201.57, and 201.80 is 0910-0572 and 0910-0001
Brief Description of Concern	The numerous prescription drug labeling requirements should be consolidated into a fewer number of regulations that would convey the same objectives. With the advent of the Physician's Labeling Rule in 2006, FDA could define 'labeling' to mean the FDA approved labeling which would serve to align revisions to 21 CFR § 202. FDA should allow for the use of electronic labeling for all drug and device products. This would allow for patients to access labeling in their native language, regardless of where they reside and significantly lower costs and better enable timely updates.

Proposed solution	These regulations should be streamlined to ensure better alignment among the requirements, which would serve to meet the same objectives. FDA should also allow for the use of electronic labeling for all drug and device products.
Name of Regulation	**§201 Labeling**
Type of Product or FDA Center Regulating the Product	CDER, CBER, CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart D Exemptions for adequate directions for use, Meaning of 'intended uses' – 21 CFR 201.128
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA's final rule amending the intended use regulation (82 FR 2193; Jan. 9. 2017) inappropriately expands the evidence that may be used to support a misbranding violation. The new final rule criminalizes innocent conduct and impedes operations important to public health. The proposed rule published on September 25, 2015 would prevent manufacturers from being prosecuted for mere knowledge of off-label use. Clarification that FDA would not consider sources related to a manufacturer's knowledge in determining use would ensure physicians continue to have access to the treatments they and their patient determine best and prevent arbitrary punishment of companies for legitimate business practices.
Proposed solution	FDA's final rule amending the intended use regulation (82 Fed. Reg. 2193, Jan. 9. 2017) should be revoked. FDA should instead enact the initial proposed changes (80 FR 57756, 57764-65) published in 2015. FDA should also clarify that it will not consider sources related to a manufacturer's knowledge in determining "intended use".

Name of Regulation	§201 Labeling
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Bar Code Label Requirements - 21 CFR 201.25
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Current guidance are not aligned with the new serialization requirements in the Drug Quality and Security Act.
Proposed solution	FDA should consider eliminating this guidance since DSCSA is being implemented
Name of Regulation	**Title 21: Food & Drugs Part 202 Prescription Drug Advertising**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Prescription drug advertising 21 CFR 202.1(e)(6)(i) and 21 CFR 202.1(e)(6)(ii).
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	These regulations state that communications not supported by "substantial evidence" will be deemed false and misleading. FDA has taken up the pressing need to reform its current approach to regulating manufacturer communications with healthcare providers ("HCPs") and payors, formulary committees and similar individuals and entities ("payors") per the following

	draft guidances: Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Public Hearing; Request for Comments (Docket No. FDA-2016-N-1149); Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities—Questions and Answers (FDA Jan. 2017) (Docket No. FDA 2016-D-1307); Medical Product Communications That Are Consistent with the FDA-Required Labeling—Questions and Answers (FDA Jan. 2017) (Docket No. FDA 2016-D-2285). Current regulations prohibit manufacturers from proactively communicating economic evidence not contained in the FDA-approved label. Real-world outcomes that are not included in product labeling would be more valuable endpoints for value-based arrangements (VBAs), but the inability of manufacturers to discuss this evidence limits the benefits of VBAs.
Proposed solution	BIO believes that reforming current regulations is urgently needed. FDA should finalize guidance on manufacturer communications regarding information not included in product labeling. We have submitted comments in response to the proposed regulations. Please see (https://www.regulations.gov/document?D=FDA-2016-N-1149-0083) for BIO's full response and proposal.
Name of Regulation	**Title 21: Food & Drugs Part 58 Good Laboratory Practice for Nonclinical Laboratory Studies**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	In general – Good laboratory practice for nonclinical laboratory studies – 21 CFR 58
Approved Information Collection and OMB Control Number (as applicable)	OMB Control Number 0910– 0119

Brief Description of Concern	FDA is proposing to amend regulations for good laboratory practices (GLP) for nonclinical laboratory studies to require a complete quality system approach (a GLP Quality System) when safety and toxicity studies support or are intended to support applications or submissions for products regulated by FDA. FDA is also proposing additional management responsibilities and standard operating procedures consistent with the proposed requirement for a GLP Quality system. FDA is also proposing to revise the testing facility definition to reflect current practices for the conduct of nonclinical laboratory studies, particularly multisite studies. These proposed regulations will likely result in diminished flexibility, confusion in roles and responsibilities and undue administrative and financial burden to companies performing nonclinical laboratory studies. The proposed NPRM as written does not provide an improved framework for modernization that is more flexible and does not help improve the quality, planning, conducting and reporting of nonclinical laboratory studies.
Proposed solution	The proposed NPRM should be withdrawn. Any new regulations should align with global standards for GLPs (e.g., consistent with OECD GLP Consensus Guidance Documents), and provide flexibility for alternative approaches to demonstrate integrity of the data.
Name of Regulation	**Title 21: Food & Drugs Part 56 Institutional Review Boards**
Type of Product or FDA Center Regulating the Product	Office of the Commissioner
Citation of Code of Federal Regulations and statutory citation (as applicable)	In general - Institutional Review Boards, Registration requirement – 21 CFR 56.106
Approved Information Collection and OMB Control Number (as applicable)	

Brief Description of Concern	The rationale for this regulation when implemented was to provide FDA with a comprehensive listing of all US IRBs in order to facilitate sharing of information with IRBs and assist FDA in scheduling and prioritizing IRB inspections. However, today FDA is already informed of IRBs overseeing research globally, by way of Form FDA 1572 (IRB for drug trials) and by clinical study reports.
Proposed solution	The regulation should be revoked and FDA should enter the information it has into a database.
Name of Regulation	**Title 21: Food & Drugs Subpart H Medical Devices Part 820 Quality System Regulation (Combination Products)**
Type of Product or FDA Center Regulating the Product	CDER, CBER, CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart C Design controls – 21 CFR 820.30
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Increased regulatory requirements for combination products with a drug primary mechanism of action (PMOA) often results in delays at FDA both in terms of study approval and overall product approval. The US-unique ASIME (analysis of similar events) requirement (CFR 312.32(c)(1)(ii)) is severely outdated.
Proposed solution	Design control regulatory requirements should be reduced and streamlined for Human Factor studies for combination products with a drug PMOA. FDA should also withdraw FDA draft guidance on Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development (February, 2016). FDA's more general guidance on Human Factor studies is sufficient.

Name of Regulation	**§312 Investigational New Drug Application**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart B Investigational new drug application, IND safety reporting – 21 CFR 312.32
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910– 0014
Brief Description of Concern	Current requirements related to individual expedited reporting to all participating investigators is overly burdensome and costly and not aligned with Europe where periodic aggregate summary reports are permitted. The US-unique ASIME (analysis of similar events) requirement (CFR 312.32(c)(1)(ii)) is severely outdated.
Proposed solution	FDA should revise regulatory requirements to decrease burdensome reporting and align with European requirements. FDA should eliminate this provision.

SECTION 1.2. Priority Guidances Suggested for Streamlining or Elimination

Name of Regulation	Submission of Quality Metrics Data (Docket No. FDA-2015-D-2537) (March 2017)
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA's proposed metrics collection would create enormous regulatory burden and would divert resources away from other programs that are more important to patient health and safety. It is also important that any guidance work to align these metrics across multiple global sites and/or products.
Proposed solution	Withdraw revised guidance and continue public dialogue between industry and the FDA. FDA should examine quality metrics requirements in all guidance document and work to streamline and decrease regulatory burden and describe benefit to FDA, industry and patients.
Name of Regulation	**Guidance for industry. Content and Format of Investigational New Drug Applications (INDs) for Phase 1 Studies of Drugs, Including Well Characterized, Therapeutic, Biotechnology-derived Products (1995);** **And Guideline on the preparation of Investigational New Drug Products (1991)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	In May 2015, FDA issued Guidance for industry entitled "IND applications prepared and submitted by Sponsors-Investigators" which not only covers all phases of development but is significantly more detailed and comprehensive than the guidance documents referenced above. Moreover, the newer guidance describes the contemporary industry practices and is consistent with the CTD (introduced after 2001) and ICH recommendations, making these two guidances outdated and obsolete.
Proposed solution	Eliminate both guidances and maintain 2015 guidance.
Name of Regulation	**Guidance on Safety Assessment for IND Safety Reporting (December, 2015)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The guidance does not align with global regulations and creates an undue burdens from a resource and operational perspectives. The guidance adds several burdensome requirements including: establishment of a Safety Assessment Committees separate and distinct from SMCs; introduces the concept of 'anticipated SAE' and excludes these from expedited reporting; and requirements for the development of Safety Surveillance Plans.
Proposed solution	Consider harmonization and alignment with global regulations to streamline the process.

SECTION 2. Priority Regulations/Guidances Suggested for Modification, Streamlining or Harmonization

SECTION 2.1. Priority Regulations Suggested for Modification

Name of Regulation	§314.70 Supplements and other changes to an approved NDA
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	In general – Supplements and other changes to an approved NDA – 21 CFR 314.70
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910–0001
Brief Description of Concern	FDA has begun to reform its approach to post-approval manufacturing changes for drugs, in line with its cGMP for the 21st Century – A Risk Based Approach Initiative. FDA should accelerate efforts to lower barriers in current regulations. Eliminate CMC portions from the 'changes being effective' regulation (and related guidance). The prescriptive elements of these regulations are out of date with respect to modern regulatory science (e.g., drug product sites transfers to CBE 30).
Proposed solution	FDA should revise regulations to remove barriers that discourage the introduction of innovative process and product improvements. The guidance is outdated based on the fact that the user must refer to several other guidances to administer a single CMC change (e.g., SUPAC Guidelines). Updating this guidance would reduce costs from having to comply with potentially discrepant requirements in other guidances, or having to address issues on an ad hoc, administrative basis (i.e., scientific advice). Eliminate the CMC portions from the 'changes being effective' regulations (CFR 314.70 & CFR 601.12; and related guidance).
Name of Regulation	**§314.70 Supplements and other changes to an approved NDA**

Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (moderate changes - 21 CFR 314.70 (c)(6)(iii); and Changes to an approved application; labeling changes requiring supplement submission – product with a labeling change that may be distributed before FDA approval - 21 CFR 601.12 (f)(2)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	While it is important to make timely labeling changes, FDA should pre-approve all labeling changes in an efficient manner to ensure consistent labeling across products. Companies do not unilaterally file CBEs updating labeling with new safety information absent consultation and approval by FDA.
Proposed solution	The regulations for changes being effective supplements for labeling revisions should be revised in a manner that streamlines operationally obsolete requirements and is updated to in manner that is consistent with current industry practice.
Name of Regulation	**§314.81 Other postmarketing reports**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Modifying Reporting requirements – Annual Report, Status reports of postmarketing study commitments – 21 CFR 314.81(b)(2)(vii)(a)(8)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	

Proposed solution	The definitions in the regulations should be revised to ensure that clinical trials and studies that have their deadlines renegotiated are not categorized as delayed.
Name of Regulation	**§314.81 Other postmarketing reports**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Modifying Reporting requirements –Other reporting, Advertisements and promotional labeling – 21 CFR 314.81(b)(3)(i)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	This requirement requires materials to be submitted at each iteration and upon dissemination to different media or audiences resulting in the submission of thousands of items to FDA each year of nearly duplicative materials.
Proposed solution	This regulation should be revised so that submissions are limited to representative materials or not include materials that make only minor changes to reduce the regulatory burden to FDA and industry. FDA should also consider allowing 'batched' submissions rather than each one 'at time of use' as it increases unnecessary burden on the Sponsor.
Name of Regulation	**§201 Labeling**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart B – Labeling requirements for Prescription Drugs, Requirements on content and format of labeling for human prescription drug and biological products – 21 CFR 201.56 (a)(3); and Subpart A – General labeling provisions, Drugs: name and place of business of manufacturer, packer, or distributor – 21 CFR 201.1
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910-0572 and 0910-0001

Brief Description of Concern	Requiring two adequate and well controlled studies to support a superiority or other comparative claims is not in the public interest. The ability to disseminate comparative data even without two head-to-head studies would result in companies generating even more comparative data about their products and this additional data would benefit payers, providers and patients.
Proposed solution	FDA should modify 21 CFR 201.56 (a)(3) to clarify that it does not limit communication of comparative data that is truthful and non-misleading and expressly permit the utilization of one robust single study to support a comparative claim in the label. Further, FDA has taken up the pressing need to reform its current approach to regulating manufacturer communications with healthcare providers ("HCPs") and payors, formulary committees and similar individuals and entities ("payors"). BIO believes that this reform is urgently needed and has submitted comments in response to the proposed FDA regulations. Please see (https://www.regulations.gov/document?D=FDA-2016-N-1149-0083) for BIO's full response and proposal.
Name of Regulation	**§201 Labeling**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart D Exemptions for adequate directions for use, Prescription drugs for human use – 21 CFR 201.100
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Paper labeling document and promotional material requirements are outdated and require a significant amount of time to update all labeling in the supply change and have significant costs associated with printing/destroying/reprinting.

Proposed solution	Modify physical labeling rules to allow paperless labeling. FDA should rely on the National Library of Medicine (NLM) labeling repository as source of up-to-date information and only require paper labeling to be printed as needed by patient or HCP. Should allow sponsors to provide electronic labeling and not "on or with the package." Allow e-labeling for all drug and device products. Currently allowed only for prescription devices. Could lead to significant cost savings and allow patient to access labeling in their native language, regardless of where they reside as well as increase safe use of a product as new approved information can be disseminated much faster.
Name of Regulation	**§ 211 Current GMP**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Validation data submitted in eCTD (ICH Q11 section VII for DS validation and ICH M4 for analytical method validation) - § 211 Current GMP
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Currently, manufacturers must submit drug substance validation data at the time of submission, significantly extending drug development timelines. Removing the application requirement and instead managing process and analytical validation as a cGMP requirement would allow manufacturers to submit earlier development or characterization data instead of final, full scale process validation.
Proposed solution	FDA should consider following a risk-based approach in alignment with their most recent Process Validation Guidance for drug products. Shift drug substance validation focus to the characterization of the manufacturing process rather than process performance qualification (PPQ), in other words, last stage of validation. Current cGMP requirements for drug product process validation leverage use of characterization and risk-assessment to reduce scope of PPQ. A similar approach should be followed for analytical test methods.

	Records and data should be subject of FDA inspectional review (i.e. pre-approval inspections; and not part of the regulatory filing).
Name of Regulation	**§312 Investigational New Drug Application**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	In general – 21 CFR 312 & [320]
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910– 0014
Brief Description of Concern	Current regulations require that a sponsor submit each IND Safety Report in a narrative format on the FDA Form 3500A or in an electronic format that the FDA can process and archive. All IND Safety Reports are submitted using FDA Form 3500A and only foreign suspected adverse reaction reports can be submitted using an alternative form (CIOMS I) form. The US FDA Form 3500A is only accepted in the US, however the CIOMS-I form is accepted globally.
Proposed solution	FDA should revise requirements to accept CIOMS-I forms for all IND Safety Reports (domestic and foreign) thus requiring that only one report is created instead of two.
Name of Regulation	**§312 Investigational New Drug Application**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart A General provisions, Promotion of investigational drugs- 21 CFR 312.7(a); and Investigational device exemptions, Prohibition of promotion and other practices - 21 CFR 812.7

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA should remove barriers preventing scientific exchange to allow manufacturers to provide physicians and other learned audiences accurate up-to-date scientific information without fear of prosecution that would further serve to support better treatment decisions and medical innovation. FDA should adopt binding regulatory safe harbors that exempt scientific exchange from FDA jurisdiction (e.g., clinical reprint dissemination, Medical Science Liaison activities).
Proposed solution	FDA should revise references to scientific exchange in 21 CFR 312.7(a) and 812.7 to create a safe harbor for scientific exchange. FDA should remove overly burdensome restrictions, and finalize its March 2014 Revised Draft Guidance for Industry on Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices and its December 2011 Draft Guidance on Responding to Unsolicited Requests for Off-label Information About Prescriptions Drugs and Devices.
Name of Regulation	**§ 610 General Biological Products Standards**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart A Release requirements, Requests for samples and protocols; official release, Licensed biological products regulated by CBER – 21 CFR 610.2 (a)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	There is no added value in waiting for CBER release and it is inconsistent with ICH Q10.
Proposed solution	Revise to align with ICH Q10.

Name of Regulation	§ 11 Electronic Records, Electronic Signatures
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Electronic records, electronic signatures – 21 CFR 11
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The regulations need to be modernized and the requirements need to be scaled back to enable utilization of new technology and personal electronic devices in clinical trials. The prescriptiveness of Part 11 (and associated guidance) does not allow for flexibility based on the organizational structure and supporting systems.
Proposed solution	Revise regulations that enable the utilization of new technology and decrease unnecessary regulatory burdens.
Name of Regulation	**§ 3.2 Definitions**
Type of Product or FDA Center Regulating the Product	CDER, CBER, CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	Definitions, Combination products – 21 CFR 3.2(e)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Regulations (and associated guidance Current Good Manufacturing Practice Requirements for Combination Products; January, 2015) regarding the definition of cross-labeled combination products should provide a more flexible approach to labeling separately packaged products.

	This regulation allows “cross labeled” products to be regulated as combination products. The U.S. is unique in this regard. The regulation impacts cross-labeled products for use with existing or new products, which may include products such as IVD tests or special delivery systems. It creates ambiguity and subjectivity in applying cGMP and other regulations across products of different identities.
Proposed solution	Revise regulations and associated guidance on cross-labeled products to enable a more flexible approach. This regulation may be interpreted and applied more broadly than products that are truly co-dependent in their use to achieve the intended purpose. FDA should modify the regulation to eliminate the ambiguity of the definition of ‘cross-labeled’ products and ensure its application in the limited circumstances of truly co-dependent products intended for use ONLY together to achieve the intended use, indication or effect.
Name of Regulation	**§ 54 Financial disclosure by clinical investigators**
Type of Product or FDA Center Regulating the Product	CDER, CBER, CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	In general, Financial disclosure by clinical investigators – 21 CFR 54
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910-0396
Brief Description of Concern	Requirements on collecting forms and signatures from all investigators and clinical trial staff is extremely time consuming, burdensome and challenging especially for sites outside the US that do not have similar local requirements, and creates enormous burdens on companies without comparable benefit.
Proposed solution	Exempt small companies not listed on the US stock exchange from these reporting requirements and allow for alternative approaches.

SECTION 2.2. Priority Guidances Suggested for Modification

Name of Regulation	**Guidance on Providing Postmarketing Periodic Safety Reports in the ICH E2C(R2) Format (Periodic Benefit-Risk Evaluation Report) (November, 2016)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Needs to better align with ICH E2C(R2) guidance without a waiver.
Proposed solution	Needs to better align with ICH E2C(R2) guidance without the necessity of a waiver.
Name of Regulation	**Guidance on Established Conditions: Reportable CMC Changes for Approved Drug and Biologic Products (May, 2015)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Guidance should be modified to permit omission of most validation data from the application. This would serve to focus review on essential requirements.

	A prior approval supplement should only be required when basic unit operations change. This guidance creates unnecessary burden as the information collected is already included in the initial marketing application.
Proposed solution	Revise guidance to permit the omission of most validation data from the application and eliminate redundancies. FDA should consider combining 21 CFR 314.50 and 314.70 - the regulations governing quality content for new and post approval regulatory applications. Combining these regulations would enable effective implementation of Established Conditions which could transform implementation of post approval change requirements consistent with emerging guidance in ICH Q12.
Name of Regulation	**Guidance on Qualification Process for Drug Development Tools (January, 2014)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The non-proprietary qualification pathway is burdensome and lacks the necessary incentives for widespread utilization. The guidance does not articulate why it is advantageous to qualify markers through this pathway as opposed to the proprietary drug development pathway.
Proposed solution	FDA should update and revise the guidance to align with 21st Century Cures Act and the PDUFA VI on the issue of qualification process for drug development tools.
Name of Regulation	**Guidance on Drug Supply Chain Security Act Implementation (December, 2016)**

Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The guidance is not very clear (particularly the sections highlighted in grey) and appears to expand the requirements of the DSCSA beyond the scope of the statute. This expansion is particularly problematic as companies' procedures in place to ensure compliance with the 2013 DSCSA law.
Proposed solution	Guidance should be revised to provide more clarity and not go beyond the scope of the statute. The FDA should enforce the preemption of DSCSA for distribution licensing. Additionally the revised guidance should: Ensure the 3911 illegitimate product reporting required under the DSCSA is not duplicative of exiting reporting requirements; Revise the post-approval change process to allow companies in good standing to provide FDA notification of changes without requiring approvals to implement every change.

SECTION 3. Outdated Regulations/Guidances Suggested for Streamlining and Harmonizing

Name of Regulation	**Guidance on Format and Content of Nonclinical Pharmacology/Toxicology Section of Application (February, 1987)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH CTC Superseded by ICH S8
Name of Regulation	**Guidance on Exploratory IND Studies (January, 2006)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines. Superseded by ICH M3(R2).
Proposed solution	Update/align with ICH

Name of Regulation	Guidance on Immunotoxicology Testing (May, 1999)
Type of Product or FDA Center Regulating the Product	CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Nonclinical Safety Evaluation of Drug or Biologic Combinations (March, 2006)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Nonclinical Safety Evaluation of Pediatric Products (February, 2006)**

Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Recommended Approaches to Integration of Genetic Toxicology Study Results (January, 2006)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH S2(R1)
Name of Regulation	**Guidance on Single Dose Acute Toxicity Testing for Pharmaceuticals (August, 1996)**

Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Analytic Procedures and Methods Validation for Drugs and Biologics (July, 2015)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	There is no alignment with ICH. The guidance also includes elements that go beyond the scope of method validation (e.g., life cycle management) Regarding guidance on the use of second-generation biologics analytical test methods: These additional/replacement methodologies are often very challenging to perform, and do not provided increased confidence in batch release as certain parameters are comparatively inconsistent (specification setting, statistical analysis, process capability, clinical relevance).

Proposed solution	Eliminate guidance and follow CFR 211.165(e) and 211.194(a)(2) which provides that validation data must merely be established and documented. ICH provides harmonized guidance on analytical method validation. There would be a reduced cost in eliminating this interpretation/requirement from the guidance.
Name of Regulation	**Guidance on Safety Testing of Drug Metabolites (November, 2016)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-derived Products (April, 1996)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH guideline on comparability (Q5E).
Name of Regulation	**Reviewer Guidance, Validation of Chromatographic Methods (1994)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH guidance for method validation.
Name of Regulation	**Guidance on NDAs: Impurities in Drug Substances (February, 2000)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated and/or duplicative with ICH guidelines
Proposed solution	Update/align with ICH
Name of Regulation	**Guidance on Immunotoxicology Evaluation of Investigational New Drugs (October, 2002)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH S8
Name of Regulation	**Reference Guide for the Nonclinical Toxicity Studies of Antiviral Drugs Indicated for the Treatment of N/A Non-Life Threatening Disease Evaluation of Drug Toxicity Prior to Phase I Clinical Studies (March, 1998)**
Type of Product or FDA Center Regulating the Product	CDER

Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH M3(R2)
Name of Regulation	**Guidance for the Submission of Chemistry, Manufacturing and Controls Information for a Therapeutic Recombinant DNA Derived Product or a Monoclonal Antibody Product for In Vivo Use (August 1996)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Superseded by ICH Quality Documents Q6b, Q8R2, and Q11
Name of Regulation	**Guidance on DSCSA Implementation: Product Tracing Requirements — Compliance Policy (December, 2014)**

Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Temporary enforcement discretion policy and is now outdated
Proposed solution	Eliminate
Name of Regulation	**Guidance for Industry: Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - Small Entity Compliance Guide (August, 2007)**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Outdated
Proposed solution	Consider updating

SECTION 4. Additional Regulations Suggested for Streamlining or Elimination

SECTION 4.1. Additional Regulations Suggested for Streamlining or Elimination

Name of Regulation	§312 Investigational New Drug Application
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart B Investigational new drug application, Annual Reports - 21 CFR 312.33
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The IND annual report date and format should be harmonized with ICH E2F Guideline to prevent unnecessary duplication and overlap.
Proposed solution	The IND annual report date and format should be harmonized with ICH E2F Guideline. (Revise Final Rule: Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans.)
Name of Regulation	**§320 Bioavailability and Bioequivalence Requirements**
Type of Product or FDA Center Regulating the Product	CDE
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart B Procedures for determining the bioavailability or bioequivalence of drug products, Criteria for waiver of evidence of in vivo bioavailability or bioequivalence – 21 CFR 320.22(b)(i)(ii)
Approved Information Collection and OMB Control Number (as applicable)	

Brief Description of Concern	The current regulation requires that composition as well as the concentrations of both the active and inactive ingredients be identical to obtain a wavier for in vivo bioavailability/bioequivalence. The regulation has become obsolete as FDA often grants waivers for IV formulations that differ both in their composition as well as concentration of their components, especially for soluble drugs.
Proposed solution	The current regulation should be revoked, and FDA should promulgate a new regulation that reflects current thinking.
Name of Regulation	**§600 Biological Products: General**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart C Establishment Inspection, Time of inspection – 21 CFR 600.21
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The regulatory requirements that each establishment is inspected every 2 years is inconsistent with a risk-based approach.
Proposed solution	The regulation should be revoked and revised to enable a risk-based approach to inspections.
Name of Regulation	**§ 610 General Biological Products Standards**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart B General provisions, Purity, Test for pyrogenic substances – 21 CFR 610.13(b)

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The current regulation requires that the rabbit pyrogen test be satisfied for each injectable product and a suitable surrogate test must be in place for each lot of drug product. FDA's historic interpretation of a suitable surrogate test has required further reliance on USP standards that may not be scientifically appropriate for all scenarios. The test is outdated and suitable in vitro tests have since been developed that provide assurance of the low endotoxin limits of each drug product lot. Additionally, this requirement does not take into account processes, facilities, and products for which suitable evidence can be generated to demonstrate low endotoxin/pyrogenic risks.
Proposed solution	This regulation is outdated and should be revised.
Name of Regulation	**Subpart B General provisions, Identity – 21 CFR 610.14**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The FDA is the only regulatory entity that requires an ID test when packaging.
Proposed solution	Revoke or revise to reduce ID testing requirements for packaging.
Name of Regulation	**§ 211 Current Good Manufacturing Practice for Finished Pharmaceuticals**
Type of Product or FDA Center Regulating the Product	CDER

Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart E Control of components and drug product containers and closures, Use of approved components, drug product containers, and closures – 21 CFR 211.86
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The current regulation of a first in first out approach is not as effective from a business or operational stand point of first expire first out as suggested by the EMA and other recognized regulatory organizations.
Proposed solution	The regulation should be revoked and revised to align with EMA (*e.g.,* Guideline on Plastic Immediate Packaging Materials, 2005).
Name of Regulation	**§ 211 Current Good Manufacturing Practice for Finished Pharmaceuticals**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart C Buildings and facilities, Design and construction features; Ventilation, air filtration, air heating and cooling – 21 CFR 211.42 and 46 & Subpart I Laboratory controls, Penicillin contamination 21 CFR 211.176
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	These regulations do not adequately take into account considerations of manufacturers that are consolidating plants and increasing the use of multiproduct facilities.
Proposed solution	The requirements for product specific facility segregation should be revised and enable a more generalized risk-based approach to multi-product facilities.
Name of Regulation	**§ 211 Current Good Manufacturing Practice for Finished Pharmaceuticals**

Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Subpart J Records and reports, general requirements – 21 CFR 211.180(e)
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The annual review of all quality standards, drug product specifications and manufacturing or control procedure specifications are overly burdensome. Companies already update these specifications and related documents as needed. The annual review requirements add record keeping and administrative obligations without corresponding benefit.
Proposed solution	Regulations requiring annual review of all quality standards, drug product specifications, and manufacturing or control procedures should be eliminated.
Name of Regulation	**§314 Subpart D – FDA Action on Applications and Abbreviated Applications**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Withdrawal of approval of an application or abbreviated application - 21 CFR 314.150 & Notice of withdrawal of approval of an application or abbreviated application for a new drug - 21 CFR 314.150
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910–0513
Brief Description of Concern	FDA regulations provide that only the agency can withdraw applications, even if the sponsor voluntarily seeks to withdraw approval. FDA response to a request for voluntary withdrawal can sometimes take years.

Proposed solution	To the extent that burdensome reporting obligations are in place following a sponsor's request for withdrawal and until FDA acts even when the product is not on the market, the regulations should be modified to remove these requirements.
Name of Regulation	**§ 208 Medication Guides for Prescription Drug Products**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	Distributing and dispensing a Medication Guide - 21 CFR §208.24
Approved Information Collection and OMB Control Number (as applicable)	OMB No. 0910–0393
Brief Description of Concern	This regulation requires manufacturers to provide a Medication Guide in sufficient numbers to permit dispensers to provide a Medication Guide to each patient. This requirement is unduly burdensome in requiring the distribution of physical copies of Med Guides when already available on company and FDA websites.
Proposed solution	The regulation should be revised to allow referencing the link to the online version of a Medication Guide available on FDA or NIH websites or providing a telephone number for patients to call will ensure that patients have access to the most up-to-date version.
Name of Regulation	**§ 801 Labeling**
Type of Product or FDA Center Regulating the Product	CDRH, CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	§ 801.30(b)(3) General exceptions from the requirement for the label of a device to bear a unique device identifier.

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA's unique device identifier (UDI) regulations require, among other things, each device to be labeled with a UDI. In addition to medical devices not in combination products, these regulations apply to certain types of combination products, including convenience kits, cross-labeled products, and co-packaged products. However, the prescription drug component of these combination products already has two unique identifiers (NDC, product identifier) which both already achieve the track/trace purposes of the UDI regulation. Requiring a UDI for these products is duplicative and unnecessary, may result in consumer confusion, and increases costs to manufacturers and patients.
Proposed solution	FDA should revise these regulations

SECTION 4.2. Additional Guidances Suggested for Streamlining or Elimination

Name of Regulation	**Guidance on Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice (September, 2004)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Guidance needs to provide more clarity and flexibility related to aseptic process for novel facility designs.
Proposed solution	Revise guidance to provide more clarity and flexibility related to aseptic process for novel facility designs.
Name of Regulation	**Guidance on Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers: Questions and Answers (January, 2017)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The DSCSA defines a wholesale distributor to exclude manufactures and manufacturer's co-licensed partner. However, the Q&A guidance requires that manufacturers meet the

	annual reporting requirements if they distribute anything but their own drugs which is in conflict with the statute creating undue burdens and duplicative activity.
Proposed solution	Guidance should be revised to provide more clarity and not go beyond the scope of the statute.
Name of Regulation	**New Drug Applications and Biologics License Applications (1987)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Presently, there is a requirement to include in any new marketing application or substantial post-approval Supplement an Executed Batch Record supporting any pivotal clinical and/or biopharmaceutics study. Although the FDA Guideline has been determined to be obsolete, FDA continues to prescribe this requirement.
Proposed solution	This requirement should be eliminated as it is superfluous with the pre-approval site inspection requirements, and thus would reduce costs in having to conduct redundant reviews of the same information.
Name of Regulation	**Guidance on Changes to an Approved NDA or ANDA (April, 2004)**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The guidance is outdated based on the fact that the user must refer to several other guidances to administer a single CMC change (e.g., SUPAC Guidelines).
Proposed solution	FDA should update this guidance as it would reduce costs from having to comply with potentially discrepant requirements in other guidances, or having to address issues on an ad hoc, administrative basis (i.e., scientific advice).
Name of Regulation	**Draft Guidance, Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The draft guidance addresses legal issues regarding products approved under a NDAs that will be deemed to be licensed under a BLA in 2020. Under the guidance, sponsors of innovative medicines will lose valuable data exclusivity rights upon transition from FDCA to the PHSA. This "taking" of intellectual property is very concerning and sets a concerning precedent on intellectual property protections that were not intended by Congress when passing the BPCIA.
Proposed solution	The guidance should be eliminated.

SECTION 4.3 Other Thematic Priorities

Name of Regulation	Novel Endpoints
Type of Product or FDA Center Regulating the Product	CDER, CBER, CDRH
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA should develop and revise guidance as appropriate designed to improve the utilization of surrogates and novel endpoints (including digital health related endpoints) for the purposes of approval and, if needed, how to most efficiently and effectively conduct any post approval studies required.
Proposed solution	
Name of Regulation	**New Medicines with Abuse Liability**
Type of Product or FDA Center Regulating the Product	
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Federal government processes, in particular at FDA, HHS, and DEA, are cumbersome and duplicative, and prevent timely access for US patients to medicines with potential for abuse liability.

	FDA should minimize burden on sponsors by responding faster (i.e., within 75 days) to abuse liability study proposals. Timely feedback will allow sponsors to move forward knowing they have considered FDA input on study design. HHS should streamline by stepping out of the process and delegating abuse liability recommendations to FDA, so that FDA can submit its recommendations to DEA directly. This simplification would eliminate an unnecessary step that slows down the process. DEA should plan to act on FDA scheduling recommendations within 30 days of receipt. There is a 90-day statutory deadline, but DEA has little to do save publish the recommendation in the Federal Register, and 30 days should be sufficient to develop the necessary Federal Register notice.
Proposed solution	
Name of Regulation	**Cardiovascular Outcome Trials (CVOTs) for Diabetes Drugs**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	The current FDA requirement to conduct a pre-market CVOT for diabetes is hindering research and development of treatments for this disease which is the fastest growing public health problem in the U.S. The premise (i.e., rosiglitazone), on which this requirement is based, has been shown to be an inaccurate interpretation of the data. CVOTs should be moved to post-approval to incentivize companies to gain CV benefit claims rather than preapproval. They should also be able to better utilize the Sentinel Network to enable more efficient post-market safety assessments.

Proposed solution	
Name of Regulation	**QT studies**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	QT studies are not a cost efficient or effective regulator requirement. QT studies can be overly sensitive and in some cases lead to false positives that can terminate the development of an otherwise promising drug candidate. QT studies are also more resource intensive than alternative methods. FDA should develop alternative in-vitro and in-silico computational methodologies for assessing proarrhythmic risk that are more accurate and cost-effective. Doing so would lead to reduced costs and better outcomes for drug development by leveraging new technologies. FDA should also examine regulations and guidance pertaining to QT to ensure they provide flexibility, enable appropriate use of waivers and are not duplicative.
Proposed solution	
Name of Regulation	**Advisory Committee Membership**
Type of Product or FDA Center Regulating the Product	

Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	Office of Government Ethics/DoJ/FDA: The Federal government process and criteria evaluating conflicts of interest should be revised to allow scientific experts to provide advice to FDA through advisory committee/panel engagement. Policies should allow alternative methods of meeting the conflict of interest requirements to enable more timely hiring of employees and qualified advisory panel members. With respect to FDA employees the need to divest of all stock and patents should be modified. Current requirements can make it difficult to hire experienced staff and top scientists, especially when rules include holdings of family members. Policies should be modified to allow recusals from participating in decisions that might impact their patents or holdings. FDA guidances such as the Guidance on Conflict of Interest for Advisory Committee Members, Consultants and Experts (http://www.fda.gov/oc/advisory/conflictofinterest/guidance.html) can be overly burdensome and barring bonafide experts from participating with the FDA. These recommendations relate to implementation of 18 USC 208(a) and (b) and 21 USC 379d-1, including 5 CFR 2635 Subparts D and E, 5 CFR 2640, and Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of interest and Eligibility for Participation in FDA Advisory Committees (August 2008).
Proposed solution	
Name of Regulation	**Standardize and Modernize Post Marketing Requirements**
Type of Product or FDA Center Regulating the Product	CDER, CBER

Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	A significant proportion of industry's R&D budget is dedicated to post-market trials and studies, which are typically agreed to at the time of FDA approval or mandated in the post-market under 505(o)(3). However, if during the conduct of a clinical trial or study, new evidence either from the study or other sources becomes available to indicate that the clinical trial or study would no longer provide useful scientific information or if medical practice changes and/or the standard of care changes due to approvals of new drugs, there should be an opportunity to end the trial or to renegotiate trial design or timelines. We suggest that FDA: 1) Streamline regulations to establish a mechanism whereby, on its own, or at the responsible person's request, FDA periodically re-evaluate the continued need for a requested post-marketing clinical trial or study and lifts the requirement if the trial or study is no longer scientifically warranted or to determine whether changes in the medical practice or standard of care warrant a need to renegotiate trial or study design or timelines, and; 2) Allow stakeholders the ability to utilize RWE studies and the Sentinel Network to satisfy post-marketing requirements for 505(o)(3) studies, pediatric studies and confirmatory studies under Accelerated Approval.
Proposed solution	
Name of Regulation	**FDA Proprietary Name (Tradename) Review**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	

Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA's process and decision criteria for evaluating proposed proprietary names for Rx and OTC drugs creates unnecessary burden on industry, duplicates efforts, and does not take into account differences between Rx and consumer needs. FDA CDER should reduce sponsor submission requirements, streamline its review process (including eliminating its own research and performing faster reviews for fast track products), and reduce and enhance clarity on decision criteria (including differentiation between Rx and OTC drug naming).
Proposed solution	
Name of Regulation	**Streamline, Modernize and Harmonize Risk Evaluation & Mitigation Strategy (REMS)**
Type of Product or FDA Center Regulating the Product	CDER, CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA should review REMS regulations and guidance and streamline/revise them and work to better align with the EU as appropriate. REMS guidance documents are overly burdensome and complex without adequate benefit to patient safety. Sponsors carry the responsibility for educating HCPs and patients on the necessity of the program. Sponsors are also required to develop new processes in a compressed timeline. However, since FDA requires approval of all changes, it is difficult to modify REMS programs to ensure compliance in a timely manner.

	FDA should consider revision of certain requirements on sponsors of REMS products that are not related to ensuring the safe use of the product. Specifically, FDA's procedural requirement to submit REMS revisions (including editorial changes) impose unnecessary burden on industry. Because these revisions do not affect safety, the guidance should be revised such that the sponsor may proceed with the revision after notification of FDA (perhaps after 30 days of submission if no objection is received). Similarly, FDA guidance imposes rigid procedural requirements for REMS modifications addressing REMS goals. The guidance should be modified so that sponsors have more procedural flexibility in modifying REMS goals to accurately reflect current scientific understanding of the product (e.g., new risk profile). FDA should also advise how products can be released from a REMS, stop considering if REMS programs should utilize CME and accelerate the implementation of the REMS Common Platform in order to incorporate complex REMS programs into HCP electronic workflows (electronic medical records). Finally, we propose that the requirement for annual reports be lessened. Sponsors rarely receive feedback on the annual reports, and we suggest that the annual reports be filed for one or two years post-approval, and then could cease to be filed if there is no substantive feedback from FDA on the previously submitted report.
Proposed solution	
Name of Regulation	**Consistent Approach to IND Requirements**
Type of Product or FDA Center Regulating the Product	CDER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	

Brief Description of Concern	FDA should clarify IND expectations through appropriate regulations and guidance to help ensure a standard approach to IND requirements is utilized across all Centers and Divisions.
Proposed solution	
Name of Regulation	**Animal Testing**
Type of Product or FDA Center Regulating the Product	CBER
Citation of Code of Federal Regulations and statutory citation (as applicable)	
Approved Information Collection and OMB Control Number (as applicable)	
Brief Description of Concern	FDA should revise regulations and guidance to reduce the need for animal testing for originator and biosimilar products and work to better align with the EU.
Proposed solution	