



March 23, 2015

NIH Office of Management Assessment
6011 Executive Boulevard, Suite 601
MSC-7669
Rockville, MD 20852-7669

RE: NIH-2011-0003: Clinical Trials Registration and Results Submission

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) for the opportunity to submit comments on the Notice of Proposed Rulemaking (NPRM) entitled *Clinical Trials Registration and Results Submission*.

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's members are committed to improving health through the development of innovative therapies. We strongly support research that aims to improve human health through better drug development and recognize that the responsibility in sharing our clinical trial data can help to advance research while reinforcing public confidence in the safety and efficacy in our medicines. Efforts to increase the availability of accurate, scientific evidence will arm patients, clinical decision makers, and scientific researchers with the best available information to help assess the relative clinical benefits and risks of a given treatment.

The drug development process is a highly complex, costly, lengthy, and competitive endeavor. Thus, the interests of all participating stakeholders must be balanced with the need for increased transparency. In order for an innovative biotechnology company to successfully attract the investment necessary to find a drug or biologic program over the decade or more required for its development, it is imperative that data not be disclosed prematurely or in a manner that does not protect confidential or proprietary information. Patients and study participants must also have confidence that their personal medical information and privacy are respected in accordance with their informed consent and in compliance with applicable laws. Finally, it must be noted that the burden associated with the NPRM's widespread application of certification, continuous updating, and self-reporting is not insubstantial, both for large companies with many clinical trials and for small companies with limited resources. These requests for additional data will not contribute added value to the core purposes of study registration or results submission on ClinicalTrials.gov and will divert resources from the primary mission of companies in developing innovative therapies for patients.



BIO is pleased to provide the following recommendations to help enhance the www.ClinicalTrials.gov study registration and results reporting process in a balanced manner that is scientifically rigorous and transparent, while not contributing to the premature disclosure of a sponsor's proprietary information while still actively seeking FDA-approval. Further, BIO recommends that the process allow for a reasonable business interval for submission of the required information, consider situations where it is sensible to allow for voluntary submission of information, and allow for batching of updates over a reasonable amount of time.

A. Data Elements/Registration and Results Submission

1. Applicable Clinical Trial

BIO believes that responsible parties should be allowed to declare whether or not a study is an applicable clinical trial (*i.e.*, that a trial fits within one or more of the four stated criteria), rather than responding for each specific sub-element. For example, if a trial is an applicable clinical trial because one of the study sites is in the United States, there is no benefit of having the responsible party further investigate and certify as to whether or not the drug under investigation is manufactured in the U.S. or one of its territories.

Additionally, the proposed distinction for "controlled" trials has the potential to be confusing, given the common reference to "well-controlled" trials. Whether or not the details of the non-concurrent control are detailed in the protocol and statistical analysis plan, there generally are some implicit comparisons to expectation (whether historic or patient as own control), giving context to the study results. In light of this, rather than trying to differentiate whether a trial meets the stated criteria for "controlled," it may be preferable to have all otherwise applicable trials be considered as applicable clinical trials. This would also align with the EU.

2. Data Elements

BIO suggests harmonization of data element format requirements including level and scope of information, data fields, and character requirements between the European Clinical Trials Database (EudraCT) and ClinicalTrials.gov. The current divergence, with respect to timelines for ClinicalTrials.gov and content requirement of EudraCT, poses a significant resource burdens on sponsors. In both cases, BIO strongly suggests that sufficient flexibility be provided to sponsors, so as not to require the completion of data fields for which the requisite information or analyses were not included in the study protocol or the statistical analysis plan.

a. Results Reporting Prior to Approval

Section 11.44 discusses when clinical trial results information should be submitted for applicable clinical trials and delayed submission of results with certification if the sponsor is seeking approval, licensure, or clearance of a new use or initial approval.



BIO's members are committed to responsibly, consistently, and transparently providing qualified researchers with clinical trial data. BIO's "Principles on Clinical Trial Data Sharing" ensure that our members fulfill requests for data transparency and that the information provided has scientific merit, protects patient privacy, and promotes biomedical innovation.¹ To that end, BIO reiterates its recommendation that results for unapproved products should only be submitted when a pivotal confirmatory trials has been terminated for safety reasons, ensuring that information pertinent to patient safety is disseminated through ClinicalTrials.gov. BIO believes this disclosure is consistent with already-existing industry statements and principles.

NIH states in the NPRM that the public availability of results information regarding trials of unapproved medicines would "help protect the safety of participants who volunteer to be in clinical trials by reducing the likelihood that people will unknowingly participate in clinical trials that "are potentially harmful." ² We believe that there are a number of other regulatory controls in place regarding the conduct and oversight of clinical trials involving unapproved drugs to protect patients from participating in clinical trials that may pose undue safety risks. If safety reasons result in an investigational medicine being withdrawn from further development, then disclosure of results would be appropriate. Indeed, in the case of completed trials for medicines that are not yet approved, patients are not using these medicines, and it is therefore hard to see the benefit to patients of the disclosure of such results.

Consistent with applicable law and regulations, proprietary results are currently protected from disclosure until the medicine is approved. The NPRM proposes disclosure at a time that is inconsistent with these legal norms and may undermine incentives to innovate by forcing premature disclosure of proprietary information.

BIO believes that timely disclosure of study results after product approval will provide the general public the opportunity to review all data relevant to a product. Because is possible for information to evolve during the regulatory review process, the disclosure of study results while approval is still being sought runs the risk of being unintentionally inconsistent once the regulatory review is complete. To avoid any potential confusion and inefficiency associated with multiple cycles of updating ClinicalTrials.gov submissions, BIO recommends timely disclosure of study results within a reasonable time frame after the conclusion of regulatory review.

According to the NPRM, general clinical trial results information must be submitted no later than one year after the completion date,³ with a two year limitation on the submission of results after the date the certification was submitted. NIH proposes to permit certification

¹ BIO Principles on Clinical Trial Data Sharing, March 25, 2014, <https://www.bio.org/sites/default/files/BIO%20Principles%20on%20Clinical%20Trial%20Data%20Sharing.pdf>

² NPRM, p. 69577

³ The NPRM states "...completion date as defined in section 402(j)(1)(A)(v) of the PHS act and LPLV [last patient last visit] are identical for most of the clinical trials. It is worth noting that the timeframe for primary income does not correspond to LPLV in many oncology, CNS, and cardiovascular clinical trials. For companies that have significant trials in these therapeutic areas, the difference between the cited definition and requirements by ClinicalTrials.gov causes a significant resource burden.



within one year of primary completion date (PCD) that one is seeking approval for a new use (21 CFR 11.44(b)) or initial approval (21 CFR 11.44(c)) so as to delay results submission until the earlier of various events, but no later than two years after the date of certification. While noting that we object to the two year backstop for initial approvals, it would simplify reporting for both NIH and sponsors if sponsors were able to certify within one year of PCD and receive a delay until three years after PCD (or within 30 days of the date of one of the earlier events).

When sponsors are seeking initial approval of a product or approval of a new use, the period after study completion but prior to approval can often take longer than these regulatory timeframes. Thus, the proposed timing for the submission of results of clinical trials as proposed in the NPRM is problematic in that the sharing of results could cause the forced release of information considered trade secrets and confidential commercial information under existing NIH and FDA regulations, as well as under the common law applicable to trade secrets. Among other concerns, this could result in the potential loss of intellectual property protection.

In the alternative, however, that NIH ultimately determines in a final rule that disclosure of results for all unapproved medicines is required, BIO suggests a bifurcated approach to the format/required elements of such disclosure, such as the use of sponsor-redacted abstracts or otherwise redacted commercially confidential information in lieu of tabular results disclosure if there is no marketing authorization for the products. Since NIH references reliance on the European Medicines Agency (EMA) as to why certain items should not be protected, then, at a minimum, NIH should reference EMA's redaction process. BIO suggests harmonizing requirements so that information posted to ClinicalTrials.gov are limited to no more than required to be posted in EudraCT.

Reasons for extensions should not be required to include anything confidential/proprietary. It is also important to differentiate the instances where a submission is "late" from where an extension has been granted.

b. Certification of Information Provided

Under proposed 42 CFR 11.6(b), NIH would require the submission of a certification by the responsible party that "to the best of his or her knowledge, the information submitted is truthful and not misleading and that he or she is aware that the submission of false and/or misleading information would subject the responsible party to civil, criminal, and/or administrative liability under U.S. law."¹ This certification is in addition to the statutory requirements that drug and device submissions to the FDA include a certification that "all applicable requirements of [section 402(j) of the PHSA] have been met" and that clinical trial information "not be false or misleading in any particular."⁴

BIO does not believe this specific certification is authorized by statute, and is unnecessary because of the certification required by statute, as described above. Indeed, we are concerned about the possible impact of such additional certification, including the potential

⁴ Section 402(j)(5)(D)(i) of the Public Health Service Act



for criminalization or significant individual or manufacturer liability for the mere “submission” of errors, rather than the intent to defraud or mislead. The mere presences of inadvertent or clerical errors should not subject individuals or entities to such potential liability. We urge NIH to remove this requirement, or at minimum to include an intent to deceive or defraud requirement.

If NIH is going to require a certification evaluating the accuracy of a submission, the use of the “truthful and not misleading” standard is inappropriate, as “truthful and not misleading” is a term of art, specifically applied to the regulatory evaluation of advertising and promotional content. Instead, NIH should move to an “information is accurate as provided” standard. Rather than potentially confusing two distinct concepts, this standard assumes that the sponsor has performed the appropriate diligence and puts the onus on the sponsor for ensuring the accuracy of the information provided. BIO would support the inclusion of a statement that the sponsor would have to specifically review and execute that states the information, “to the best of the sponsor’s knowledge,” is accurate as provided.

c. Timing of Updates

Section 11.64 discusses when clinical trial information must be updated. The NPRM proposes requiring all submitted information to be updated at least once a year if there are changes. More rapid updating is proposed for several data elements to help ensure that users of ClinicalTrials.gov have access to accurate, up-to-date information about important aspects of a clinical trial. The deadlines by which data elements need to be updated varies by type.

Even for interventional trials that are closely monitored, updating data elements, such as individual site status and human subject protection review board status within 45 days of a change is unduly burdensome. With the move to risk-based monitoring underway within the clinical trial community, updated information may not be collected as often as it has been historically. These timelines are particularly burdensome to smaller and/or emerging companies, which may have fewer resources to be able to devote solely to these reporting tasks. For study sponsors that have upward of hundreds of studies active on ClinicalTrials.gov, a monthly update schedule would be administratively burdensome. Additionally, observational studies that are voluntarily submitted to ClinicalTrials.gov present a unique set of challenges, as these studies are not as closely monitored and status changes are often not collected in real time.

BIO suggests that, rather than updating this information within 45 days of a change, sponsors’ changes to the site status, Institutional Review Board (IRB) status, and protocol amendments should be batched and updated on an annual basis. If there are no changes to report, then no action should be taken.

d. Timely Corrections

Section 11.66 discusses timely corrections to any errors discovered by the responsible party or by NIH as it reviews submissions upon receipt.



While simple edits and corrections may be made within 15 calendar days of noticing an error, additional time may be needed to move more substantive corrections (e.g., changes to data values) through the sponsor's quality system and approve for release. When a data value is erroneous, for example, the corrections will need to follow the same internal quality processes as the original values - the corrected value may need to be generated by Statistics and checked by Medical prior to uploading to ClinicalTrials.gov. Thus, the deadline of 15 calendar days is difficult to meet when approvals are required to change information that was originally submitted.

Rather than submit the corrected information within 15 calendar days of the error being noticed, BIO suggests that corrections be submitted no later than 45 business days of when identified.

e. Timing for PI Publishing/Presenting Data for Multi-Site Studies

NIH proposes that sponsors identify three categories of publication/presentation restrictions that they place on Principal Investigators (PIs): 1) review and embargo period less than or equal to 60 days, no obligation for PI to accept changes; 2) review and embargo period more than 60 days but less than or equal to 180 days, no obligation for PI to accept changes; and 3) other disclosure agreement that restricts the PI to discuss or publish clinical trials. BIO proposes an additional, scientifically appropriate category that more accurately and specifically characterizes restrictions on multi-site studies and helps the end user better understand the rationale for any publication/presentation restrictions.

While multi-site studies could reasonably fit within the "other disclosure agreement" category, we believe that a distinction should be made between agreements where, for instance, PIs are obligated to accept changes made by the sponsor and multi-site studies where the PI is restricted from publishing or presenting single-site results until multi-centered data are published.

f. Inclusion of Current and Former Names in the Clinical Trial Listing

NIH proposes requiring the inclusion of current and former names of the same product. This requirement could be onerous, particularly when different names for the same product are used in different countries. This requirement could also be challenging because, in the case of devices, there are common "technology" names in addition to trade names. BIO recommends that, rather than requiring sponsors to include current and former names, NIH requires the use of a universally recognized standard, such as the international nonproprietary name (INN) for drugs or the unique device identification (UDI) for devices.

g. Trials of Combination Products to be Treated as Applicable Drug Clinical Trials

Under proposed 42 CFR 11.10, NIH proposes that trials of combination products be treated as applicable drug clinical trials for the purposes of trial registration and results submission. This is contrary to how FDA determines which regulatory pathway a product should follow. BIO recommends that primary mode of action (PMOA) of the combination should determine



whether trials of combination products are treated as drug clinical trials or device clinical trials, similar to the way FDA would regulate a combination product.

3. Results Submission

a. Voluntary Submissions

We agree with the NPRM's proposal regarding voluntary submissions, specifically, the three following points: 1) if a responsible party voluntarily registers a study, the responsible party should complete all the required fields/documents for registration; 2) if a responsible party voluntarily posts results, the responsible party should complete all required fields/documents for results; and 3) a responsible party may voluntarily register a study without being obligated to post the results of that study. We suggest that for voluntarily registered trials, there should be a disclaimer that makes the reader aware that these results are not mandated, and that the results may be not submitted at all.

b. Corrections and Falsifications

BIO recommends removing references to "falsification" altogether from the final rule. In 2010, FDA published a proposed rule that would have required sponsors to report information regarding falsification of data to FDA.⁵ As the FDA proposed rule has not been finalized, we are concerned that including a "falsification" standard to ClinicalTrials.gov circumvents the rulemaking process without addressing or responding to public comments and creates a new requirement though reporting that is different from the normal routes of discussion with FDA.

We encourage the finalization of the proposed FDA rule and believe that cases of falsification should be dealt with separately from ClinicalTrials.gov reporting requirements, and in a coordinated way with other stakeholders, as potential falsification has legal, publication, and other ramifications, and investigations into falsifications may be lengthy.

Additionally, the proposed rule does not support any real distinction between an error and falsification. BIO supports the idea that errors should simply be corrected with no additional notification to NIH.

c. Retroactivity

BIO opposes the retroactive imposition of new requirements. We believe that the regulations regarding registration should apply to initial registrations after the effective date, and that regulations regarding results apply only to new initial results posted after the effective date of the rule.

⁵ "Reporting Information Regarding Falsification of Data," 75 Federal Register 33 (19 February 19 2010), pp. 7412-7426



d. Quality Controls

Sponsors employ their own quality control methods prior to submitting the required information to ClinicalTrials.gov. BIO believes it would be useful for NIH and sponsors to agree on common criteria and standards for quality control, or a verification of quality control for key data fields so that public disclosure of study information is not delayed. Quality control of data should not include imposing additional statistical evaluations by the sponsor not originally planned for in the protocol or the study statistical analysis plan.

The NPRM requires that responsible parties will be “required to correct the errors, deficiencies and/or inconsistencies no later than 15 calendar days after being informed of them by the Agency or otherwise becoming aware of them...” Often, the Agency requires additional data analyses if it makes a sponsor aware of a data deficiency. We note that these activities can take significant resources and take longer than 15 days. BIO suggests extending this deadline to at least 45 days.

B. Effective Date/Compliance Date

NIH proposes that the rule would be effective 45 days after issuance (meaning that ClinicalTrials.gov would be modified to reflect the rule by that date) and that the compliance date would be 90 days after the effective date. Sponsors would therefore have 135 days to update registration and results information in ClinicalTrials.gov to be in compliance with the final rule. This is highly unlikely to be enough notice for sponsors to complete this work, as they will 1) need to determine what changes are needed; 2) pull together the required information; 3) perform analyses necessary to make the changes; and 4) input and submit the information. Indeed, sponsors may have to make significant system alterations or manage data preparations in order to provide data in the form and format the final rule may require. This creates workload burdens for both large and small companies, as large companies could have 100 or more records to update, while small companies may not have the resources available to make the changes.

BIO requests that both the effective date and the compliance date be extended: the effective date should be changed from 45 days to 90 business days and the compliance date from 90 days to 180 business days.

C. Narrative Summaries and Protocols

1. Narrative Summaries

The Food and Drug Amendments Act (FDAAA) states that the expanded registry and results databank should include summaries of clinical trials and their results *if* this can be accomplished without such information being misleading or promotional, charging the Secretary to address first, whether it would be feasible for a summary to be written in non-technical language understandable to patients without being misleading and promotional and second, if a technical summary can be non-misleading or promotional. If these feasibility questions are answered in the affirmative, then the Secretary shall require



regulations. The NPRM has asked for additional comments from companies on narrative, non-technical summaries.

While non-technical summaries can be an important source of information to patients and their families, it is challenging to translate technical language into consumer- and patient-friendly language in such a way that it could not be misconstrued as misleading. BIO strongly encourages NIH and FDA to work with stakeholders to develop standards that ensure that these non-technical summaries present the information in a neutral, factual, and easily understandable manner.

The multi-stakeholder Multi Regional Clinical Trials Center at Harvard University (Harvard MRCT) has developed a draft guidance document⁶ and toolkit⁷ that addresses the challenges faced by sponsors when developing non-technical summaries and provides guidance and examples on the effective use of non-misleading and non-promotional language. Harvard MRCT's approach aims to harmonize requirements with EudraCT and presents best practices for the return of results to patients, including recommended timing and processes for developing content, while incorporating patient-centric methods based on health literacy principles. Harvard MRCT has also developed comprehensive examples of neutral language that could be used to avoid misleading or promotional language alongside templates and examples for creating the summary.

It must be noted that companies are concerned about potential liability considerations on the basis of non-technical (and technical) summaries. Physician (and patient) reliance should be on the product label only, not on a technical or non-technical summary of the trial results. In any summary, technical or non-technical, efforts must be taken to mitigate the potential liabilities, including a clear notation on the summaries page that reliance should be on the product label alone; a voluntary advisory process from FDA as to the non-promotional/non-misleading nature of a proposed summary; and agreement between the sponsor and FDA on the approved narrative summary for submission to ClinicalTrials.gov at the product approval stage for new products and clinical trials only.

2. Protocols

As noted by NIH, FDAAA provides that the regulations shall require information within the category of "[t]he full protocol or such information on the protocol for the trial as may be necessary to help to evaluate the results of the trial."⁸ Based on comments and feedback previously received at the April 2009 Public Meeting, and further based on the proposed submission of additional registration and results information, NIH is not at this time proposing to require submission of the full protocol or other "information on the protocol."⁹ Rather, NIH is seeking public comment on whether the additional information proposed for submission (registration and results) in this proposed rule is sufficient to meet the statutory

⁶ Harvard Multi Regional Clinical Trials Center "Return of Results MRCT Guidance Document."

http://mrct.globalhealth.harvard.edu/files/mrct/files/mrct_at_harvard_ror_guidance_5_feb_2015b.pdf

⁷ Harvard Multi Regional Clinical Trials Center "Return of Results MRCT Toolkit."

http://mrct.globalhealth.harvard.edu/files/mrct/files/mrct_at_harvard_ror_toolkit_5_feb_2015.pdf

⁸ NPRM, at p 69582, quoting 42 USC 282(j)(3)(D)(iii)(III).

⁹ NPRM, at 69582.



definition of “information on the protocol” such that no further information on the protocol would be required.

BIO concurs that submission of the full protocol should not be required, and further believes that the “information on the protocol” requirement would be met by registration and results (in full or partial) submission. Indeed, information required for registration of trials with the NIH including purpose, study design, and eligibility criteria, is sufficient for evaluating the results of the trials. It seems unlikely that submission of the protocol or any other information about the protocol would significantly assist patients or practicing physicians in evaluating the results of a trial or the completeness of the results, and in some cases, such as in medical devices, reveal proprietary information.

D. Adverse Event Reporting

BIO notes that it is questionable whether NIH has the authority to require the additional adverse event information proposed in 21 CFR 11.48(a)(4)(ii)(D) and (E), as the statute provides a default adverse event reporting requirement if NIH failed to issue a proposed rule within 24 months of enactment of FDAAA, and NIH failed to do that. However, for the sake of completeness, BIO is providing comments on the proposed rule below and is seeking further clarification illustrated by two examples, in order to gain a better understanding about what is proposed by the rule.

Proposed Section 11.48(a)(4)(D) and (E) would require reporting of the total number affected and the total number at risk for each organ system for which there is one or more serious adverse events or one or more adverse events that occur with a frequency that exceeds five percent. BIO believes there is little value to this requirement, and that if this requirement is retained, a sponsor should be allowed to include a disclaimer¹⁰ that these data do not necessarily reflect a conclusion by either the sponsor or FDA that the information constitutes an admission that the drug caused or contributed to an adverse experience.

As this requirement is new, we are seeking clarification on how to implement the additional requirement to add the number affected and number at risk at the System Organ Class¹¹ for the “adverse events other than serious that exceed a frequency of 5 percent”. One could only include the events that met the five percent threshold at the Preferred Term level and then calculate the number affected for the System Organ Class. However, the statement that for Organ Systems not presented in the table, ClinicalTrials.gov will assume the total number of participants affected by that organ system is less than five percent is an issue. Therefore, we would like to get clarification on how to handle implementation of the rule illustrated by the following examples.

¹⁰ For example, a disclaimer similar to 21 CFR 312.32 IND Safety Reports (e) disclaimer or 21 CFR 314.80 Postmarketing Adverse Event Experience (k) disclaimer

¹¹ Or other comparable nomenclature when alternative adverse event data systems are employed, such as the Common Terminology Criteria for Adverse Events (CTCAE) in oncology trials



For the two examples below, assume that no subjects had more than one event, such that adding the number affected for each event gives the total number affected for the System Organ Class (note this may not be the case in real data but makes it easy to illustrate the issues/question).

Example 1

System Organ Class	Preferred Term	# affected / # Risk	Percent
Nervous System Disorders	Dizziness	5/100	5%
Nervous System Disorders	Headache	5/100	5%
Nervous System Disorders	Tremor	2/100	2%
Nervous System Disorders	Total	12/100	12%

In Example 1, would a sponsor only include Dizziness and Headache in the table for the “adverse events other than serious” on ClinicalTrials.gov as they exceed five percent as individual line items with the accompanying Total Number Affected by Organ System as 10 percent (*i.e.*, only including the events present in the table on ClinicalTrials.gov) or should it be 12 percent for the organ system entirely (*i.e.*, including events not shown in the table)?

Example 2

System Organ Class	Preferred Term	# affected / # Risk	Percent
Nervous System Disorders	Dizziness	2/100	2%
Nervous System Disorders	Headache	2/100	2%
Nervous System Disorders	Tremor	2/100	2%
Nervous System Disorders	Total	6/100	6%

In Example 2, the Nervous System Disorders organ system would not be present in the table for “adverse events other than serious” in ClinicalTrials.gov as no individual line items exceeds five percent. However, the Total Number Affected for the Organ System is six percent. Should the six percent be included despite the contradiction with the text offered in the NPRM (in bold below):

“(D) Total Number Affected, by Organ System. For each organ system that has one or more adverse events listed in either the table of serious adverse events or the table of adverse events other than serious adverse events that exceed a frequency of 5 percent within any arm of the clinical trial, the overall number of human subjects affected, by arm or comparison group, within each table. **For organ systems that do not have a submitted adverse event, ClinicalTrials.gov will automatically assume that the total number of participants affected by that organ system is 0 (zero) for serious adverse events, and less than the 5 percent threshold for other adverse events,** which will reduce the burden of this proposed requirement.”

Finally, including any abnormal lab results with a clinical consequence as adverse events is unusual, and in addition to being burdensome to the responsible party, will most likely overwhelm those looking at results and thus dilute truly meaningful changes that could be made clear separately.



E. Expanded Access

BIO suggests that the final rule narrow the definition of “Availability of Expanded Access” as “an indication of whether there is expanded access to the drug under section 561(c) of the Federal Food, Drug and Cosmetic Act (21 USC 360bbb(c)) for those who do not qualify for enrollment in the applicable clinical trial. Under this definition, “expanded access” applies only to intermediate-size and large-size treatment INDs¹² with established inclusion/exclusion enrollment parameters and excludes emergency situations and individual patient access to INDs intended for serious diseases.

Conclusion:

BIO appreciates this opportunity to comment on the *Clinical Trials Registration and Results Submission NPRM*. We would be pleased to provide further input or clarification of our comments as needed.

Sincerely,

Andrew J. Emmett

/S/

Managing Director
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/S/

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¹² Per MAPP 6030.6 definitions, when an access protocol that provides for widespread access to an investigational drug is submitted to an existing IND, the submission is referred to as a treatment protocol. When such a protocol is submitted in an original IND and is the only protocol under that IND, the submission is referred to as a treatment IND.