

## NIH Issues Proposed Rule Expanding Clinical Trial Registration and Reporting Obligations

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On November 21, 2014, the National Institutes of Health (“NIH”) published a notice of proposed rulemaking regarding requirements for clinical trial registration and the reporting of results (“Notice” or “Proposed Rule”).<sup>1</sup> These regulations, once implemented, will expand and clarify the registration and results reporting requirements established by Section 801 of the Food and Drug Administration Amendments Act of 2007, which added Section 402(j) of the Public Health Service Act (“PHS Act”).<sup>2</sup>

The Proposed Rule is divided into four subparts. The first, Subpart A, sets forth general provisions including the overarching definitions. Subparts B and C outline the registration requirements and results reporting requirements. The final subpart, Subpart D, addresses additional reporting requirements for voluntary submissions and for updating and correcting registration and results information.

Due to the potentially significant consequences of the Notice, entities sponsoring applicable clinical trials should review the Proposed Rule and consider submitting comments, on or before the **February 19, 2015**, deadline. Comments may be submitted electronically at <http://www.regulations.gov>.

A significant portion of the proposed regulations merely clarify or make slight changes to the requirements that were already in place. This is because the requirements were either codified in Section 402(j) of the PHS Act, such as timing requirements for reporting results from clinical trials of approved, licensed, or cleared products or the requirement to submit clinical trial information when the NIH Director determines that such submission is necessary to protect the public health (which generally must be done within 30 days of notification), or they were implemented as part of sub-regulatory action, such as requiring responsible parties to indicate which FDA center issued an IND or IDE when registering a clinical trial on [clinicaltrials.gov](http://clinicaltrials.gov). However, NIH proposes

<sup>1</sup> 79 Fed. Reg. 69,566 (Nov. 21, 2014).

<sup>2</sup> Codified at 42 U.S.C. § 282(j).

a few significant, and potentially controversial, modifications to the results reporting requirements.

The more significant changes, which are discussed in more detail below, include:

- further defining the scope of applicable clinical trials and proposing a process for determining whether a specific trial is an applicable clinical trial;
- proposing additional registration data elements and the implementation of structured data entry for clinical trial registration information;
- expanding the scope of clinical trial reporting requirements to include results of applicable drug and device clinical trials investigating drugs and devices that have not been approved, cleared, or licensed for marketing;
- requiring responsible parties for applicable device clinical trials to report additional results information that is substantially similar to the information that is required to be submitted during the registration process, as the results information may be required to be publically disclosed before NIH is permitted to disclose the device clinical trial's registration information;
- clarifying the adverse event reporting requirements; and
- expanding the scope of data elements that must be updated within 30 days of the responsible party becoming aware of the need to update the data.

In addition to the key changes in the Proposed Rule, NIH chose not to adopt certain proposals at this time. For example:

- NIH did not propose to require the submission of either a technical or non-technical summary of the results of an applicable clinical trial. Instead, NIH noted that it will study this further and is requesting comments on methods that NIH may employ to evaluate whether such summaries should be required, and if so, how they can be provided in a manner that is objective and not misleading.
- NIH also did not provide a pathway for responsible parties conducting applicable clinical device studies to permit NIH to publicly disclose registration information prior to the device receiving marketing authorization.

### **Subpart A – General Provisions**

NIH adopted the statutory definitions of “applicable clinical trial” and “applicable device clinical trial” without significant modification.<sup>3</sup> In the Proposed Rule, however, NIH significantly broadens the statutory definition of “applicable drug clinical trial” to include clinical trials of combination products that are subject to regulation as drugs, biologics,

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<sup>3</sup> 79 Fed. Reg. at 69574; See Section 402(j)(1)(A)(i) & (ii) of the PHS Act.

or devices. Thus, a clinical trial of a combination product that is evaluated under an IDE that is being performed in support of a PMA would be considered to be a drug clinical trial.

As a result of being considered an applicable drug clinical trial, the registration information for such a combination product will be published within 30 days after the registration information is submitted, regardless of whether the combination product has been previously approved. This is unlike registration information for applicable device trials for previously unapproved or uncleared products, which is not made available to the public until after approval or clearance of the device. This expansion of the scope of trials considered “applicable drug clinical trials” has the potential benefit of ensuring that the study is compliant with ICMJE requirements that clinical trials be registered in a public trials registry at or before the first patient enrolls. However, for those sponsors that do not intend to publish the study results, this requirement may place substantial burdens on their commercial interests.

In addition to interpreting each element of these definitions, NIH is proposing a method to determine whether a clinical trial is an “applicable clinical trial,” using a subset of the data elements that are required to be provided when registering a clinical trial.<sup>4</sup> In order to be deemed an applicable clinical trial, among other requirements, at least one of the following must apply: “(A) At least one Facility Location for the clinical trial is within the U.S. or one of its territories; (B) A drug under investigation is a Product Manufactured in the U.S. or one of its territories and exported for study to another country; or the clinical trial has [an FDA] IND Number.”<sup>5</sup> Because NIH has determined that all combination product clinical trials are drug clinical trials, such a trial may not be considered an “applicable drug clinical trial” if the study is conducted under an IDE, all sites are located outside of the United States, and the combination product is not manufactured in the United States.

### **Subpart B – Registration of Applicable Clinical Trials**

NIH is proposing to use structured data entry for certain data elements required for registration (e.g., requiring responsible parties to pick elements from a preset list).<sup>6</sup> The use of structured data elements is an effort to make the database easier to use for the public and reduce the burden on responsible parties. In addition, the use of defined data elements will allow interested parties to confirm that a clinical trial is an applicable clinical trial through the use of a subset of the registration data elements.

NIH is also proposing adding several additional data elements that it feels are necessary to “allow the effective implementation of, [and] compliance with” other requirements of Section 402(j) of the PHS Act.<sup>7</sup> Other provisions are being added in an effort to improve the quality of the database and make it easier to use the data. These additional data elements include:

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<sup>4</sup> See proposed 42 C.F.R. § 11.22(b), 79 Fed. Reg. at 69670-71.

<sup>5</sup> Proposed 42 C.F.R. § 11.22(b)(v), 79 Fed. Reg., 69671.

<sup>6</sup> 79 Fed. Reg. 69611-31.

<sup>7</sup> 79 Fed. Reg. 69575.

- whether the product was manufactured in the United States or one of its territories;<sup>8</sup>
- any other current or former names of the interventions being studied in the clinical trial;<sup>9</sup>
- an “intervention description” that includes additional information about the intervention beyond the intervention name, which can help distinguish the intervention being studied in the clinical trial from other interventions being used in the control arms or in other clinical trials;<sup>10</sup>
- whether the product being studied in the clinical trial is an FDA-regulated device or FDA-regulated drug;<sup>11</sup> and
- the scientific and ethical review status of the clinical trials listed in the database.<sup>12</sup>

### Subpart C – Results Reporting

The requirements for reporting clinical trial results proposed in Subpart C of the Proposed Rule include the most significant substantive changes proposed by NIH. Specifically, in Subpart C, NIH proposes a significant expansion of the scope of studies subject to reporting obligations to include clinical studies involving unapproved, uncleared, or unlicensed products, regardless of whether a marketing authorization is being sought for the products. This subpart also establishes the timing requirements for results data reporting, which include the requirements for delaying the submission of results data and seeking waivers for such requirements. Additionally, NIH expanded the scope of results information that must be reported for clinical trials involving unapproved and uncleared medical devices.

#### Expansion of the Clinical Trials Subject to Results Reporting Requirements

Exercising the authority granted by Section 402(j)(3)(D)(ii)(II) of the PHS Act, NIH proposes to require responsible parties to submit results of applicable clinical trials involving unapproved, unlicensed, or uncleared products.<sup>13</sup> This represents a significant expansion of the current requirements under the PHS Act, which requires reporting of results information only from applicable clinical trials of products that are approved, licensed, or cleared. In making this proposal, NIH determined that the potential public health benefits of the timely disclosure of results information outweigh the potential competitive disadvantages resulting from such disclosures.

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<sup>8</sup> 79 Fed. Reg. 69618.

<sup>9</sup> 79 Fed. Reg. 69616.

<sup>10</sup> *Id.*

<sup>11</sup> 79 Fed. Reg. 69617-18.

<sup>12</sup> 79 Fed. Reg. 69653.

<sup>13</sup> Proposed 42 C.F.R. § 11.42, 79 Fed. Reg. 69673-74.

Consistent with its rationale for other proposed changes, NIH determined that submitting the results of applicable clinical trials of products that are not available for commercial distribution furthers the express statutory purpose of the expanded data bank “to provide more complete results information and to enhance patient access to and understanding of the results of clinical trials.”<sup>14</sup> NIH further observed that the adverse impact of this new requirement is mitigated by sponsors’ ability to delay reporting the data for up to three years following the completion of the clinical trial. NIH also noted that the European Medicines Agency is contemplating a similar disclosure requirement.

### Timeline for Reporting and Methods for Requesting a Delay

NIH declined to exercise its authority to extend the results submission timeline to 18 months and is instead proposing that clinical trial results data for all applicable clinical trials be submitted by the *earlier* of: (1) one year after the completion date of the primary outcome measures;<sup>15</sup> or (2) 30 calendar days after initial FDA approval, licensure, or clearance of the drug or device for any indication studied in the applicable clinical trial.<sup>16</sup> As a result, if a responsible party obtains approval or clearance of the drug or device for any indication studied in the applicable clinical trial, the timeline for reporting results data may be accelerated significantly.

The Proposed Rule outlines two methods for delaying the submission of results beyond the standard submission deadline: (1) delay by certification, or (2) submission of a request for an extension based on good cause. If a responsible party delays submission by certification or receives an extension, NIH will post on [clinicaltrials.gov](http://clinicaltrials.gov) that the results submission has been delayed but will not indicate the mechanism used to delay the submission or the reason for which an extension may have been granted for a particular applicable clinical trial.

In addition to these two methods for obtaining a delay in the submission of results data, NIH is proposing a pathway to request a waiver of the results submission requirement if the Secretary of the Department of Health and Human Services determines that extraordinary circumstances justify the waiver and that providing the waiver is consistent with the protection of public health or national security interests.<sup>17</sup> If granted, the waiver would excuse the sponsor from compliance with any requirements for which a waiver is granted, and the Secretary will notify and explain to the appropriate committees of Congress why the waiver was granted.

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<sup>14</sup> 79 Fed. Reg. 69577, citing Section 402(j)(3)(D)(i) of the PHS Act.

<sup>15</sup> With respect to pediatric postmarket surveillance of a device that is not part of a clinical trial, the results data must be submitted no later than 30 calendar days after the date on which the final report of the approved pediatric postmarket surveillance of the device is submitted to FDA.

<sup>16</sup> Proposed 42 C.F.R. § 11.44, 79 Fed. Reg. 69674.

<sup>17</sup> Section 402(j)(3)(H) of the PHS Act, Proposed 42 C.F.R. § 11.54. The Proposed Rule provides an opportunity to appeal a denied waiver request to the Secretary or delegated official. The delegated official deciding waiver appeals would, as a matter of practice, not be the delegated official that reviewed the initial waiver request. 79 Fed. Reg. 69646.

Certifications for delay, requests for extensions, and requests for waivers must be made prior to the applicable deadline for submitting clinical trial results information.

### *Delay by Certification*

For applicable clinical trials investigating new uses of already marketed products, the certification requirements mirror those set forth in the PHS Act, which permit a manufacturer to delay the reporting of results of applicable clinical trials of products for which it certifies that FDA clearance or approval has been, or will be, sought.<sup>18</sup> For those applicable clinical trials investigating unapproved, uncleared, or unlicensed products, however, the Proposed Rule departs from the statutory requirements that permit delay by certification that the clinical trial was completed prior to the product's initial approval, licensure, or clearance by FDA,<sup>19</sup> and instead creates a certification process similar to the process for new uses of currently marketed products described above.<sup>20</sup>

By pursuing a delay by certification, a responsible party is permitted to delay submission of results for up to an additional two years, regardless of whether the applicable clinical study involved a new use of an already marketed product or a new product. In addition to certain other triggering events, if the product obtains marketing authorization for the use investigated in the applicable clinical study in the intervening two years, the results data must be submitted within 30 calendar days of receipt of that authorization.<sup>21</sup>

NIH explained that two years provides sufficient time for the sponsor of the applicable clinical trial to protect its competitive advantage and that, within this time frame, a sponsor would likely make a decision about whether to halt product development, initiate another clinical trial, or submit a marketing application or premarket notification to FDA. NIH noted that subsequent trials would most likely be required to register at [clinicaltrials.gov](http://clinicaltrials.gov), and the clinical trial registration would be posted in the data bank, thereby providing some information to competitors about the outcome of previous trials and the objectives of future trials.

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<sup>18</sup> Proposed 42 C.F.R. § 11.44(b), 79 Fed. Reg. 69674. (The responsible party must certify that (1) the drug or device studied has been previously approved, licensed, or cleared; (2) the sponsor of the clinical trial is the manufacturer of the product; and (3) the manufacturer has filed, or will file within one year, an application to FDA for approval or clearance of the use being studied.)

<sup>19</sup> Submission is only required within 30 days of receipt of authorization by FDA and is not limited to a maximum of two years.

<sup>20</sup> Proposed 42 C.F.R. § 11.44(c), 79 Fed. Reg. 69674 (requiring the responsible party to certify that (1) the product has not been previously approved, licensed, or cleared, and (2) the sponsor of the applicable clinical trial intends to continue with product development and is seeking, or may at a future date seek, FDA approval, licensure, or clearance of the product under study).

<sup>21</sup> For certifications relating to a new use of a product, submission is required within 30 calendar days of any one of the following triggering events: (1) the new use is approved, licensed, or cleared by FDA; (2) FDA issues a letter that ends the regulatory review cycle for the application or submission; or (3) the manufacturer withdraws the application or premarket notification and does not resubmit within 210 days. Only the first and third triggering event applies to certifications relating to applicable clinical trials investigating unapproved, uncleared, or unlicensed products. Proposed 42 C.F.R. § 11.44(b), 79 Fed. Reg. 69674.



Recognizing the importance of understanding when a product is being submitted for “initial approval” versus a “new use,” NIH attempted to establish a bright line rule to assist responsible parties. Specifically, NIH stated that it proposes to interpret the term “initial approval” to apply to a new application (i.e., NDA, ANDA, BLA, PMA) or new premarket notification (i.e., 510(k)) for a new product, while a “new use” is evidenced by the submission of a supplemental application or a 510(k) for a new indication.

Although NIH made an attempt to develop a bright line rule, it is unclear whether this distinction is meaningful with respect to 510(k) devices, as there may be little difference between a 510(k) submitted for a new indication and one submitted for a new device.

### *Good-Cause Extensions*

Pursuant to its authority to grant good-cause extensions of the reporting requirements, NIH proposes a detailed process for the submission, review, and appeal of determinations of requests for good-cause extensions.<sup>22</sup> Written requests for good-cause extensions must be submitted prior to the date on which results information is due and must include an explanation of why an extension is necessary and the estimated date that the information will be submitted. Requests for good-cause extensions will be decided by an NIH official, designated by the director, on a case-by-case basis.<sup>23</sup> Although NIH may grant the extension for a period of time that is shorter than requested, responsible parties are not precluded from requesting and receiving more than one good-cause extension. Further, should a request be denied or a shorter extension period be granted than was requested, the Proposed Rule provides responsible parties with an opportunity to submit a written appeal to the NIH Director explaining the reasons why the initial decision should be overturned or revised.<sup>24</sup>

NIH has not defined “good cause.” Whether a request satisfies this requirement will be determined on a case-by-case basis. However, the Notice does include the following examples of circumstances in which NIH may grant or deny a request for a good-cause extension:

- NIH may grant a request if such a delay is necessary to preserve the scientific integrity of an applicable clinical trial for which data collection is ongoing (e.g., if submission of the results of the primary outcomes would require unblinding before all data for secondary outcome measures are collected).
- NIH may grant a request for a delay in the event an emergency (e.g., natural disasters or other catastrophes outside the responsible party’s control) prevents the timely submission of clinical trial results.

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<sup>22</sup> Proposed 42 C.F.R. § 11.44(e), 79 Fed. Reg. 69674-75; see Section 402(j)(3)(E)(vi) of the PHS Act.

<sup>23</sup> 79 Fed. Reg. 69636.

<sup>24</sup> If a request for an extension or a subsequent appeal is denied, the responsible party must submit results information by the later of the original submission deadline (including any applicable delay period or grant of extension period) or 15 calendar days after the electronic notification of denial is sent to the responsible party. Proposed 42 C.F.R. § 11.44(e), 79 Fed. Reg. 69675.

- NIH stated that it would not grant a request for a delay due to pending publications.<sup>25</sup>

Further, NIH stated that it would develop additional guidance clarifying the circumstances that would and would not be considered “good cause” for a delay.

### General Results Information Requirements

In general, the required results information proposed by NIH is consistent with the current requirements for submission of clinical trials results information set out in the PHS Act. Specifically, responsible parties must submit tables of data summarizing:

- participant flow;
- demographics and baseline characteristics of the study population;
- outcome measures, including results of any scientifically appropriate statistical tests;
- adverse events information; and
- certain additional administrative information.

The required information would have to be submitted even if an applicable clinical trial is terminated early, unless no participants are enrolled in the trial prior to termination. NIH also encourages responsible parties to voluntarily submit additional information about the clinical trial to clarify situations where the available data is limited by insufficient enrollment in the trial.

### Adverse Event Information

In general, the requirements proposed by NIH are consistent with the submission requirements codified in Section 402(j) of the PHS Act with a few notable additions. NIH’s proposal to require submission of additional information is intended to help the public better understand the adverse event information included in the database. Specifically, responsible parties will be required to submit two tables of information summarizing the adverse events collected in accordance with the protocol.<sup>26</sup> The first will include data on all serious adverse events, and the second will include data on all other adverse events that occurred at a frequency greater than 5 percent within any arm

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<sup>25</sup> 79 Fed. Reg. 69636-37.

<sup>26</sup> The Proposed Rule would not require responsible parties to collect adverse event data that is not specified to be collected in the protocol. Therefore, in the event that a protocol specifies the collection of only a limited set of adverse event data, the responsible party would be required to submit only the information collected along with a description of how the types of adverse events collected in the clinical trial differ from the types of adverse events defined in the Proposed Rule. 79 Fed. Reg. 69589; see also Proposed 42 C.F.R. § 11.48(a)(4)(ii)(H), 79 Fed. Reg. 69676.



of the trial. Under the Proposed Rule, data on adverse events would need to be included regardless of whether the adverse event is anticipated or determined not to be attributable to clinical trial interventions.

At this time, NIH has decided not to require the use of standard vocabulary for adverse event terms or require the submission of the following information relating to adverse events:

- information specifying when during the clinical trial adverse event information was collected;
- information describing whether the adverse event data was collected using a systematic approach or non-systematic approach; or
- an all-cause mortality table.

However, NIH is requesting comment on the potential benefits and burdens of implementing such requirements.

### Additional Information Required for Medical Device Clinical Trials

Expanding the results reporting requirements to applicable medical device clinical trials involving unapproved or uncleared medical devices creates the potential for a responsible person to be required to submit, and NIH to publish, clinical trial results data before NIH is permitted to publish the clinical trial's registration data.<sup>27</sup> NIH not only recognized this potential, but it realized that publishing results data without some of the registration data could hinder the public's understanding of the results data. Therefore, NIH proposed expanding the scope of results data required to be submitted for such studies to include certain information that was also provided as part of the registration of the clinical trial.<sup>28</sup>

### Pediatric Postmarket Surveillance Requirements

NIH acknowledged the potential difficulty in specifying particular data elements that must be reported for pediatric postmarket surveillance of a medical device because such surveillance may take many forms. As such, the Proposed Rule would instead require that sponsors conducting pediatric postmarket surveillance submit the final report that is submitted to FDA, according to 21 C.F.R. 822.38. NIH is proposing that this report be submitted to the database within 30 calendar days after the report is

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<sup>27</sup> Section 402(j)(2)(D)(ii) of the PHS Act requires the NIH Director to ensure that clinical trial information for an applicable device clinical trial of an unapproved or uncleared device submitted in accordance with the clinical trial registration requirements will not be posted publicly until the product is approved or cleared.

<sup>28</sup> 79 Fed. Reg. 69645; see also Proposed 42 C.F.R. § 11.48(a)(6)(i), 79 Fed. Reg. 69677. As this information would have already been submitted during the registration, NIH proposes to require that sponsors "submit" this information by submitting an affirmation that the information previously submitted to clinicaltrials.gov has been updated and is to be included as clinical trial results information.

submitted to FDA. NIH intends to post the contents of these reports, in their entirety, on [clinicaltrials.gov](https://clinicaltrials.gov). Therefore, NIH instructs responsible parties to redact any:

- personally identifiable information (other than that required to be submitted under the Proposed Rule); and
- information that is not required to be submitted under the Proposed Rule and that is commercial confidential information.

### Subpart D – Requirements

Subpart D of the Proposed Rule covers three aspects of the requirements for submission of clinical trial information. First, it outlines requirements for the voluntary submission of information for clinical trials that are not otherwise subject to the Proposed Rule's reporting requirements. Second, it sets forth requirements for the submission of information when the NIH Director determines that the posting of such information is necessary to protect the public health. Third, it provides the processes and time frames that responsible parties must follow in updating and correcting submitted information.

#### Voluntary Submission

Responsible parties that are not subject to the Proposed Rule's reporting requirements may nevertheless elect to submit trial information voluntarily (either registration information, results information, or both). There are a number of motivations for voluntary reporting, including reducing publication biases in the medical literature and assisting with subject recruitment. Therefore, parties who voluntarily submit information should be aware of their obligations under the Proposed Rule. For example:

- A responsible party may voluntarily submit only results information without registration information; however, it must submit the full results information (as required by proposed Section 11.48) as well as certain additional data elements (including many of the same additional data elements required to be submitted with the results data from applicable device clinical studies of unapproved or uncleared devices).<sup>29</sup> NIH believes that this additional information is needed to make the results information meaningful to the public and demonstrate that the relevant clinical trial is not an "applicable clinical trial."
- A responsible party that voluntarily submits clinical trial information may be required to submit additional information regarding applicable clinical trials that are submitted in FDA pre-market submissions for the same use studied in the voluntarily submitted clinical trial. However, this requirement is only triggered if the applicable clinical trial is required to be submitted in an FDA premarket application for the use studied in the voluntarily submitted trial (i.e., "triggered

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<sup>29</sup> Examples of these data elements include an FDA IND or IDE number and the availability of expanded access. For the full list of required elements, see Proposed 42 C.F.R. § 11.60(a)(2)(i)(B) at 79 Fed. Reg. 69678.

trials”) and the responsible party for the voluntarily submitted trial is the sponsor of the premarket submission. The requirement is designed to reduce the likelihood of responsible parties making selective voluntary submissions as well as limit the burden on responsible parties that submit information voluntarily to the database. NIH specifically invited comments on the appropriateness of this approach.<sup>30</sup>

### Responses to NIH Requests for Additional Information

In addition to clarifying the scope of responsible parties’ obligations with respect to voluntary submissions, proposed Subpart D addresses the requirements surrounding the mandatory submission of clinical trial information in cases where the NIH Director finds that the posting of such information is necessary to protect the public health. Although this mandatory submission requirement is codified in the PHS Act, the Proposed Rule further defines some of the contours of the requirement. For instance, the Proposed Rule states that the waiver provisions of Section 402(j)(3)(H) of the PHS Act and proposed Section 11.54 do not permit a responsible party to request a waiver of the requirement to submit information when notified that submission is necessary to protect the public health. NIH has asked for feedback on this interpretation and, more generally, on the types of situations that might fall under the “necessary to protect the public health” umbrella.<sup>31</sup>

### Requirements for Updating and Correcting Data

The proposed Subpart D details the requirements for updating and correcting submitted information. Notably, *all* responsible parties who submit information (whether pursuant to a mandatory requirement or voluntarily) would be subject to NIH’s proposed time frames for updating and correcting information. Parties who are considering voluntarily reporting should consider whether they have the processes in place to update and correct information in accordance with these time frames before deciding to voluntarily submit data.

Generally, updates to submitted information will need to be made at least once every 12 months (unless there are no changes during those 12 months). However, NIH proposes that certain data elements be updated not later than 30 days after the change occurs. Currently, this accelerated, 30-day update time frame only applies to two data elements (completion date and recruitment status).<sup>32</sup> In the Notice, NIH proposes to expand the number of elements subject to this accelerated time frame to include eight additional elements, which are:

- study start date,
- intervention name,

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<sup>30</sup> 79 Fed. Reg. 69648 (discussing Proposed 42 C.F.R. § 11.60(a)(2)(ii)).

<sup>31</sup> 79 Fed. Reg. 69650.

<sup>32</sup> PHS Act §§ 402(j)(4)(C)(i)(III) & (IV).

- availability of expanded access,
- expanded access status,
- individual site status,
- human subjects protection review board status,
- responsible party or his/her official title, and
- responsible party contact information.<sup>33</sup>

NIH also proposes that several additional elements be subject to more rapid update time frames under certain circumstances. For example, responsible parties would have to update:

- FDA approval, licensure, or clearance status data not later than 15 calendar days after a change in approval, licensure, or clearance of the product being studied;
- relevant registration information not less than 30 days after a protocol amendment is approved by a human subjects protection review board if the protocol is amended and the amendment is so material that changes must be communicated to enrolled subjects (with respect to this proposal, NIH has asked for comments on whether there should be an alternate trigger for when the 30-day update timing is required (one alternative trigger may be when any protocol amendment is reported to a human subjects protection review board));
- record verification date any time the responsible party reviews the complete set of submitted information for accuracy, even if no other updates are submitted at that time; and
- registration information at the time they submit results information (if there are updates).<sup>34</sup>

With respect to errors in submitted information, responsible parties will be required to correct errors not later than 15 calendar days after becoming aware of them (either through self-identification or notification from NIH or other parties). NIH differentiates between updates and corrections, explaining that “updates modify clinical trial information to reflect changes in the status or conduct of an ongoing clinical trial or the associated analysis,” while “[c]orrections revise submitted clinical trial information that is found to be false, invalid, incorrect, inconsistent, or incomplete.”<sup>35</sup>

The Proposed Rule also includes proposals for the actions that a responsible party must take if it determines that information it submitted was falsified or based on falsified

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<sup>33</sup> 79 Fed. Reg. 69651-53 (discussing 42 C.F.R. § 11.64(b)(1)).

<sup>34</sup> *Id.* at 69653-54 (discussing Proposed 42 C.F.R. §§ 11.64(b)(2) through (b)(4) & 11.64(c)).

<sup>35</sup> *Id.* at 69654 (discussing Proposed 42 C.F.R. § 11.66).

information. Upon making such a determination, the responsible party would be required to (1) submit corrected information, within 15 days of it being available, and explain that the correction was necessary because the data was falsified; or (2) report the falsification, within 15 days of discovering the falsification, and notify NIH either that corrected information cannot be generated or that the falsification did not result in incorrect information being submitted.

NIH requested feedback on an alternative approach that would require a responsible party to notify NIH shortly (i.e., less than 15 days) after it determines that it submitted falsified information or data based on falsified information, but then provide the responsible party with additional time to submit the corrected information, explain that the information as submitted was correct, or explain why the submitted data cannot be corrected.<sup>36</sup>

### Compliance Date

Finally, the Proposed Rule would make the deadline for compliance with the changes 90 days after the effective date of any final rule. As a result, by any compliance date:

- responsible parties for applicable clinical trials initiated on or after, or ongoing as of, the effective date would have to comply with the rule's registration information requirements;
- responsible parties for applicable clinical trials would be required to submit results information by a date that is on or after the rule's effective date (including trials whose completion dates were before the effective date, but for which results are due on or after the effective date) and would have to comply with the rule's results information requirements;
- responsible parties who make voluntary submissions on or after the rule's effective date would have to comply with the rule's voluntary submission requirements; and
- responsible parties that submit information (whether by requirement or voluntarily) on or after the rule's effective date would be required to update such information in accordance with the rule.<sup>37</sup>

### **Conclusion**

Much of the Proposed Rule is intended to merely codify existing requirements; however, as discussed above, NIH is proposing several significant changes to the registration and reporting requirements for applicable clinical trials. Several of these changes could significantly impact a sponsor's ability to dictate what information about clinical trials is disclosed and the timing of such disclosure. Therefore, stakeholders may want to consider submitting comments in order to explain the potential consequences of these

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<sup>36</sup> *Id.* at 69655 (discussing Proposed 42 C.F.R. § 11.66(b)).

<sup>37</sup> *Id.* at 69592 (discussing Proposed 42 C.F.R. § 11.64).

changes. Additionally, stakeholders may also want to consider submitting comments responding to the specific questions NIH has asked in the Notice.

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