

GUIDANCE FOR ENSURING YOUR CLINICAL STUDY IS  
BEING DESIGNED, EXECUTED, AND MONITORED  
**IN ACCORDANCE WITH THIS  
INTERNATIONAL DEVICE  
STANDARD**

## Introduction:

An increasing trend in the clinical device research industry is the inclusion of the International Organization for Standardization 14155:2011 (ISO 14155) guidelines into research protocols. IMARC previously published a whitepaper titled "[Conducting Global Clinical Research Trials: Comparing and Contrasting FDA Medical Device Regulations for Clinical Investigators with ISO 14155:2011](#)," which provided readers with a detailed comparison between the FDA regulations for clinical studies and the ISO 14155 standards. The focus of that paper was on clinical investigator compliance with both the required FDA regulations and ISO 14155, specifically on where these guidelines overlap and what additional steps are necessary to comply with ISO 14155.



The Sponsor's goal may be to utilize international clinical data for a trial run in the U.S.; or, perhaps the Sponsor plans to only use sites outside of the U.S. for their study. In either case, incorporating the guidelines from ISO 14155 in addition to any other required regulations can only increase the quality of the subsequent trial data, barring that measures to ensure compliance with ISO 14155 are clearly outlined from the start. Here, the focus will be to dig deeper into what exactly it means from a Sponsor's perspective to ensure a clinical device study follows ISO 14155, from the design and execution phase of the protocol to the subsequent monitoring that will accompany the trial to ensure compliance with this guidance.

## Background:

As referenced above, as a medical device CRO, we have seen Sponsors increasingly include a requirement in their protocols that the study will follow ISO 14155, in addition to the applicable FDA regulations-namely 21 CFR Part 11 (Electronic Records), Part 50 (Informed Consent), Part 54 (Financial Disclosure), Part 56 (IRBs), and Part 812 (IDEs), and typically ICH GCP:E6. Historically, clinical trial protocols were often written to follow both the FDA regulations and ICH GCP: E6, since the ICH GCP guidance was released in 1996. As those in the industry are aware, ICH GCP mostly focuses compliance in regards to drug studies, whereas ISO 14155 was created in 2003 as a specific guideline for clinical device studies to follow. As such, the trend has been progressively moving toward the inclusion of the ISO 14155 guidance for device studies, so it is important to understand exactly what is included that may be in addition to the requirements of the FDA regulations and ICH GCP. If the overall goal of the Sponsor is to follow ISO 14155, in addition to the FDA regulations and ICH GCP to meet international regulatory agency device standards, understanding how to appropriately design protocols and instruct sites on this requirement from the start will aid in compliance, thus benefitting the clinical trial as a whole.



## Planning, Design, and Execution of Clinical Trial:

In the planning and design of a new clinical device trial, what additional steps should be considered to ensure the study complies with the elements included in ISO 14155? What extra measures should be considered for Sponsors and sites to take into account to ensure they are meeting the requirements of ISO 14155 that go above and beyond the FDA regulation stipulations?

The following tables list several additional requirements encompassed in ISO 14155, which go above and beyond the stipulations noted in the FDA regulations.

<b>RECORD MAINTENANCE</b>	
Requirements per 21 CFR	Requirements per ISO 14155
21 CFR 11.1: Electronic records, electronic signatures, and handwritten signatures executed to electronic records are considered trustworthy, reliable, and generally equivalent to paper records and handwritten signatures executed on paper.	ISO 14155 6.8.1: Copies of the original source documents as well as printouts of original electronic source documents shall be signed and dated with a statement that it is a true reproduction of the original source document.
Not specifically required.	ISO 14155 6.8.3 (h): When electronic clinical databases or remote electronic clinical data systems are used, written procedures shall be implemented to ensure that all completed CRFs are signed by the principal investigator or authorized designee.
Not specifically required.	ISO 14155 6.8.2: Case report forms shall be signed and dated by the Principal Investigator or designee.
21 CFR 812.100: An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator’s care.	<p>ISO 14155 8.2.1(e): Ensure the members of the investigation site team and their designated authorization(s) are identified in a log with details.</p> <p>AND</p> <p>ISO 14155 6.2: A log shall be initiated identifying names, initials, signatures, functions, and designated authorizations for the principal investigator and members of the investigation site team.</p>

As evidenced above, ISO 14155 requires four additional items in addition to FDA 21 CFR Parts 11 and 812, in regards to record keeping. Taking this a step further, when designing a clinical protocol following ISO 14155, the following recommendations may be taken into consideration to aid with site compliance:

1

Any printed records shall be signed and dated with a statement that it is a true reproduction of the original.

*A. Discuss this with sites during site assessments and/or site initiation visits, to reiterate the importance and also to assess their familiarity with this process. Determine whether the sites have current processes in place to comply with this requirement (i.e., the EMR can print a certificate, they use a sticker or stamp to certify the printed documents, etc.).*

*i. Depending on the site's current process and whether or not this is considered sufficient, it may be beneficial to provide sites with a document to file in the subject(s) and/or regulatory binders to confirm that all available medical records up to a certain date have been printed from the site's EMR system; request that the site sign and date this form, if utilized.*

*B. Consider modifying the site agreements and/or protocol itself to refer to this requirement, as sites will likely be referring to these documents often.*

2

When electronic databases/systems are used, written procedures shall be implemented to ensure that all completed CRFs are signed by the principal investigator or authorized designee.

*A. When choosing an EDC system, ensure that it has the capability for Principal Investigator signoffs within the database.*

*i. Further, it would be helpful to think about the level of training required for this activity— is it a user-friendly system? Can Investigators “batch sign” eCRFs per subject, or do individual forms require signoff?*

*B. It may also be beneficial to include in the site agreements and/or protocol who would be an appropriate designee for PI signoff. Is a co-investigator acceptable? What about a physician's assistant participating on the study or another research team member?*

C. The expectations of when the PI should sign eCRFs (i.e., when the study is closed, when a subject reaches the primary endpoint for analysis, when a subject exits the study, etc.) should be clearly communicated to the site via training and/or included in the site agreements or protocol.

D. Consider documenting the entire eCRF signoff process in a separate monitoring or data management plan, if not in the protocol itself. Wherever this is documented, the process for eCRF signoff should be clear. Do the forms need to be monitored and query-free ahead of PI signoff? Does data management need to review and lock the forms ahead of or after PI signoff?

3

Case report forms shall be signed and dated by the Principal Investigator or designee.

A. Similarly to the above point, it may be wise to consider adding specifics to the site agreements and/or protocol to clarify who the Sponsor feels is acceptable as a designee for eCRF signoff.

4

Each study team member should be identified in a log (including names, initials, signatures, and functions) to document that personnel's designated authorization(s) by the investigator.

A. Consider creating a Delegation Log to provide to sites at the start of a study, to allow them to clearly document each study team member and which task(s) are delegated to each by the Principal Investigator. Ensure the log includes initials and signatures to be compliant with ISO 14155.

B. During a site initiation visit or other site training, train the site on how to properly complete the Delegation Log and make appropriate changes as necessary throughout the course of the study.



## PRODUCT ACCOUNTABILITY

Requirements per 21 CFR	Requirements per ISO 14155
<p>21 CFR 812.140 (a) (2): A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator’s participation in an investigation: 2) Records of receipt, use, or disposition of a device that relate to:</p> <p>i) The type and quantity of the device, the dates of its receipt, and the batch number or code mark.</p> <p>ii) The names of all persons who received, used, or disposed of each device.</p> <p>iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of. 21 CFR 812.140 (a) (3) (iii): A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.</p>	<p>ISO 14155 6.9 (c) and (d): The principal investigator or an authorized designee shall keep records documenting the receipt, use, return and disposal of the investigational devices, which shall include:</p> <p>a) the date of receipt,</p> <p>b) identification of each investigational device (batch number/serial number or unique code),</p> <p>c) the expiry date, if applicable,</p> <p>d) the date or dates of use,</p> <p>e) subject identification,</p> <p>f) date on which the investigational device was returned/explanted from subject, if applicable, and</p> <p>g) the date of return of unused, expired or malfunctioning investigational devices, if applicable.</p>

One additional item is noted for ISO 14155 requirements, for sites to include in their records the expiry date of investigational devices when applicable.

As the Sponsor, when designing the product log, *include a section for the expiration date of each investigational device on the Investigational Device Accountability Log*, in addition to the elements already required by 21 CFR 812, to ensure that sites are given the appropriate tools to maintain the device expiration information appropriately.

## INFORMED CONSENT DOCUMENTATION

Requirements per 21 CFR	Requirements per ISO 14155
21 CFR 50.27: A copy of the informed consent shall be provided to the subject	ISO 14155 4.7.2 (h): Provide the subject with a signed and dated copy of informed consent
21 CFR 50.25 (b): Statement that significant new findings during the course of the trial which relate to willingness to continue participation will be provided	ISO 14155 4.7.6: New information shall be provided in written form, and confirmed in writing
Not specifically required	ISO 14155 09.5 (c): The Principal Investigator should ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process
Not specifically required	ISO 14155 9.7 (h): Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation
Not specifically required	ISO 14155 9.7 (f): Ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation

Here, ISO 14155 takes the FDA regulations a step further in several instances. The following suggestions may easily be incorporated into study documents as follows:

1

Subjects are required to be provided with a signed and dated copy of the informed consent document.

*A. Consider including this statement in the informed consent template.*

*B. Ensure sites are made aware of this additional requirement during the site initiation training.*

*C. Consider a request for sites to write an informed consent note to document that subjects were given a signed and dated copy of the ICF.*

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2

New information is required to be provided in written form and confirmed in writing.

*A. When new information becomes known, consider a requirement that subjects are re-consented on a revised informed consent document that includes the new information, thus clearly meeting the requirement that the new information is provided to the subject, and that he or she agrees to continue participating in the study by signing and dating the revised ICF. Alternately, the Sponsor may require that sites complete a progress note to document that new information was provided to the subjects in writing, in lieu of re-consenting; any written documentation should be approved by each site's IRB/EC prior to distributing this information to subjects.*

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3

The Principal Investigator should ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

*A. Include training on informed consent requirements per the regulations and ISO 14155 on study training that is required for any new study team member.*

*B. Include on the Delegation Log "obtain informed consent" as a specific task that may be delegated, to clearly document any authorized designees for this task.*

4

**With the subject's approval**, the subject's personal physician should be informed about the subject's participation in the clinical

*A. The Sponsor may want to include a section in the informed consent template with a section similar to the following:*

- I agree to notify my PCP
- If yes, add PCP name and address here: \_\_\_\_\_
- I do not agree to notify my PCP
- The study physician is my PCP
- Notify other physician

*B. When subjects choose to notify their PCPs, consider having a template PCP notification letter with important requirements that the PCP should know, including any device description, study schedule, medication requirements, etc. If a notification letter is used, have the site confirm with their IRB/EC whether or not this needs to be approved by the IRB/EC before utilizing.*

*C. Consider adding a requirement to the protocol for the informed consent document to be added to subject medical records. However, keep in mind that oftentimes, a subject's PCP is at another institution and would not have access to the medical records (and hence the study informed consent) at a particular site, which could prompt the use of the PCP notification letter.*

5

**Clinical records should be clearly marked to indicate that the subject is enrolled in a particular clinical investigation.**

*A. Ensuring that a site is including the study ICF in the subjects' medical records may make it easier for study personnel to verify inclusion/exclusion information and to confirm that subjects are not enrolled in other investigational studies. Similarly to the above example regarding record keeping, discuss with the site whether or not they have a current process in place to comply with this requirement, to determine if their process for identifying subjects participating in investigational studies within the subject's medical record or EMR system is sufficient.*

## SAFETY REPORTING

Requirements per 21 CFR	Requirements per ISO 14155
<p>21 CFR 812.140 (a)(3): A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator’s participation in an investigation:</p> <p>(ii) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.</p> <p>AND</p> <p>21 CFR 812.150 (a): Investigator reports. An investigator shall prepare and submit the following complete, accurate, and timely reports: (1) Unanticipated adverse device effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator.</p>	<p>ISO 14155 9.8: The principal investigator shall</p> <p>a) record every adverse event and observed device deficiency, together with an assessment,</p> <p>b) report to the sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect; this information shall be promptly followed by detailed written reports, as specified in the CIP,</p> <p>c) report to the EC serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or CIP or by the EC,</p> <p>d) report to regulatory authorities serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations, and</p> <p>e) supply the sponsor, upon sponsor’s request, with any additional information related to the safety reporting of a particular event.</p>

Finally, ISO 14155 has a more rigorous adverse event reporting requirement, although this guidance does not provide specific timelines on when certain AEs need to be reported to the Sponsor.

Keep the following suggestions in mind, specifically regarding the requirement that any device deficiencies that could have led to a serious adverse device effect to be reported to the Sponsor, IRB/EC, and regulatory authorities:

1

All serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to the Sponsor.

*A. Add to the site agreements and/or protocol the requirement that serious adverse events that could lead to serious adverse device effects must be reported.*

*B. Create an adverse event source worksheet to include specific questions such as “was the AE related to the device,” “was the AE caused by a device deficiency”, “could the event have led to a serious adverse device effect” and require that the investigator assess each AE in relation to these questions.*

*C. Consider adding to the site agreements and/or protocol a reporting requirement and timeline for reporting any device issues. A separate CRF and/or source worksheet for device deficiencies may be included, and review of device deficiencies may be added to the monitoring and/or data management plan.*

*D. Serious adverse events and device deficiencies that could have led to a serious adverse device effect could be included in CEC and/or DSMB reviews.*

2

Similarly, all serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to the EC (or IRB) if required by the protocol or EC/IRB policies.

*A. Be familiar with the sites’ EC or IRB policies to assist with reporting applicable events as necessary.*

3

Finally, all serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to regulatory authorities, as required.

*A. Consider outlining in the protocol and/or site training the process for how sites should communicate when one of these events occurs, to ensure timely submissions to regulatory authorities as necessary. For example, many Sponsors request that any particular SAEs or SADEs are reported within 24 hours, with subsequent documentation to follow.*

4

The site should provide the Sponsor with any additional information related to the safety reporting of a particular event.

*A. In addition to the above suggestion, ensure sites are properly trained on any specific process required for the sites to communicate safety information in a timely manner. Should de-identified documents be sent via email or fax? Is there a place in the EDC system or Trial Master File to maintain documentation surrounding safety events where sites can upload this information themselves?*



## Monitoring to Ensure Compliance:

Now that some suggestions have been made to ensure the study has been designed and executed appropriately to follow ISO 14155, with suggestions to add these requirements into the study documents themselves, how should monitors adjust their practices to ensure that they are reviewing for compliance with this guideline?

On-site monitors play a crucial role in determining whether sites are in compliance with all necessary requirements. Taking each of the bullet points from above into consideration, some suggestions for ensuring compliance through monitoring are as follows:

### 1 Record Maintenance:

ISO 14155 requires four additional items in addition to FDA 21 CFR Parts 11 and 812, in regards to record keeping. To ensure compliance with ISO 14155 in regards to these requirements, let's examine each of the points separately from a monitoring perspective and what may be seen on-site:

A. Any printed records shall be signed and dated with a statement that it is a true reproduction of the original.

*i. Monitors may see that sites are printing the electronic medical records, which are then maintained, and using a certified stamp or sticker to document that the printed record is equivalent to the EMR.*

*ii. Monitors may also see sites which have a note-to-file in the regulatory binder outlining their process for printing electronic records and confirming these match the original records.*

*iii. The Sponsor may also have provided a document for the site to file in the subject(s) and/or regulatory binders to confirm that all available medical records up to a certain date have been printed from the EMR system; if used, the site may be requested to sign and date this form.*

*iv. The EMR system itself may have the capability to create a certificate when medical records are printed. If this is the case, monitors may recommend that the document explain that all available medical records between specified dates have been printed to ensure that all records are available for monitoring.*



B. When electronic databases/systems are used, written procedures shall be implemented to ensure that all completed CRFs are signed by the principal investigator or authorized designee.

i. *Monitors should confirm with the Sponsor that the EDC system has eCRF signoff capabilities.*

ii. *Monitors should be aware if there is any requirement in the protocol or agreement for a timeline surrounding when the PI should sign off on eCRFs or any conditions surrounding eCRF signoff. If so, monitors should assess whether or not the PI signoff is occurring within the required timeframe and meeting all expectations.*

iii. *It should also be determined whether or not the PI has authorized a designee to sign off on eCRFs in his or her place. If so, the monitor should determine whether this is appropriately documented on a Delegation Log and that proper training has been provided and is documented.*

iv. *The monitor should be familiar with the process for eCRF signoff, including the order when each party needs to sign the forms, to be able to re-train the site as necessary; this may be outlined in a separate monitoring or data management plan, if it is not in the protocol itself.*

C. Case report forms shall be signed and dated by the Principal Investigator or designee.

i. *As noted above, monitors should confirm whether the protocol or agreement includes any language surrounding which study personnel could appropriately be delegated this responsibility. If such language exists, the monitor should confirm if appropriate study personnel were delegated this duty.*

ii. *Monitors should be able to confirm through an audit trail the date the PI (or designee) signed an eCRF and should confirm this is in alignment with the Sponsor's expectations.*

D. Each study team member should be identified in a log (including names, initials, signatures, and functions) to document that personnel's designated authorization(s) by the investigator.

*i. Monitors should confirm that a Delegation Log has been provided to the site and is completed appropriately to confirm the site is complying with this requirement.*

*1. Attention should be paid to ensure that all study team members are listed on the log, that tasks delegated to each study team member are appropriate, that the date(s) of participation are accurate, etc.*

*2. Monitors should ensure the log includes signatures and initials for each team member included.*

*3. Monitors should ensure that appropriate training documentation is on file to correlate with the authorized task(s) for each study personnel, as noted on the Delegation Log.*

*4. Monitors should check the Delegation Log during review of subject data and regulatory documents to ensure that anyone noted as participating on the study is documented appropriately on the Delegation Log, as noted above.*

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## 2

## Product Accountability

A. ISO 14155 requires sites to include in their records the expiry date of investigational devices when applicable.

*i. Monitors should confirm that the Device Accountability Log contains the expiration dates of devices.*

*ii. If expiration dates are missing from the Device Accountability Log, monitors should determine if these dates can be found elsewhere (packing slips, for example).*

## 3

## Informed Consent Documentation

ISO 14155 takes the FDA regulations a step further in several instances. The monitor can ensure compliance in the following ways:

A. Subjects are required to be provided with a signed and dated copy of the informed consent document.

*i. The monitor may look to the protocol and/or agreement to see if the Sponsor has required this to be documented in a particular way. Often, sites may be writing an informed consent note to document the consent process, which could include that the subject was given a signed and dated copy of the informed consent document.*

*ii. If a monitor does not see anything documented in the site's files regarding their consent process, or sees other issues surrounding the process of ensuring that subjects are given copies of the signed and dated ICFs, the monitor may suggest that this be clarified or documented in a formal consent note.*

B. New information is required to be provided in written form and confirmed in writing.

*i. Monitors should look for documentation that new information was provided to study subjects and suggest that sites document this process, if it is not clear. A copy of the information provided to the subjects should be included in the study files. If the Sponsor requires a consent note or other form of documentation, the monitor should ensure the site is meeting the Sponsor's expectations.*

*ii. One suggestion for monitors to ensure compliance with this requirement would be to use a table or other format to track when subjects are required to be re-consented and follow up to ensure that this is completed, within the required timeframe if one is specified.*

C. The Principal Investigator should ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

*i. The monitor should be aware of any IRB/EC requirements regarding which study personnel the PI may delegate this task to and ensure appropriate training (minimally the protocol and general informed consent requirements) is on file for the delegated personnel.*

*ii. Monitors should confirm that an appropriate Delegation of Authority Log is being maintained to ensure the site is complying with this requirement.*

**D. With the subject's approval**, the subject's personal physician will be informed of the subject's participation in the clinical investigation

*i. Monitors should first look for documentation of the subject's approval to notify their PCP of their participation in the study. This may be found within the informed consent itself, via a consent note, or in another form of documentation.*

*ii. The monitor may look to the protocol and/or agreement to see if the Sponsor has required this to be documented in a particular way.*

*1. One example would be confirming whether the study informed consent form has been added to the subject's paper or electronic medical record for any other physician to access the study ICF within that institution.*

*2. Another example may be documentation that the subject's primary care physician was mailed a letter from the Principal Investigator to communicate the subject's participation in the study. If a notification letter to the PCP was utilized, the monitor should confirm whether or not the IRB/EC needed to approve the letter.*

**E. Clinical records should be clearly marked to indicate that the subject is enrolled in a particular clinical investigation.**

*i. As noted above, the monitor may see this being documented in a number of ways, but the monitor should ensure that the site has a process in place to comply with this requirement. The site may be uploading the study ICF document to the subject's electronic medical record, the EMR system may have the capability to label or tag subjects participating in an investigational study, etc.*



## 4

## Safety Reporting

ISO 14155 has a more rigorous adverse event reporting requirement, although this guidance does not provide specific timelines on when certain AEs need to be reported to the Sponsor.

The monitor can work with sites to ensure compliance in the following ways:

A. All serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to the Sponsor.

*i. Monitors should specifically keep in mind that ISO 14155 requires any device deficiencies that could have led to a serious adverse device effect to be reported to the Sponsor, IRB/EC, and regulatory authorities. Because of this, the Sponsor may have added a requirement to the protocol and/or agreement that all potentially - related device AEs should be reported to the Sponsor.*

*ii. Even if this is not spelled out in the protocol, monitors should be aware of this requirement and guide their sites to report these types of events appropriately to ensure compliance with ISO 14155.*

*iii. The monitor should be familiar with any specific questions the Sponsor has included in the AE CRF, and also whether device deficiencies are being reported on a separate CRF, if they were unrelated to an AE.*

*iv. For any reportable AEs or device deficiencies, the monitor should ensure that the PI (or designee) is appropriately assessing the relatedness of the device deficiency to an AE. In addition, there should be adequate documentation to demonstrate that the PI (or designee) is indeed assessing all AEs and device deficiencies.*

*v. If the Sponsor has outlined the process for monitoring AEs and/or device deficiencies in the protocol or a separate monitoring or data management plan, the monitor should be familiar with those requirements.*

B. Similarly, all serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to the EC (or IRB) if required by the protocol or EC/IRB policies.

*i. As with all studies, monitors should be well-versed in the site's IRB/EC policies and should be able to appropriately guide them on these reporting requirements.*

*ii. As each site may have different requirements regarding the reporting of device deficiencies (separately from AEs), the monitor should become familiar with these policies as well, to guide sites appropriately.*

C. Finally, all serious adverse events and device deficiencies that could have led to a serious adverse device effect should be reported to regulatory authorities, as required.

*i. Monitors should ensure that all events meeting these criteria are reported to the Sponsor in a timely manner, so that the Sponsor can communicate to regulatory authorities as necessary. If the Sponsor has a report timeline for adverse events and/or device deficiencies, the monitor should be aware of these and confirm that the site is in compliance with the Sponsor's expectations.*

D. The site should provide the Sponsor with any additional information related to the safety reporting of a particular event.

*i. In the event that a serious adverse device effect occurs, monitors may be asked to copy relevant source documentation for the Sponsor to review and/or include in their regulatory submissions. Monitors can assist on-site with determining what source would be relevant to send, how to properly de-identify the source to avoid any PHI being sent to the Sponsor, and to ensure that all necessary source has been obtained and sent.*

*ii. The monitor should be familiar with the Sponsor's requested timeline for obtaining this documentation and the process for how this should be sent to ensure that all necessary information is being submitted to the Sponsor in a timely manner.*

If the site does not have any of these processes in place, the monitor should suggest that the site consider whether any of these processes outlined could work for them and document how they will do so, following one of these or an equivalent method, to ensure they are meeting the requirements of ISO 14155.

If the monitor notes any deficiencies in the above areas, these should be discussed with the PI and applicable site personnel and any re-training should be performed.



## Summary:

We have previously compared the FDA regulations outlining the requirements of conducting clinical trials with the ISO 14155:2011 guidelines and noted the similarities between the two. The goal of this paper was to introduce some suggestions on how to set up a study for successful compliance with both the FDA regulations and ISO 14155, giving some practical advice on how these additional ISO 14155 requirements can be added. In addition, monitors in the field should be able to identify where a site may not be in compliance with ISO 14155 and provide sites with guidance on how to improve or alter their processes to meet these requirements.

## References

1 International Standard ISO 14155, second edition (2011). Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice.

2 U.S. Food and Drug Administration, Code of Federal Regulations. Title 21, Parts 11, 50, and 812.

3 "Conducting Global Clinical Research Trials: Comparing and Contrasting FDA Medical Device Regulations for Clinical Investigators with ISO 14155:2011", IMARC Whitepaper, 2014.



### Stephani Hulec, Assistant Director of Clinical Monitoring Services

Stephani has been part of the IMARC team since August 2010 and is currently serving as an Assistant Director of Clinical Monitoring Services. Stephani has been involved in a variety of clinical trials, including studies investigating treatments for aortic, abdominal, and thoracic aneurysms; imaging modalities, such as intravascular ultrasound in patients with coronary stenosis; electrical stimulation to treat post-stroke pain and Parkinson's symptoms; orthopedic studies to treat hip, shoulder, and knee injuries; wound healing studies for patients with diabetic ulcers or trauma; and several other studies in the genitourinary area.

Stephani joined IMARC from The Cleveland Clinic where she served for several years as a research coordinator in the department of hematologic malignancies and blood disorders. While there, she coordinated several Sponsor and Investigator-initiated clinical trials, including studies focused on myelodysplastic syndromes, bone marrow failure and leukemia. Prior to working as a research coordinator, Stephani worked at the University of North Carolina, where she performed preclinical testing using drug compounds affecting liver fibrosis.

Stephani currently maintains Certified Clinical Research Associate (CCRA) credentials through the Association for Clinical Research Professionals (ACRP) and formerly was a Certified Clinical Research Professional (CCRP) from the Society of Clinical Research Associates. She received her Bachelors degree in Biology from Thiel College (Greenville, PA) and her Master of Science degree in Biology from the University of North Carolina (Charlotte, NC).

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For more information on how you can help prepare your sites for a better outcome, starting from Day One, please contact John Lehmann at 440.801.1540 or via e-mail at [jlehmann@imarcresearch.com](mailto:jlehmann@imarcresearch.com).



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