# Live Case Presentations During Investigational Device Exemption (IDE) Clinical Trials

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# Draft Guidance for Institutional Review Boards, Industry, Investigators, and Food and Drug Administration Staff

***DRAFT GUIDANCE***



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**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Devices and Radiological Health**
**Office of Device Evaluation**
**Program Operations Staff**
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# Preface

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# Live Case Presentations During Investigational Device Exemption (IDE) Clinical Trials

# Draft Guidance for Institutional Review Boards, Industry, Investigators, and Food and Drug Administration Staff

***This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.***



## 1 Introduction

The purpose of this document is to provide draft guidance on important information that should be provided in an original investigational device exemption (IDE) application or a supplement to an IDE application when a sponsor anticipates including a live case presentation during a clinical investigation. This document is also intended to provide guidance to Institutional Review Boards (IRBs) on factors to consider when evaluating an investigation that contains a live case presentation.[1]

**Definition:** For the purpose of this guidance document, a live case presentation is defined as:

"The treatment of a human subject under the auspices of an approved or conditionally approved IDE, conducted and broadcast in real time, or recorded for broadcast at a later time"[2]

[1] Although this guidance is written primarily for IDEs and significant risk devices, the information may also be applied to non-significant risk (NSR) device studies.

[2] Although live case presentations with approved or cleared medical devices used in accordance with their approved or cleared indications may also occur, they are excluded from the definition of a "live case presentation" for purposes of this guidance document.

Generally, a live case presentation involves a video broadcast of an on-going surgical or percutaneous procedure, often accompanied by live narration by, or audience or expert panel interaction with, the operating surgeon, or a video recording of the procedure for later broadcast.

A live case presentation differs from telemedicine; telemedicine is defined as "the use of medical information exchanged from one site to another via electronic communications to improve patients' health status."[3]

It is expected that very few investigations conducted under an IDE will have the need for live case presentations. However, in a few studies, live case presentations may increase awareness of the study for potential investigators and facilitate the recruitment of subjects. Increased awareness of the IDE clinical study by other health care professionals resulting from a live case presentation might accelerate enrollment of eligible subjects which, in turn, may lead to new therapies being made available sooner.

This draft guidance is intended, in part, to improve the quality of information submitted by sponsors in an IDE application or supplement to an IDE application and to ensure consistency in the review of those submissions. It is expected to reduce the need to submit an IDE supplement solely for purposes of conducting a live case presentation after an IDE application has been approved. This guidance aims to shift the Food and Drug Administration's (FDA's or the Agency's) evaluation of the inclusion of a live case presentation in an investigation to a one-time prospective protocol review at the time the original IDE application is submitted. Also, it is anticipated that this will improve the Agency's feedback to sponsors about measures taken to ensure adequate human subject protection, follow-up, reporting, and data analysis for live case presentations.



This document is intended to clarify FDA's regulations and policies regarding live case presentations using unapproved or uncleared investigational devices in the U.S. We recommend that live case presentations performed outside the U.S. and broadcast to audiences within the U.S. also comport with the guidance provided in this document. Regulations and standards of practice may differ for studies conducted outside the U.S. Foreign manufacturers and study sponsors should follow the laws and regulations of the country that is the site of the investigational treatment, which may have their own policies for the broadcast of live case presentations.

Investigations involving a significant risk device,[4] including those investigations involving live case presentations, must be approved by an IRB and must also have an

[3] American Telemedicine Association http://www.americantelemed.org/i4a/pages/index.cfm?pageid=3333

[4] A significant risk device is defined as an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. 21 CFR 812.3(m).

FDA-approved IDE application. See 21 CFR 812.62 and 21 CFR 812.20(a)(1). Investigations involving a non-significant risk device, including those investigations involving live case presentations, must also be approved by an IRB but generally do not require submission to FDA of an IDE application. See 21 CFR 812.62 and 21 CFR 812.2(b)(1)(ii).

Suggestions and recommendations presented in this document are not mandatory requirements, but reflect methodologies that we believe could be acceptable. In this context, please note the following:

- If the objectives in this document can be accomplished by means that present less risk than those stated herein, then you should use those means.

- Some of the following recommendations may have to be modified, and/or additional information may be needed, to address the individual circumstances of a particular request for a live case presentation of a specific investigation.

- If there are any questions regarding the contents of a request for a live case presentation, please contact FDA's IDE Staff or the appropriate Agency review division.



Not all IDE studies are appropriate for live case presentations. For example, high risk procedures that may adversely impact the subject or certain pediatric studies may not be suitable. Additionally, a live case presentation may not be appropriate for novel devices for which the risk profile is unknown or only limited information is available.

FDA regulations referred to in this guidance include:

- Protection of Human Subjects; Informed Consent of Human Subjects and Additional Safeguards for Children in Clinical Investigations (21 CFR Part 50)
- Standards for Institutional Review Boards for Clinical Investigations (21 CFR Part 56)
- Investigational Device Exemptions (21 CFR Part 812)

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

# 2 Background

Requests for live case presentations have been submitted to the Agency as multiple supplements to an approved IDE application as either protocol deviations, changes to the investigational plan, or study expansion requests. Live case presentations have not generally been prospectively identified and described as components of the overall study design in original IDE applications.

Although it is expected that very few investigations conducted under an IDE will have the need for live case presentations, FDA has seen an increase in the number of requests for certain investigations to conduct live case presentations. Live case presentations may increase awareness of the study for potential investigators and facilitate the recruitment of subjects. Increased awareness of the IDE clinical study by other health care professionals resulting from a live case presentation might accelerate enrollment of eligible subjects which, in turn, may lead to new therapies being made available sooner. However, because of concerns related to human subject protection and uncertainty about potential differences between outcomes of subjects participating in live case presentations compared to subjects not participating in live case presentations, this guidance was developed for IRBs, review staff, the regulated industry and clinical community.

# 3 Promotion and Advertising



FDA's regulations provide that a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not promote or test market an investigational device until after FDA has approved the device for commercial distribution. 21 CFR 812.7(a). Additionally, 21 CFR 812.7(d) prohibits a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator from representing that an investigational device is safe or effective for the purposes for which it is being investigated. 21 CFR 812.7(d). These regulations apply to live case presentations involving investigational devices.

Broadcasts of live case presentations may be considered promotional in nature. Therefore, sponsors should provide a rationale in the application for an IDE or supplement for why the live case presentation would not be in violation of the prohibited practices, including promotion, test marketing and representing the investigational device as safe and effective for the purposes for which it is being investigated. Additionally, live case presentations of unapproved or uncleared medical devices or investigational use of marketed devices should be clearly identified as involving investigational devices that are not approved or cleared by FDA for the indication used in the live case presentation at the beginning of the broadcast of the case.

# 4 Human Subject Protection Measures

Investigations involving live case presentations conducted under 21 CFR Part 812, which includes investigations involving significant risk and non-significant risk devices, must

be reviewed and approved by an IRB (*see* 21 CFR 812.62). That IRB, in turn, must comply with the requirements in 21 CFR Part 56. 21 CFR 812.60.

21 CFR 56.111 sets forth the criteria for IRB approval of research, including research involving live case presentations of investigational devices. Among the criteria listed that are particularly important when evaluating an investigation involving live case presentations is a determination by the IRB that: (1) risks to human subjects are minimized (see 21 CFR 56.111(a)(1)); (2) informed consent will be sought in accordance with 21 CFR Part 50 (see 21 CFR 56.111(a)(4)); (3) where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data (see 21 CFR 56.111(a)(7)); and (4) when some or all of the subjects are children, the research complies with 21 CFR Part 50, Subpart D (see 21 CFR 56.111(c)). Thus, any live case presentation must meet these requirements in order to obtain IRB approval. 21 CFR 56.111.

## 4.1 Risk Analysis

All potential risks and benefits of conducting the procedure as a live case presentation should be identified and discussed in detail in the investigational plan. The risk analysis must describe and analyze all increased risks to which the subjects will be exposed by participating in a live case presentation, discuss the manner in which these risks will be minimized, and provide a justification for the live case presentation. 21 CFR 812.25(c). Live case presentations may increase risks to subjects in several ways. The additional risks that should be addressed in the investigational plan may include, but are not limited to, the following:



- Increased risk of infection due to the increased number of non-medical personnel and broadcast equipment in the sterile environment of the operating room or procedure room;
- Prolongation of the medical procedure, resulting in increased blood loss, anesthesia time, radiation exposure, and risk of infection;
- Distraction of the operator from the highly technical and/or high risk procedure;
- Increased pressure on the operator as a result of public scrutiny of the procedure, or conflicting advice from a panel of experts moderating the live case session;
- Invasion of the subject's privacy in the operating room or procedure room because of the presence of persons not directly involved in medical care, as well as the public viewing of the subject's medical procedure.
- Inadvertent broadcasting of the subject, subject identifiers, the subject's voice, or conversations in which the subject's identity is revealed.

A subject who agrees to participate in a live case presentation should have the same expectation of benefit as a subject participating in the clinical trial who did not participate in the live case demonstration. However, the increased awareness of the IDE clinical study by other health care professionals resulting from a live case presentation might accelerate enrollment of eligible subjects. This in turn may lead to new therapies being made available sooner.

A discussant/narrator should be present to explain the procedure, answer questions, and reduce the distraction of the surgeon performing the procedure. If the sponsor does not elect to use a discussant/narrator, this should be discussed with FDA (or an IRB for non-significant risk studies) when the live case presentation is requested. Recording the procedure is recommended as a means of limiting the need for additional live case presentations as the recorded procedure can be reviewed by investigators at their convenience.

## 4.2 Informed Consent

A subject may be asked to participate in a live case presentation after enrolling in a study. It should be made clear to the subject that participation in a live case presentation is optional and that there is no additional direct benefit conferred on the subject by his or her participation in the live case presentation. It should also be made clear to the subject that there will be no favoritism from the investigator as an acknowledgement or reward for consenting to participate in a live case presentation. The informed consent document and process must comply with the requirements of 21 CFR 50.20, and minimize the possibility of coercion or undue influence for subjects who are asked to participate in a live case presentation. Subjects should be able to enroll in the study without agreeing to participate in a live case presentation.



Valid informed consent must be obtained prior to study participation per 21 CFR 50.20, and a separate informed consent must be obtained prior to participating in a live case presentation, outlining the protocol deviations and any additional risks including any additional confidentiality/privacy concerns. A subject who participates in a live case presentation must be informed in writing by the investigator (or his or her designated representative) of the investigational nature of the device and the additional risks posed by the conduct of the live case presentation. 21 CFR 50.25. Therefore, the informed consent form should include, at a minimum:

1. that the procedure will be recorded for future viewing and/or broadcast to an audience during the conduct of the procedure,
2. that there is no additional direct benefit to the subject for participating in the live case presentation
3. any additional risks posed by performing the procedure in this manner, such as increased anesthesia and/or procedure time (see previous discussion under “Risk Analysis”), and
4. any additional issues related to subject confidentiality, such as privacy concerns related to the live case broadcast, and subsequent distribution and/or use of a video or other type of stored media of the procedure.

The informed consent document must be approved by FDA and the IRB for significant risk studies, and by the IRB for non-significant risk studies. *See* 21 CFR 56.109(a). IRB approval for the live case presentation must be obtained prior to the procedure (21 CFR812.42) and a copy of the informed consent must be provided to FDA as part of the

submission of the IDE application for studies involving significant risk devices (21 CFR 812.20(b)(11)).

## 4.3 Additional Considerations for Children

The Agency believes there will only be rare instances in which it might be appropriate to have live case presentations of pediatric subjects.[5] Live case presentations involving pediatric subjects should be reviewed by the IRB with particular concern for the protection of the rights, safety, and welfare of children. In addition to the risks described in the section "Risk Analysis," pediatric live case presentations pose unique considerations. For example, children, on average, are smaller than adults, which may make the procedure involved more technically challenging. Safe performance of the procedure may therefore require a heightened degree of concentration, which may be more difficult to achieve given the distractions associated with live case presentations. In addition, children's sensitivities should be considered when designing a "child friendly" setting. ICH E11[6] suggests a physical setting with furniture, play equipment, activities, and food appropriate for children as an example of a child friendly setting.

In addition to other responsibilities assigned to IRBs under 21 CFR Parts 50 and 56, each IRB must review clinical investigations involving children as subjects covered by 21 CFR Part 50, Subpart D and approve only those clinical investigations that satisfy the criteria described in 21 CFR 50.51, 50.52, or 50.53, and the conditions of all other applicable sections of 21 CFR Part 50, Subpart D. *See* 21 CFR 50.50; *see also* 21 CFR 56.111(c). Since live case presentations neither offer the prospect of additional direct benefit nor result in generalizable knowledge about the subject's disorder or condition, the added risk of the live case presentation must present no more than minimal risk to the child in the clinical investigation in order to conduct a live case presentation with pediatric subjects. *See* 21 CFR 50.51. In addition, the IRB must determine that adequate provisions are made for soliciting the assent of the children when, in the judgment of the IRB, the children are capable of providing assent and that the permission of their parents or guardians is granted as set forth in 21 CFR 50.55.



## 4.4 Data Collection and Analysis

The record-keeping requirements for investigators conducting live case presentations consists in part of maintaining records that include all relevant observations, including adverse effects (whether anticipated or unanticipated). 21 CFR 812.140(a)(3)(ii). There should be no less data collection for live case presentations than there is for the general investigational cohort.

[5] For the purposes of this guidance, the term "pediatric" is used interchangeably with "child," as defined in 21 CFR 50.3(o).

[6] ICH E11 Clinical Investigation of Medicinal Products in the Pediatric Population (December 2000) http://www.fda.gov/ohrms/dockets/ac/04/briefing/4028B1_07_GFI-ICH%20E11.pdf

As mentioned above, all per protocol follow-up requirements are applicable to live case presentations and should be reported on in a separate cohort in the annual report to the IDE. *See* 21 CFR 812.150(b)(10). These reports should include:

- Summary information:
  - diagnostic indications for the procedure;
  - description of all deviations from investigational protocol:
  - number of live case presentations;
  - names of the investigator(s) who performed the live case presentation(s);
  - investigational site(s);
  - the IRB(s) and IRB chair(s) that approved the live case presentation(s);
  - the name(s) of the meeting(s) at which the live case presentation was broadcast, date(s) of the live case presentations(s) and the date(s) of the broadcast (if different from the date of the live case presentation);
  - location(s) of meetings for live case presentations;
- subject-specific information:
  - the subjects' identification codes for the particular study;
  - subject demographics;
  - how subject(s) will be selected, (e.g., fewest risk factors, prognosis, etc).
  - results and conclusions of the procedure, including a complete description of any adverse effects; and
  - any other pertinent information relating to the safety of the device as used under conditions of a live case (e.g., lot number, serial number, etc.).



In addition, if a live case presentation was planned but not performed, this should be submitted to FDA in a report including the reason why it was not performed (e.g., lack of suitable subject for meeting date, business reasons).

Clinical outcomes of those subjects who participate in live case presentations should be collected and analyzed separately. The clinical outcomes of subjects who participated in live case presentations should be compared with those observed in the rest of the study population to assess whether live case subjects were exposed to additional risks and to compare outcomes (including frequency/severity of adverse events) of the live case presentations against those of the remainder of the study cohort. The results of this analysis should be reported in the sponsor's annual progress reports and the final report to the reviewing IRB and FDA. If an unanticipated adverse device effect occurs during a live case presentation, the investigator must report the unanticipated adverse device effect to the sponsor and reviewing IRB as soon as possible, but no later than 10 working days after the investigator first learns of the effect. 21 CFR 812.150(a)(1). The sponsor must then immediately conduct an evaluation (21 CFR 812.46(b)(1)) and report the results of the evaluation to FDA and all reviewing IRBs and participating investigators within 10 working days after the sponsor first receives notice of the effect. 21 CFR 812.150(b)(1).

Study monitors should review all live case presentation informed consent documents and subject files to ensure appropriate adherence to the protocol and all applicable regulations.

# 5 Information to Include in IDE Applications When Seeking to Conduct Live Case Presentations

FDA believes live case presentations performed during an investigation may affect the rights, safety or welfare of subjects enrolled in the clinical trial. Therefore, for investigations of significant risk devices conducted under an IDE, the sponsor of the investigation must obtain FDA approval of the necessary changes to the investigational plan per 21 CFR 812.35(a) and IRB approval per 21 CFR 812.62 prior to conducting a live case presentation. 21 CFR 812.42. For investigations of non-significant risk devices, sponsors must obtain IRB approval per 812.2(b)(1)(ii) prior to conducting a live case presentation. The IRB should determine whether the potential additional risks introduced by a live case presentation would change the risk level from non-significant risk to significant risk.

Live case presentations represent protocol deviations to the approved research; the investigational plan must be modified to account for these uses of the investigational device. 21 CFR 812.35. For example, subjects are pre-selected to participate in the broadcast which may result in breaking treatment assignment protocols, unblinding investigators and subjects, and introducing selection bias. Even if the study is designed as a single arm study, the live case presentation represents a change to the approved research since there may be additional anesthesia time or other additional risks. Subjects may experience changes in treatment regimen, and have their privacy compromised. Data analysis, risk analysis, and reporting may also be altered.



A live case presentation request should be submitted at least 30 days prior to the planned presentation; original IDE applications and supplements have a 30 day review period. A live case presentation request is not appropriate for a study nearing completion since the purpose of a live case presentation is to increase awareness of the study for potential investigators and facilitate recruitment of subjects.

If live case presentations are anticipated for any part of an investigation conducted under an IDE, sponsors should provide the following information at the time the original IDE application is submitted, or as soon as possible thereafter as a supplement to the IDE application for a change to the investigational plan, pursuant to 21 CFR 812.35(a):

- The total number of live case presentations anticipated over the duration of the study;
- A justification for the live case presentation; if more than one live case presentation is requested, provide a justification as to why more than one is necessary;
- The names, dates and locations of scientific meeting(s) (if known) where the live case presentation will be presented and the site where the procedure will be conducted;
- The name and qualifications of the operator/investigator performing the procedure, if not included in the investigator section of the IDE submission;

- A copy of the informed consent for the live case presentation, which includes all additional potential risks to the subject due to the nature of the live case presentation and a clear statement that there is no additional direct benefit to the subject for participating in the live case presentation, in addition to the other elements of informed consent;
- A discussion of methods utilized to minimize risks; and
- A discussion of how the live nature of the case will affect the scientific soundness of the study and how the live case data will be handled in the statistical analysis or otherwise be used to support device approval or clearance.

FDA also has concerns related to clinical study execution as identified below. FDA therefore recommends that the following additional items be specifically addressed when designing or revising an investigational plan to include live case presentations:

- Live case presentations necessitate prior subject selection and may result in unblinding the investigator and subject. The potential for investigator and selection bias should be addressed, as well as how this bias will be minimized (e.g., comparing the results of the live case subjects to the remainder of the study cohort).
- Live case presentations should not result in enrollment beyond the total approved number of subjects in the study. Because these subjects may need to be excluded from the primary study analysis, sample size adjustments may be necessary.
- The sponsor should provide assurance that the live presentation will not be used for commercial promotion of an investigational device (see "Guidance for Industry and FDA Staff on Preparing Notice of Availability of Investigational Medical Devices and for Recruiting Study Subjects" http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073585.pdf ).
- Since a live case presentation presumably means that a subject is assigned the investigational treatment, the IDE protocol for treatment assignment may be violated if there is a randomization schedule. The sponsor should address this protocol deviation and discuss how this protocol deviation with regard to change in treatment assignment will impact the study analysis.
- Live case presentations should not require any significant changes to the investigational protocol, other than potentially altering treatment assignment if the trial is randomized. The sponsor should describe in detail and justify any anticipated changes to the protocol, including subject follow-up and evaluation.
- Data for subjects participating in live case presentations should be collected and reported to FDA according to the protocol in the approved IDE application (or to the IRB, for non-significant risk studies). FDA will review the data from the live case presentation for safety and effectiveness, whether or not the data is used in the statistical analysis or otherwise used to support a marketing submission, in order to determine whether the live case presentation affects subject outcome. Live case presentations should also be separately reported and compared to the remaining investigational cohort in the annual report submissions as well as any marketing application.

- If an unanticipated adverse device effect requiring investigation and reporting to the Agency and all reviewing IRB's (*see* 21 CFR 812.150) occurs during a live case presentation, it should be noted in the report that it took place during a live case presentation, and include a discussion of how the nature of the live case presentation may have impacted the adverse event.
- Sponsors should include a discussion of how subjects participating in live case presentations will be handled in the planned endpoint analyses. For example, will these subjects be included in safety analysis but excluded from the overall effectiveness analysis and reported in a separate cohort?
- A risk analysis must be provided that includes a discussion of the potential increased risks to the subject posed by the live case presentation. 21 CFR 812.25(c).

The live case presentation should be conducted only at an investigational site by an investigator who has signed the Investigator Agreement and is currently participating in the study under an approved IDE. A live case presentation for a non-significant risk device requires IRB approval. A live case presentation for a significant risk device should not be conducted until IRB approval is obtained and certification of that IRB approval is submitted to FDA.

The Agency believes that live case presentations are not appropriate under the IDE Continued Access program since the purpose of a live case presentation is to increase awareness of the study for potential investigators and facilitate recruitment of subjects. By definition, Continued Access occurs after the investigation has been completed and permits continued access to the device while a marketing submission is being prepared and reviewed. Since the IDE Continued Access Program is only available after the investigation is completed, the Agency believes there is no reason to conduct a live case presentation during the continued access phase.



The Agency also believes that live case presentations are not appropriate under the Compassionate Use Program because subjects in the Compassionate Use Program do not meet the study inclusion/exclusion criteria, and the device may be used for a different indication.

# 6 Summary

The goal of this guidance is to provide recommendations as to the type of information that will be useful in reviewing requests for live case presentations during IDE studies. By proactively anticipating the need for live case presentations, and prospectively identifying the study parameters around such live case presentations, the Agency believes that protections to human research subjects will be improved, burdens to the sponsor and the Agency will be minimized, and study validity related to live case presentations using investigational devices will be assured.

# ATTACHMENT A:

## SUGGESTED ELEMENTS OF A PROPOSAL TO INCLUDE LIVE CASE PRESENTATIONS FOR INVESTIGATIONAL DEVICE EXEMPTION STUDIES

The following is a list of items to consider in an original Investigational Device Exemption (IDE) application or a supplement to an IDE application when requesting inclusion of live case presentations during an IDE clinical investigation. Suggestions and recommendations presented in this list are not mandatory requirements, but reflect data and methodologies that FDA believes could be acceptable.

General Information

The sponsor should provide:

- ☐ A detailed rationale for why the live case presentation is needed, including an explanation of the status of subject enrollment and investigator recruitment, as well as a specific rationale for why a live case presentation would not constitute promotion or advertising.

- ☐ The name, date and location of the scientific meeting(s) where the live case presentation will be broadcast and site(s) where the procedure will be conducted

- ☐ A discussion of how the live case nature of the procedure will affect the scientific soundness of the study or necessitate any revisions of the investigational protocol and planned statistical analysis



- ☐ Criteria for how potential subjects will be selected

- ☐ The potential effects of subject selection for live case presentations on unmasking investigator and subject

- ☐ Treatment assignment and the effect on the randomization schedule

- ☐ Information about the potential for selection bias and how this will be minimized; e.g., data submitted to FDA for review should be stratified and compared to the remainder of the study cohort

- ☐ Justification for sample size. Live case presentations may not result in enrollment beyond the approved total number of subjects in the study. Since these subjects may be excluded from the efficacy analyses, sample size adjustments may be necessary

- ☐ A revised risk analysis that includes a discussion of the increased risks posed by the live case presentation

- ☐ Specification that the live case presentations will be conducted only at previously approved investigational sites by investigators who have signed the Investigator Agreement and who are currently participating in the study

Informed Consent

In addition to the other elements of informed consent, the informed consent document should include the following information:

- ☐ The procedure will be recorded for future viewing and/or broadcast to an audience during the conduct of the procedure

- ☐ There is no additional direct benefit to the subject for participating in the live case presentation, and in fact, it is not known if participating in a live case presentation will affect clinical outcome compared to subjects who do not participate

- ☐ Any additional risks posed by performing the procedure in this manner, such as increased anesthesia and/or procedure time (see previous discussion under "Risk Analysis")

- ☐ Any additional issues related to subject confidentiality, such as privacy concerns related to the live case broadcast, and subsequent distribution and/or use of a video or other type of stored media of the procedure.

- ☐ A statement that additional follow-up and evaluation may be needed as a result of the subject's participation in a live case presentation.



Reporting and analysis plans

- ☐ The sponsor should provide a detailed description of proposed data collection and reporting for subjects participating in a live case presentation. Sponsors should address whether data collection and reporting will be according to the IDE protocol, and if not, provide a detailed description of (and justification for) any anticipated changes to the protocol. Subject follow-up and evaluation should be specifically discussed, and should be the same as that specified in the IDE protocol, unless the patient's condition requires additional follow-up and evaluation.

- ☐ The sponsor should provide analysis plans for the live case presentations that include all relevant observations, including adverse device effects (whether anticipated or unanticipated), and specifying that live case presentation data will be stratified and included in safety and/or efficacy analyses.

- ☐ The sponsor should provide separate reporting and a comparison to the remaining investigational cohort in Annual Report submissions as well as any marketing submission. Outcomes for these subjects should be compared to the rest of the study population to assess whether these subjects were exposed to additional risks

or had different outcomes. This information should be submitted in the annual progress reports and final report. These reports should include the subjects' ID codes for the particular study; number of live case presentations; names of the investigator(s) who performed the live case presentation(s); investigational site(s); the IRB(s) and IRB chair(s) that approved the live case presentation(s); the name(s), date(s) of the live case presentation(s) and the date(s) of the broadcast (if different); location(s) of meetings for live case presentations; subject demographics, diagnostic indications, surgical or procedural methods (if different from the investigational protocol), description of all changes to the investigational protocol, results and conclusions of the procedure, including a complete description of any adverse events; and any other pertinent information relating to the safety of the device as used under conditions of a live case presentation.

☐ If an unanticipated adverse device event occurs during a live case presentation, the investigator must report it to the sponsor and reviewing IRB as soon as possible, but no later than 10 working days after the investigator first learns of the event. 21 CFR 812.150(a)(1). The sponsor must then immediately conduct an evaluation of the unanticipated adverse device event (21 CFR 812.46(b)(1)) and report the results of the evaluation to FDA and all reviewing IRBs and participating investigators within 10 working days after the sponsor first receives notice of the event. 21 CFR 812.150(a)(1).



☐ The sponsor should ensure that it is up-to-date in providing Annual Reports and other reports as required by 21 CFR 812.150(b) before requesting or conducting live case presentations.

IRB review

☐ IRB approval and an informed consent document are needed before conducting a live case presentation, regardless of whether the investigational device is a significant risk device or a non-significant risk device. The sponsor should provide a statement that it will obtain IRB approval before adding a live case presentation to the clinical study protocol.

☐ The sponsor should provide a statement that the clinical outcomes of those subjects who were treated in live case presentations will be collected and separately analyzed and reported in the sponsor's progress reports and in the final report to the IRB (and to FDA, for significant risk devices), and that the clinical outcomes will be compared to the rest of the study population to assess whether these subjects were subjected to additional risks and/or had different outcomes.

Additional Safeguards for Children

If live case presentations involve pediatric subjects, assurance of the following additional safeguards for the protection of the rights, safety and welfare of the children should be included in a proposal to include live case presentations in investigational device exemption studies:

- ☐ The added risks of being involved in a live case presentation will involve no more than minimal risk to the enrolled child per 21 CFR 50.51; and;
- ☐ Permission of the parent or guardians will be obtained per 21 CFR 50.55; and
- ☐ Adequate provisions will be made for soliciting the assent of the child as set forth in 21 CFR 50.55.