

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

Draft Guidance for Institutional Review Boards, Industry, Investigators, and Food and Drug Administration Staff

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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
Investigational Device Exemption Staff

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Preface

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1 **Live Case Presentations During**
2 **Investigational Device Exemption (IDE)**
3 **Clinical Trials**

4 _____
5 **Draft Guidance for Institutional Review**
6 **Boards, Industry, Investigators, and Food**
7 **and Drug Administration Staff**
8

9 *This draft guidance, when finalized, will represent the Food and Drug*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

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17 **1 Introduction**

18 The purpose of this document is to provide draft guidance on important information that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

24
25 **Definition:** For the purpose of this guidance document, a live case presentation is
26 defined as:

27
28 “The treatment of a human subject under the auspices of an approved or conditionally
29 approved IDE, conducted and broadcast in real time, or recorded for broadcast at a later
30 time”²

31

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.

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

36
37 A live case presentation differs from telemedicine; telemedicine is defined as “the use of
38 medical information exchanged from one site to another via electronic communications
39 to improve patients' health status.”³

40
41 It is expected that very few investigations conducted under an IDE will have the need for
42 live case presentations. However, in a few studies, live case presentations may increase
43 awareness of the study for potential investigators and facilitate the recruitment of subjects.
44 Increased awareness of the IDE clinical study by other health care professionals resulting
45 from a live case presentation might accelerate enrollment of eligible subjects which, in
46 turn, may lead to new therapies being made available sooner.

47
48 This draft guidance is intended, in part, to improve the quality of information submitted
49 by sponsors in an IDE application or supplement to an IDE application and to ensure
50 consistency in the review of those submissions. It is expected to reduce the need to
51 submit an IDE supplement solely for purposes of conducting a live case presentation after
52 an IDE application has been approved. This guidance aims to shift the Food and Drug
53 Administration's (FDA) or the Agency's evaluation of the inclusion of a live case
54 presentation in an investigation to a case-by-case prospective protocol review at the time the
55 original IDE application is submitted. Also, it is anticipated that this will improve the
56 Agency's feedback to sponsors about measures taken to ensure adequate human subject
57 protection, follow-up, reporting, and data analysis for live case presentations.

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

66
67 Investigations involving a significant risk device,⁴ including those investigations
68 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).

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69 FDA-approved IDE application. See 21 CFR 812.62 and 21 CFR 812.20(a)(1).
70 Investigations involving a non-significant risk device, including those investigations
71 involving live case presentations, must also be approved by an IRB but generally do not
72 require submission to FDA of an IDE application. See 21 CFR 812.62 and 21 CFR
73 812.2(b)(1)(ii).

74
75 Suggestions and recommendations presented in this document are not mandatory
76 requirements, but reflect methodologies that we believe could be acceptable. In this
77 context, please note the following:

- 78
- 79 • If the objectives in this document can be accomplished by means that present less
80 risk than those stated herein, then you should use those means.
 - 81
 - 82 • Some of the following recommendations may have to be modified, and/or
83 additional information may be needed, to address the individual circumstances of
84 a particular request for a live case presentation of a specific investigation.
 - 85
 - 86 • If there are any questions regarding the contents of a request for a live case
87 presentation, please contact FDA's IDE Staff or the appropriate Agency review
88 division.

89
90 Not all IDE studies are appropriate for live case presentations. For example, high risk
91 procedures that may adversely impact the subject or certain pediatric studies may not be
92 suitable. Additionally, a live case presentation is not the appropriate for novel devices
93 for which the risk profile is unknown or only limited information is available.

94
95 FDA regulations referred to in this guidance include:

- 96
- 97 • Protection of Human Subjects; Informed Consent of Human Subjects and Additional
98 Safeguards for Children in Clinical Investigations (21 CFR Part 50)
 - 99 • Standards for Institutional Review Boards for Clinical Investigations (21 CFR Part
100 56)
 - 101 • Investigational Device Exemptions (21 CFR Part 812)

102
103 FDA's guidance documents, including this guidance, do not establish legally enforceable
104 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and
105 should be viewed only as recommendations, unless specific regulatory or statutory
106 requirements are cited. The use of the word *should* in Agency guidances means that
107 something is suggested or recommended, but not required.

108 **2 Background**

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

114
115 Although it is expected that very few investigations conducted under an IDE will have
116 the need for live case presentations, FDA has seen an increase in the number of requests
117 for certain investigations to conduct live case presentations. Live case presentations may
118 increase awareness of the study for potential investigators and facilitate the recruitment of
119 subjects. Increased awareness of the IDE clinical study by other health care professionals
120 resulting from a live case presentation might accelerate enrollment of eligible subjects
121 which, in turn, may lead to new therapies being made available sooner. However,
122 because of concerns related to human subject protection and uncertainty about potential
123 differences between outcomes of subjects participating in live case presentations
124 compared to subjects not participating in live case presentations, this guidance was
125 developed for IRBs, review staff, the regulated industry and clinical community.

126 **3 Promotion and Advertising**

127 FDA's regulations provide that a sponsor, investigator, or any person acting for or on
128 behalf of a sponsor or investigator shall not promote or test market an investigational
129 device until after FDA has approved the device for commercial distribution. 21 CFR
130 812.7(a). Additionally, 21 CFR 812.7(d) prohibits a sponsor, investigator, or any person
131 acting for or on behalf of a sponsor or investigator from representing that an
132 investigational device is safe or effective for the purposes for which it is being
133 investigated. 21 CFR 812.7(d). These regulations apply to live case presentations
134 involving investigational devices.

135
136 Broadcasts of live case presentations may be considered promotional in nature.
137 Therefore, sponsors should provide a rationale in the application for an IDE or
138 supplement for why the live case presentation would not be in violation of the prohibited
139 practices, including promotion, test marketing and representing the investigational device
140 as safe and effective for the purposes for which it is being investigated. Additionally,
141 live case presentations of unapproved or uncleared medical devices or investigational use
142 of marketed devices should be clearly identified as involving investigational devices that
143 are not approved or cleared by FDA for the indication used in the live case presentation at
144 the beginning of the broadcast of the case.

145 **4 Human Subject Protection Measures**

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

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

150
151 21 CFR 56.111 sets forth the criteria for IRB approval of research, including research
152 involving live case presentations of investigational devices. Among the criteria listed
153 that are particularly important when evaluating an investigation involving live case
154 presentations is a determination by the IRB that: (1) risks to human subjects are
155 minimized (*see* 21 CFR 56.111(a)(1)); (2) informed consent will be sought in accordance
156 with 21 CFR Part 50 (*see* 21 CFR 56.111(a)(4)); (3) where appropriate, there are
157 adequate provisions to protect the privacy of subjects and to maintain the confidentiality
158 of data (*see* 21 CFR 56.111(a)(7)); and (4) when some or all of the subjects are children,
159 the research complies with 21 CFR Part 50, Subpart D (*see* 21 CFR 56.111(c)). Thus,
160 any live case presentation must meet these requirements in order to obtain IRB approval.
161 21 CFR 56.111.

162 **4.1 Risk Analysis**

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

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

184
185 A subject who agrees to participate in a live case presentation should have the same
186 expectation of benefit as a subject participating in the clinical trial who did not participate
187 in the live case demonstration. However, the increased awareness of the IDE clinical
188 study by other health care professionals resulting from a live case presentation might
189 accelerate enrollment of eligible subjects. This in turn may lead to new therapies being
190 made available sooner.

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

199 **4.2 Informed Consent**

200
201 A subject may be asked to participate in a live case presentation after enrolling in a study.
202 It should be made clear to the subject that participation in a live case presentation is
203 optional and that there is no additional direct benefit conferred on the subject by his or
204 her participation in the live case presentation. It should also be made clear to the subject
205 that there will be no favoritism from the investigator as an acknowledgement or reward
206 for consenting to participate in a live case presentation. The informed consent document
207 and process must comply with the requirements of 21 CFR 50.20, and minimize the
208 possibility of coercion or undue influence for subjects who are asked to participate in a
209 live case presentation. Subjects should be able to enroll in the study without agreeing to
210 participate in a live case presentation.

211
212 Valid informed consent must be obtained prior to study participation per 21 CFR 50.20,
213 and a separate informed consent must be obtained prior to participating in a live case
214 presentation, outlining the protocol deviations and any additional risks including any
215 additional confidentiality/privacy concerns. A subject who participates in a live case
216 presentation must be informed in writing by the investigator (or his or her designated
217 representative) of the investigational nature of the device and the additional risks posed
218 by the conduct of the live case presentation. 21 CFR 50.25. Therefore, the informed
219 consent form should include, at a minimum:

- 220
221
- 222 1. that the procedure will be recorded for future viewing and/or broadcast to
223 an audience during the conduct of the procedure,
 - 224 2. that there is no additional direct benefit to the subject for participating in
225 the live case presentation
 - 226 3. any additional risks posed by performing the procedure in this manner,
227 such as increased anesthesia and/or procedure time (see previous
228 discussion under “Risk Analysis”), and
 - 229 4. any additional issues related to subject confidentiality, such as privacy
230 concerns related to the live case broadcast, and subsequent distribution
231 and/or use of a video or other type of stored media of the procedure.

232 The informed consent document must be approved by FDA and the IRB for significant
233 risk studies, and by the IRB for non-significant risk studies. *See* 21 CFR 56.109(a). IRB
234 approval for the live case presentation must be obtained prior to the procedure (21
235 CFR 812.42) and a copy of the informed consent must be provided to FDA as part of the

236 submission of the IDE application for studies involving significant risk devices (21 CFR
237 812.20(b)(11)).

238 **4.3 Additional Considerations for Children**

239 The Agency believes there will only be rare instances in which it might be appropriate to
240 have live case presentations of pediatric subjects.⁵ Live case presentations involving
241 pediatric subjects should be reviewed by the IRB with particular concern for the
242 protection of the rights, safety, and welfare of children. In addition to the risks described
243 in the section “Risk Analysis,” pediatric live case presentations pose unique
244 considerations. For example, children, on average, are smaller than adults, which may
245 make the procedure involved more technically challenging. Safe performance of the
246 procedure may therefore require a heightened degree of concentration, which may be
247 more difficult to achieve given the distractions associated with live case presentations. In
248 addition, children’s sensitivities should be considered when designing a “child friendly”
249 setting. ICH E11⁶ suggests a physical setting with furniture, play equipment, activities,
250 and food appropriate for children as an example of a child friendly setting.

251
252 In addition to other responsibilities assigned to IRBs under 21 CFR Parts 50 and 56, each
253 IRB must review clinical investigations involving children as subjects covered by 21
254 CFR Part 50, Subpart D and approve only those clinical investigations that satisfy the
255 criteria described in 21 CFR 50.51, 50.52, or 50.53, and the conditions of all other
256 applicable sections of 21 CFR Part 50, Subpart D. *See* 21 CFR 50.50; *see also* 21 CFR
257 56.111(c). Since live case presentations need to be conducted for the prospect of a direct
258 benefit nor result in generalizable knowledge about the subject’s disorder or condition,
259 the added risk of the live case presentation must present no more than minimal risk to the
260 child in the clinical investigation in order to conduct a live case presentation with
261 pediatric subjects. *See* 21 CFR 50.51. In addition, the IRB must determine that adequate
262 provisions are made for soliciting the assent of the children when, in the judgment of the
263 IRB, the children are capable of providing assent and that the permission of their parents
264 or guardians is granted as set forth in 21 CFR 50.55.

265 **4.4 Data Collection and Analysis**

266 The record-keeping requirements for investigators conducting live case presentations
267 consists in part of maintaining records that include all relevant observations, including
268 adverse effects (whether anticipated or unanticipated). 21 CFR 812.140(a)(3)(ii). There
269 should be no less data collection for live case presentations than there is for the general
270 investigational cohort.
271

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

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

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

294
295 In addition, if a live case presentation was planned but not performed, this should be
296 submitted to FDA in a report including the reason why it was not performed (e.g., lack of
297 suitable subject for meeting date, business reasons).

298
299 Clinical outcomes of those subjects who participate in live case presentations should be
300 collected and analyzed separately. The clinical outcomes of subjects who participated in
301 live case presentations should be compared with those observed in the rest of the study
302 population to assess whether live case subjects were exposed to additional risks and to
303 compare outcomes (including frequency/severity of adverse events) of the live case
304 presentations against those of the remainder of the study cohort. The results of this
305 analysis should be reported in the sponsor's annual progress reports and the final report to
306 the reviewing IRB and FDA. If an unanticipated adverse device effect occurs during a
307 live case presentation, the investigator must report the unanticipated adverse device effect
308 to the sponsor and reviewing IRB as soon as possible, but no later than 10 working days
309 after the investigator first learns of the effect. 21 CFR 812.150(a)(1). The sponsor must
310 then immediately conduct an evaluation (21 CFR 812.46(b)(1)) and report the results of
311 the evaluation to FDA and all reviewing IRBs and participating investigators within 10
312 working days after the sponsor first receives notice of the effect. 21 CFR 812.150(b)(1).

313
314 Study monitors should review all live case presentation informed consent documents and
315 subject files to ensure appropriate adherence to the protocol and all applicable regulations.

316 **5 Information to Include in IDE Applications When Seeking**
317 **to Conduct Live Case Presentations**

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

328
329 Live case presentations represent protocol deviations to the approved research; the
330 investigational plan must be modified to account for these uses of the investigational
331 device. 21 CFR 812.35. For example, subjects are pre-selected to participate in the
332 broadcast which may result in breaking treatment assignment protocols, unblinding
333 investigators and subjects, and introducing selection bias. Even if the study is designed
334 as a single arm study, the live case presentation represents a change to the approved
335 research since there may be additional anesthesia time or other additional risks. Subjects
336 may experience changes in treatment regime, and have their privacy compromised.
337 Data analysis, risk analysis, and reporting may also be altered.

338
339 A live case presentation request should be submitted at least 30 days prior to the planned
340 presentation; original IDE applications and supplements have a 30 day review period. A
341 live case presentation request is not appropriate for a study nearing completion since the
342 purpose of a live case presentation is to increase awareness of the study for potential
343 investigators and facilitate recruitment of subjects.

344
345 If live case presentations are anticipated for any part of an investigation conducted under
346 an IDE, sponsors should provide the following information at the time the original IDE
347 application is submitted, or as soon as possible thereafter as a supplement to the IDE
348 application for a change to the investigational plan, pursuant to 21 CFR 812.35(a):

- 349
- 350 • The total number of live case presentations anticipated over the duration of the
351 study;
 - 352 • A justification for the live case presentation; if more than one live case
353 presentation is requested, provide a justification as to why more than one is
354 necessary;
 - 355 • The names, dates and locations of scientific meeting(s) (if known) where the live
356 case presentation will be presented and the site where the procedure will be
357 conducted;
 - 358 • The name and qualifications of the operator/investigator performing the procedure,
359 if not included in the investigator section of the IDE submission;

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- 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.

370 FDA also has concerns related to clinical study execution as identified below. FDA
371 therefore recommends that the following additional items be specifically addressed when
372 designing or revising an investigational plan to include live case presentations:
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- 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 not be excluded from the primary study analysis, sample size adjustments may be necessary.
 - The sponsor should provide assurance that the live case presentation will not be used for commercial promotion of an investigational device (see [“Guidance for Industry and FDA Staff on Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects”](http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073585.pdf) <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.

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- 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).

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

425

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

434

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

439 **6 Summary**

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

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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

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- 492 Specification that the live case presentations will be conducted only at previously
493 approved investigational sites by investigators who have signed the Investigator
494 Agreement and who are currently participating in the study
495

496 Informed Consent

497 In addition to the other elements of informed consent, the informed consent document
498 should include the following information:
499

- 500 The procedure will be recorded for future viewing and/or broadcast to an audience
501 during the conduct of the procedure
502
- 503 There is no additional direct benefit to the subject for participating in the live case
504 presentation, and in fact, it is not known if participating in a live case presentation
505 will affect clinical outcome compared to subjects who do not participate
506
- 507 Any additional risks posed by performing the procedure in this manner, such as
508 increased anesthesia and/or procedure time (see previous discussion under “Risk
509 Analysis”)
510
- 511 Any additional issues related to subject confidentiality, such as privacy concerns
512 related to the live case broadcast, and subsequent distribution and/or use of a
513 video or other type of stored media of the procedure.
514
- 515 A statement that additional follow-up and evaluation may be needed as a result of
516 the subject's participation in a live case presentation.
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518 Reporting and analysis plans

- 519
- 520 The sponsor should provide a detailed description of proposed data collection and
521 reporting for subjects participating in a live case presentation. Sponsors should
522 address whether data collection and reporting will be according to the IDE
523 protocol, and if not, provide a detailed description of (and justification for) any
524 anticipated changes to the protocol. Subject follow-up and evaluation should be
525 specifically discussed, and should be the same as that specified in the IDE
526 protocol, unless the patient's condition requires additional follow-up and
527 evaluation.
528
- 529 The sponsor should provide analysis plans for the live case presentations that
530 include all relevant observations, including adverse device effects (whether
531 anticipated or unanticipated), and specifying that live case presentation data will
532 be stratified and included in safety and/or efficacy analyses.
533
- 534 The sponsor should provide separate reporting and a comparison to the remaining
535 investigational cohort in Annual Report submissions as well as any marketing
536 submission. Outcomes for these subjects should be compared to the rest of the
537 study population to assess whether these subjects were exposed to additional risks

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

551

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

560

561 The sponsor should ensure that it is in compliance with providing Annual Reports and
562 other reports as required by 21 CFR 812.144(b) before requesting or conducting
563 live case presentations.

564

565

566 IRB review

567

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

573

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

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581 Additional Safeguards for Children

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

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