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| University of Washington Human Subjects DIvision | **CHECKLIST Exception from Informed Consent** |

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| **PURPOSE AND APPLICABILITY** |

This checklist is used by the IRB to document that the criteria are met to grant IRB approval for research involving the exception to informed consent. HSD staff complete this regulatory checklist and upload it to the Zipline application.

“FDA-FAQ” refers to the FDA Guidance, “Exception from Informed Consent Requirements for Emergency Research”, April 2013. It is an excellent source of explanation and guidance.

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| **STUDY INFORMATION** |

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| **Zipline # (initial app):** | Click or tap here to enter text. |
| **PI last name:** | Click or tap here to enter text. |
| **Checklist completion date:** | Click or tap here to enter text. |
| **Staff person:** | Click or tap here to enter text. |

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| 1. **INSTITUTIONAL REVIEW BOARD REQUIREMENT** | **Met** |
| **1.1** A **licensed physician**, who is a member or consultant to the IRB and who is not otherwise an investigator or participant in the research, concurs with the IRB’s findings that this study may be approved without requiring that consent be obtained for all subjects.  *21 CFR 50.24(a)* |  |
| **+ Guidance**  At the UW, this requirement is fulfilled by ensuring that at least one IRB member who is a physician has attended all of the meetings and votes in favor of granting consent exception. The physician’s concurrence or affirmative vote must be recorded in the IRB meeting minutes. |  |

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| 1. **CONDITION AND TREATMENT** | **Met** |
| **2.1** The subjects are in a **life-threatening situation** which requires intervention.  *21 CFR 50.24(a)(1); 21 CFR 50.24(a)(3)(i); FDA-FAQ 22* |  |
| **+ Guidance**  “Life-threatening” includes research that is evaluating conditions of severe morbidity that are closely associated with mortality. For example, patients with stroke or head injury are at risk of both death and severe disability. |  |
| **2.2 Available treatments are unproven or unsatisfactory.**  *21 CFR 50.24(a)(1); FDA-FAQ 23-25* |  |
| **+ Guidance**  “Available treatment” means (for FDA regulated products) treatment that is specified in the approved labeling of regulated products.  The IRB should consider these questions: **(1)** What is the current standard of care?; **(2)** What treatments are available?  “Unproven” means that there is not substantial evidence that a treatment is effective for the condition. These may reflect the absence of any data or the absence of studies of acceptable quality. It includes: **(1)** treatment that is considered “standard of care”, but which has never been subjected to rigorous scientific testing or submitted to FDA for approval; **(2)** treatment for which there are no or insufficient clinical or pre-clinical data to support safety or efficacy; **(3)** a product that is not approved for, nor does the labeling for the product contain, the specific indication or patient population under study.  “Unsatisfactory” means that the available product or therapy is effective, but there are drawbacks to its use, such as: **(1)** safety issues (e.g., high incidence of adverse effects); **(2)** efficacy issues including poor survival rate, treatment is only partially effective, treatment fails to prevent a significant permanent disability, established efficacy is low; **(3)** the time for the treatment to be effective is too long; **(4)** the treatment has limitations related to the setting in which it is needed (e.g., should be administered in the field but needs refrigeration; it is not portable). |  |
| **2.3** The **collection of valid scientific evidence**, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.  *21 CFR 50.24(a)(1); FDA-FAQ 27, 28* |  |
| **+ Guidance**  In virtually all studies, it is expected that when a placebo is used, standard of care (if any) would be given to all subjects, with subjects randomized additionally to receive either a test treatment or placebo. An exception to this would be the situation in which the study objective is to determine whether some aspect of the standard treatment is in fact useful. In that case, there would be a group that does not receive that aspect of the standard treatment.  Non-inferiority trials are acceptable. This means that the study seeks to show that the test treatment is not materially worse that or inferior to the control treatment. For a non-inferiority trial to be informative, there needs to be clear data about the effectiveness of the control treatment (to make the study interpretable) and about known safety or other problems associated with the control treatment. Non-inferiority trials are generally used when a placebo-controlled trial would be unethical and where there are no data to suggest the new treatment would be more effective than the standard treatment. |  |
| **2.4** The research plan defines the **length of the therapeutic window** based on scientific evidence.  *21 CFR 50.24(a)(5); FDA-FAQ 34-36, 43* |  |
| **+ Guidance**  “Therapeutic window” means the time period after onset of the event, based on available scientific evidence, within which the product or procedure must be used or administered to have its potential clinical effect (diagnostic or therapeutic).  The therapeutic window for some emergency research may be very brief, or, in some cases, almost non-existent.  The sponsor is required to determine the therapeutic window, to the extent possible, using available data (e.g., pathophysiological data, animal data).  Review [5.1](#LARtherapeutic) for a discussion of the relationship between the length of the therapeutic window and the time spent on attempting to contact a LAR or family member. |  |
| **2.5** For research involving a drug or device: the researcher has obtained a separate **investigational new drug application (IND) or investigational device exemption (IDE)** from the Food and Drug Administration that clearly identifies the research as a study that may include subjects who are unable to consent.(check ‘met’ if n/a)  *21 CFR 50.24(d)* |  |
| **+ Guidance**  This is required even if an IND for the same drug product or an IDE for the same device already exists. |  |

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| 1. **BENEFIT AND RISK** | **Met** |
| **3.1** Participation in the research holds out the[**prospect of direct benefit**](https://www.washington.edu/research/glossary/prospect-direct-benefit/)to the subject because **all of the following are true:** |  |
| **a.** Subjects are facing a[**life-threatening**](#lifethreat)situation that necessitates intervention.  *21 CFR 50.24(a)(1); 21 CFR 50.24(a)(3)(i)* |  |
| **b.** Appropriate **animal studies and other pre-clinical studies** have been conducted, and the information derived from those studies and other evidence supports the potential for intervention to provide direct benefit to the individual subjects.  *21 CFR 50.24(a)(3)(ii); FDA-FAQ 13, 14, 22* |  |
| **+ Guidance**  Note that there is no requirement that a study be a Phase 1, Phase 2, or Phase 3 study. However, most Phase 1 studies would not generally meet the criterion of direct benefit (review 3.1.c below). To establish potential benefits, Phase 2 trials in consenting subjects (if possible) may be needed to explore dose response for safety or biomarkers before research involving the consent exception. However, feasibility/pilot trial **can** be conducted with devices, provided the study holds out the prospect of direct benefit. |  |
| **c. Risks associated with the research are reasonable** in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, and what is known about the risks and benefits of the intervention.  *21 CFR 50.24(a)(3)(iii)* |  |
| 1. **CONSENT OR OBJECTION** (when it is obtained) | **Met** |
| **4.1 The IRB has reviewed and approved informed consent procedures and an informed consent document** consistent with standard human subjects regulatory requirements.  *21 CFR 50.24(a)(6); FDA-FAQ 97* |  |
| **+ Guidance**  A consent form must be prepared and approved even if all subjects will not be able to give consent because it may be possible to use it: **(1)** to obtain consent from LARs; **(2)** when providing an opportunity for a family member to object to a subject’s participation;  **or (3)** to inform subjects, LARs, or family members afterwards. |  |
| **4.2** These **procedures and the informed consent document will be used** with subjects or their legally authorized representatives (LARs) in situations where use of such procedures and documents is feasible.  *21 CFR 50.24(a)(6)* |  |
| **+ Guidance**  The consent exception can be granted even if there will be some subjects who are able to provide consent. The UW IRB has historically interpreted circumstances in which subjects are conscious and able to communicate but full consent is very difficult or impossible, to be circumstances in which true informed consent is neither feasible nor practicable. |  |
| **4.3** The IRB has reviewed and approved procedures and information to be used when providing **an opportunity for a family member to object** to a subject’s participation in research.  *21 CFR 50.24(a)(6)* |  |

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| 1. **ATTEMPTS TO OBTAIN CONSENT OR OBJECTION** | **Met** |
| **5****.1** The researcher has committed to **attempting to contact a LAR for each subject within the therapeutic window** and, if feasible, toask the LAR for consentwithin that window rather than proceeding without consent.  *21 CFR 50.24(a)(5); FDA-FAQ 43, 95-102* |  |
| **+ Guidance**  Researchers are not required to exhaust the entire therapeutic window attempting to contact a LAR or family member before the intervention is administered. It is expected that in most cases the potential benefit of the intervention will decrease as the delay in delivering the intervention increases. Thus, the effect of delaying the intervention should be taken into account when determining the portion of the therapeutic window to be devoted to obtaining consent from a LAR or providing the opportunity for a family member to object.  Researchers should specify the amount of time that will be devoted to these efforts, within the therapeutic window. |  |
| **5.2 The researcher will summarize efforts made to contact the LARs** and will make this information available to the IRB at the time of continuing review.  *21 CFR 50.24(a)(5)* |  |
| **5.3** If obtaining informed consent is not feasible and a LAR is not reasonably available, the investigator has committed, if feasible, to **attempting to contact within the therapeutic window** the subject’s family member who is not a LAR, and asking whether they object to the subject’s participation in the research.  *21 CFR 50.24(a)(7)(v); FDA-FAQ 42, 43, 96-102* |  |
| **+ Guidance**  This criterion applies to situations where the family member is not LAR for the subject (and therefore cannot legally provide consent). This would be rare in Washington State. The purpose of contacting a family member who is not a LAR is to provide the opportunity for the family member to object to enrolling the subject in the study.  If the non-LAR family member is present or accompanying the subject to the emergency room, the healthcare professionals or researchers must ask their family member immediately if there is any objection to enrolling the subject in the study.  Researchers are not required to exhaust the therapeutic window attempting to contact a LAR or family member before the intervention is administered. It is expected that in most cases the potential benefit of the intervention will decrease as the delay in delivering the intervention increases. Thus, the effect of delaying the intervention should be taken into account when determining the portion of the therapeutic window to be devoted to obtaining consent from a LAR or providing the opportunity for a family member to object. |  |
| **5.4** The **researcher will summarize efforts made to contact family members** and make this information available to the IRB at the time of continuing review.  *21 CFR 50.24(a)(7)(v)* |  |

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| 1. **FEASIBILITY AND PRACTICABILITY OF OBTAINING CONSENT** | **Met** |
| **6.1** Obtaining consent is not feasible because **all of the following are true:** |  |
| **a.** Subjects cannot give consent as a result of theirmedical condition.  *21 CFR 50.24(a)(2)(i)* |  |
| **b.** The intervention must be administeredbefore consent from the subject’s LAR is feasible.  *21 CFR 50.24(a)(2)(ii)* |  |
| **c.** There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the investigation.  *21 CFR 50.24(a)(2)(iii)* |  |
| **6.2** The research **could not practicably be carried out** without the waiver.  *21 CFR 50.24(a)(4); FDA-FAQ 29* |  |
| **+ Guidance**  This means that: **(1)** the results obtained in consenting subjects could not be generalizable to subjects who are unable to provide consent; **or (2)** the research would be unduly delayed by restricting it to consenting subjects.  For example, it may or may not be reasonable to generalize results from a less ill population (that was able to provide consent) to a more ill population that is unable to consent. Subjects who are not able to provide consent may have better prospects for full recovery than subjects who are unable to consent or may be less susceptible to the risks of the treatment.  Even if the population at risk can be identified in advance (e.g., cardiac patients entering a hospital who may be at risk for cardiac arrest), it may be impracticable to obtain consent from all of them because the event (cardiac arrest) may occur in a very small fraction of those patients; therefore, subject enrollment would take too long to conduct the study in a reasonable time. |  |

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| 1. **AFTER ENROLLMENT** (when consent was not obtained) | **Met** |
| **7.1** There are procedures for **informing each subject, at the earliest feasible opportunity** or, if the subject remains incapacitated, a LAR, or if a LAR is not reasonably available, a family member, of the subject’s inclusion in the research, the details of the research, and other information contained in the consent document.  *21 CFR 50.24(b); FDA-FAQ 103-114* |  |
| **7.2** If a **subject is enrolled in the study without consent and dies** before a LAR or family member can be contacted, information about the research is to be provided to the LAR or family member, if feasible.  *21 CFR 50.24(b); FDA-FAQ 107* |  |
| **7.3** If a LAR or family member is told about the research and **the subject’s condition improves,** the subject will be informed as soon as is feasible about the subject’s inclusion in the research, the details of the research, and other information contained in the consent document.  *21 CFR 50.24(b)* |  |
| **7.4** There is a procedure to inform the subject, or if the subject remains incapacitated, a LAR, or if a LAR is not reasonably available, a family member, that they may **discontinue the subject’s participation** at any time without penalty or loss of benefits to which the subject is otherwise entitled.  *21 CFR 50.24(b)* |  |

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| 1. **ADDITIONAL PROTECTIONS** | **Met** |
| **8.1 Community consultation, type 1** (including, where appropriate, consultation carried out by the IRB) will occur with representatives of the *communities in which the research will be conducted*.  *21 CFR 50.24(b)(7)(i); FDA-FAQ 47, 48, 54-77* |  |
| **+ Guidance**  “Communities in which the research will be conducted” means the geographic area (e.g., hospital or other facility or city or region) where the research will be conducted.  The IRB must review and approve the plans for community consultation and public disclosure before the plans are implemented.  Though not required, it is considered best practice to review the study protocol together with the plans for community consultation and public disclosure.  There is no single acceptable way to accomplish community consultation, nor will all studies require the same amount, type, or extent of community consultation. More or less consultation may be appropriate, depending on the study. For example, a study involving a novel treatment that is being compared with placebo may require extensive consultation. Less extensive consultation may be appropriate for a study comparing an available treatment that is considered unsatisfactory with another product about which much is known (e.g., an approved product that is not approved for the specific indication that is the subject of the emergency research).  The IRB is expected to consider the concerns and objections raised during community consultation activities before completing its review of the initial application.  There is no requirement to evaluate the effectiveness of the community consultation and public disclosure processes.  The FDA guidance document provides extensive discussion and guidance about community consultation (FDA-FAQ 47, 48, 54-77). |  |
| **8.2 Community consultation, type 2.** Consultation, (including, where appropriate, consultation by the IRB) will occur with representatives of the *communities from which the subjects will be drawn*.  *21 CFR 50.24(b)(7)(i)* |  |
| **+ Guidance**  “Communities from which the subjects will be drawn” means the group of patients who share a particular medical or other characteristic that increases the likelihood that they (or a family member) may be enrolled in the study. |  |
| **8.3 Public disclosure, type 1.** Public disclosure of the plans for the investigation and its risks and expected benefits will be made prior to the initiation of the research, to the communities in which the research will be conducted and from which the subjects will be drawn.  *21 CFR 50.24(b)(7)(iii); FDA-FAQ 46, 47, 78-84* |  |
| **+ Guidance**  The IRB must find that the public disclosure will have or has taken place prior to the study. |  |
| **8.4 Public disclosure, type 2.** Public disclosure of sufficient information following the completion of the research will be conducted, to apprise the community and researchers of the study, its results, and the demographic characteristics of the research population.  *21 CFR 50.24(b)(7)(iii); FDA-FAQ 85-94* |  |
| **8.5 An independent data monitoring committee will be established to exercise oversight over the research.**  *21 CFR 50.24(b)(7)(iii); FDA-FAQ 46* |  |
| **+ Guidance**  The IRB cannot grant full approval until it has been documented that the DMC has been arranged. |  |

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| 1. **ADDITIONAL CONSIDERATIONS** | **Met** |
| **9.1 Prisoners.** If the researcher wishes to retain the data and/or participation of prisoners who were inadvertently provided with the emergency intervention, IRB should review the study for prisoner involvement. (check ‘met’ if n/a)  *For research governed by 45 CFR 46 or FDA regulations (not EFIC)* |  |
| **+ Guidance**  This is a requirement for federally funded research. It is not a specific EFIC requirement. |  |
| **9.2 The IRB considers opt out mechanisms.** Opt out mechanisms refer to ways in which individuals can indicate for themselves that they do not want to participate in an emergency exception study. Opt out mechanisms are not required. The decision to use them is left to the discretion of the IRB.  *FDA-FAQ 68, 69* |  |
| **+ Guidance**  There are advantages and drawbacks, as well as valid concerns about the effectiveness of opt out mechanisms. Consider, for example, a trauma study and the number of potential subjects who might be motorists driving a freeway or road in a geographical area.  Community consultation activities should make communities aware of any opt out mechanisms and ensure that the community understands that efforts to inform the community may not reach all community members. |  |
| **9.3 Involvement of first responders and healthcare personnel.**   * Are the procedures for training, oversight, and involvement of these groups adequate to ensure that the study protocol will be carried out as accurately as possible under the conditions of the study? * Are the procedures for communication with them adequate?   *UW application of 45 CFR 11(a)(2) (not EFIC)* |  |
| **9.4 Coordination with other emergency medicine studies.** If there are competing emergency medicine studies or sequential studies (e.g., where patients might experience an intervention in one study, followed by an intervention in another study) the IRB must determine that:   * The scientific benefit of the study will not be negatively affected (taking into account any ways in which the impact of multiple studies will be mitigated or controlled). * The study procedures appropriately consider and manage the impact on LARs and family members of being approached by multiple studies.   *UW application of 45 CFR 11(a)(2, 3, 7) (not EFIC)* |  |

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| 1. **REQUIRMENT IF IRB CANNOT APPROVE THE CONSENT EXCEPTION** | **Met** | **n/a** |
| **10.1** The IRB will **provide its determination and rationale promptly and in writing** to the researcher and sponsor if the exception to consent is disapproved.  *21 CFR 50.24(e)* |  |  |

**Keywords:** EFIC; FDA