Emergency use of a test article / treatment use of investigational drugs

University of Nebraska Medical Center

"I'm not sure what these are, but take them for a couple of weeks and let me know how you feel."

Emergency use is different than Expanded Access ("compassionate use")

- Emergency Use
  - Life threatening situation, no other option, not time for IRB approval
  - Not research*
  - Does not require IRB approval (only notification)
  - Requires sponsor and FDA approval
  - Requires informed consent
  - Only one use
- Expanded Access
  - Serious disease, no other satisfactory alternative (may be urgent but not emergent)
  - Research*
  - Requires IRB approval (or IRB chair concurrence)
  - Requires sponsor and FDA approval
  - Requires informed consent
  - Single patient or larger population

Emergency use of a test article

- Investigators may be confronted with the need to use a test article in an emergency situation
- In these circumstances review by a full IRB may not be feasible
- FDA regulations allow for an emergency waiver of prior IRB review (21 CFR 56.104(c))

Emergency use of a test article

- Life-threatening situation exists requiring treatment with the test article
  - likelihood of death or severe debilitation is high unless the course of the disease is interrupted
- No standard acceptable treatment is available
- Insufficient time is available to obtain IRB approval at a convened meeting (21 CFR 56.102(d))

Emergency use of a test article

- Emergency use provision in the FDA regulations is an exemption from prior review and approval by the IRB
- It is not "emergency IRB approval"
  - IRB only acknowledges compliance with 21 CFR 56.104(c)

Emergency use of a test article

- FDA regards emergency use of a test article (other than a medical device) as a "clinical investigation"
  - may require data from an emergency use to be reported in a marketing application
- However, DHHS states "emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity"
  - single case reports may be allowable

Process

- Treating physician will contact IRB Office and/or Chair prior to use of the test article
  - IRBORA@unmc.edu
  - (402) 559-6463
  - bgordon@unmc.edu
  - (402) 559-6045

Process

- Treating physician will contact IRB Office and/or Chair prior to use of the test article
- Treating physician will contact:
  - P&T Committee to obtain P&T emergency use approval
  - Investigational Drug Pharmacist resolve financial responsibility for the pharmacy costs
  - Sponsor and FDA

Process

- Treating physician will contact IRB Office and/or Chair prior to use of the test article
- Treating physician will contact:
  - P&T Committee to obtain P&T emergency use approval
  - Investigational Drug Pharmacist resolve financial responsibility for the pharmacy costs
  - Sponsor and FDA
- Obtain consent

Consent

- Consent from the subject or their LAR must be obtained (21 CFR 50.23(a)) unless
  - life threatening situation
  - consent of the subject cannot be obtained
  - not enough time to obtain consent from the LAR
  - no alternatives which provide equal or greater likelihood of saving the life of the subject
- Investigator and an uninvolved physician must certify the above in writing
- Consent template available on IRB website
  - IRB › Procedures & Deadlines › Procedures › Emergency Treatment

Process

- Treating physician will contact IRB Office and/or Chair prior to use of the test article
- Treating physician will contact:
  - P&T Committee to obtain P&T emergency use approval
  - Investigational Drug Pharmacist resolve financial responsibility for the pharmacy costs
  - Sponsor and FDA
- Obtain consent
- Treating physician will complete and submit the Emergency Use of a Test Article Report to the IRB within 5 business days following initiation of the treatment

New Application

INSTRUCTIONS: Carefully read the descriptions below and click on the one that best repre
questions or are unsure as to which option to select, please contact the Office of Regulat

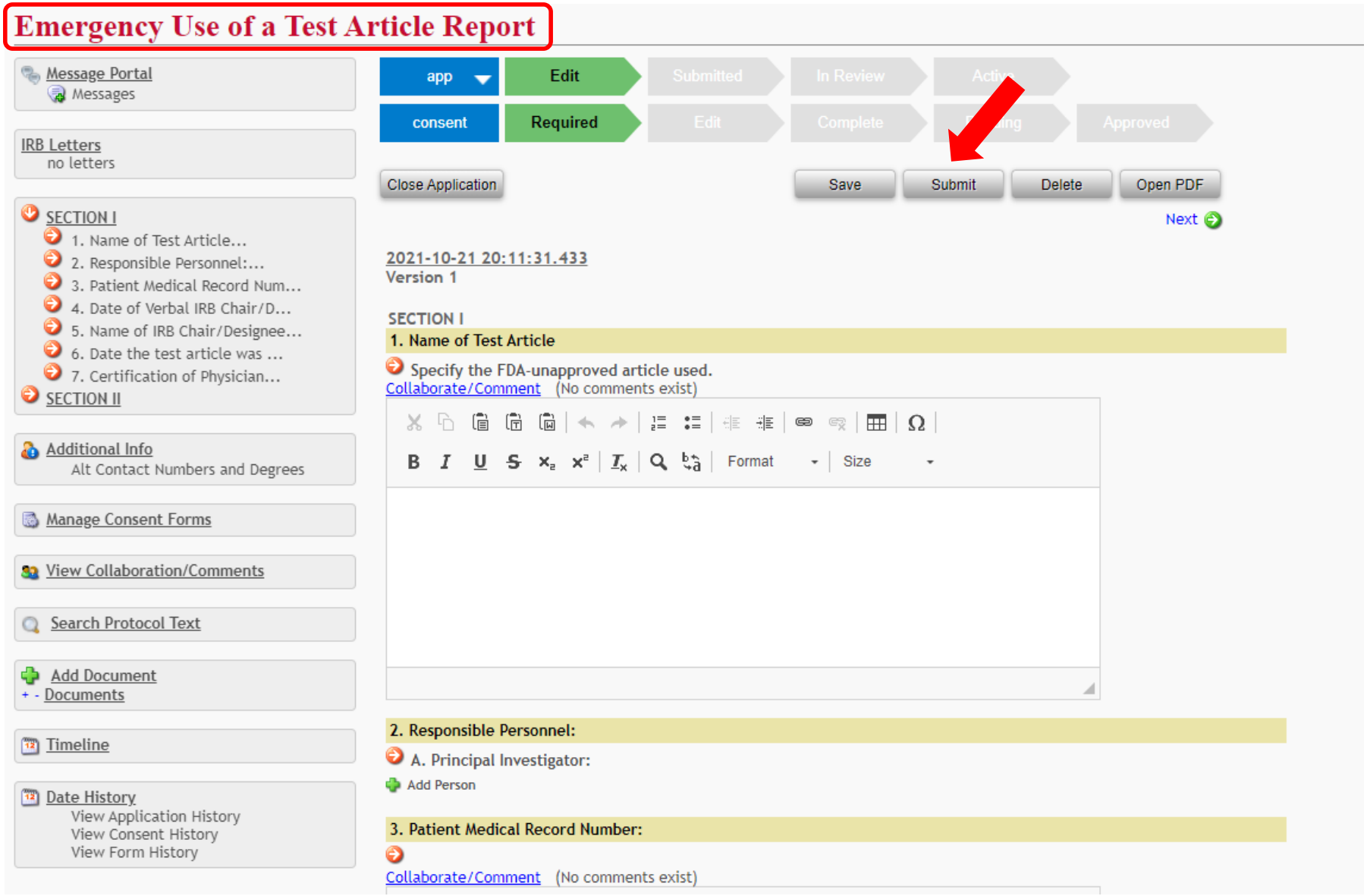
Create New Application

A. Biomedical Research OR Behavioral and Social Science Research
B. Research involving the collection and/or use of human biological material (HB
C. Exempt research (Note: only use this application if your research falls into on
D. Research involving medical records
E. Tissue bank ONLY- the collection of human biological material (HBM) with no c
F. Humanitarian Use Device (HUD) click here for description
G. Data Registry ONLY- the collection of information/data (typically from medica
H. Existing Paper Format Protocol
I. Central IRB Application (CIRB)
J. Single Patient Expanded Access Protocol (Drugs) view
K. Single Patient Expanded Access Protocol (Device) view
L. Emergency Use of a Test Article Report view

Create Single IRB Request

A. Single IRB (sIRB) Request Form view

Emergency Use of a Test Article Report



- Any subsequent use of the test article must have prospective IRB review and approval
  - "FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue" (FDA Guidance, Emergency Use of an Investigational Drug or Biologic, January 1998)

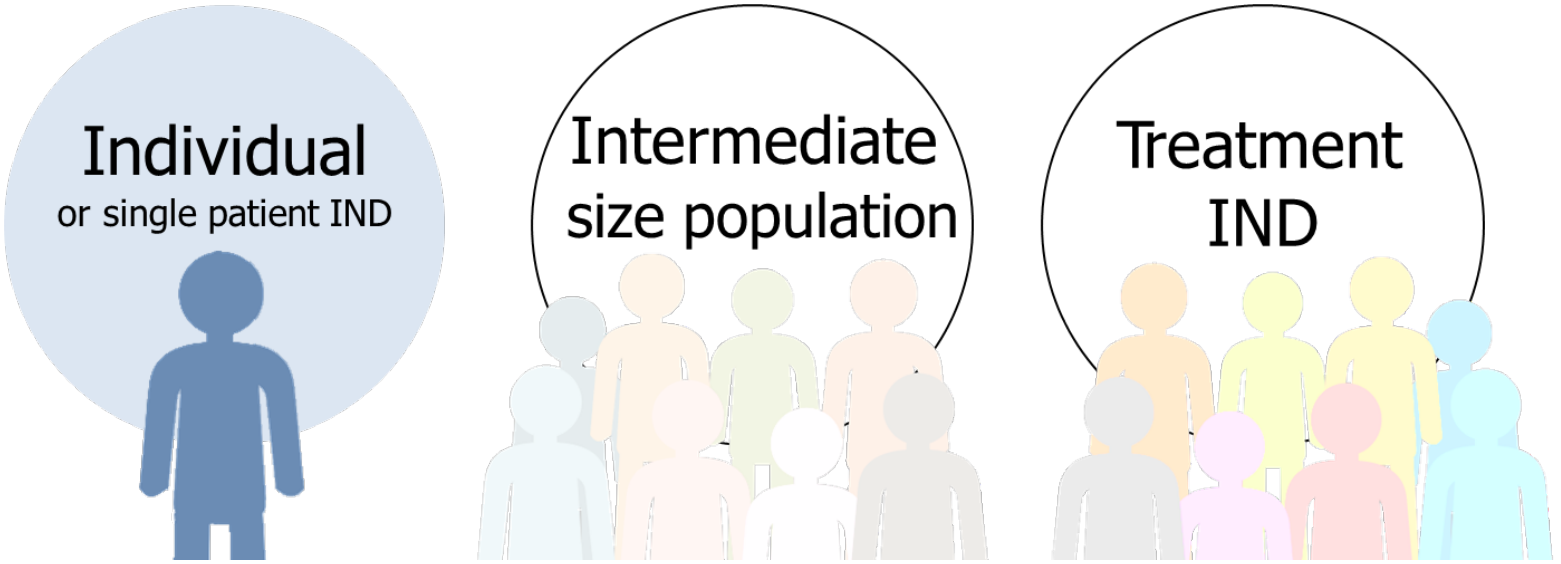
"I go home today. They cured me using this new miracle drug. I'm afraid it'll be years before it's approved for humans."

Expanded Access ("compassionate" use)

- The aim of the FDA Expanded Access regulations (21 CFR 312 Subpart I) is to facilitate availability of investigational new drugs to patients with serious disease when there is no satisfactory alternative therapy
- Requires prospective IRB approval*
- Requires informed consent

21 CFR 312 subpart I

- Three distinct categories of access:



Individual patient EAP
(21 CFR 312.310)

- Physician often takes role of sponsor/investigator
  - responsible for sponsor activities such as tracking and reporting
- Physician must determine probable risk from drug does not exceed that from disease
- FDA must determine that the patient cannot obtain access under another type of IND
- Treatment generally limited to one course (though FDA may allow ongoing therapy)

Individual patient EAP
(21 CFR 312.310)

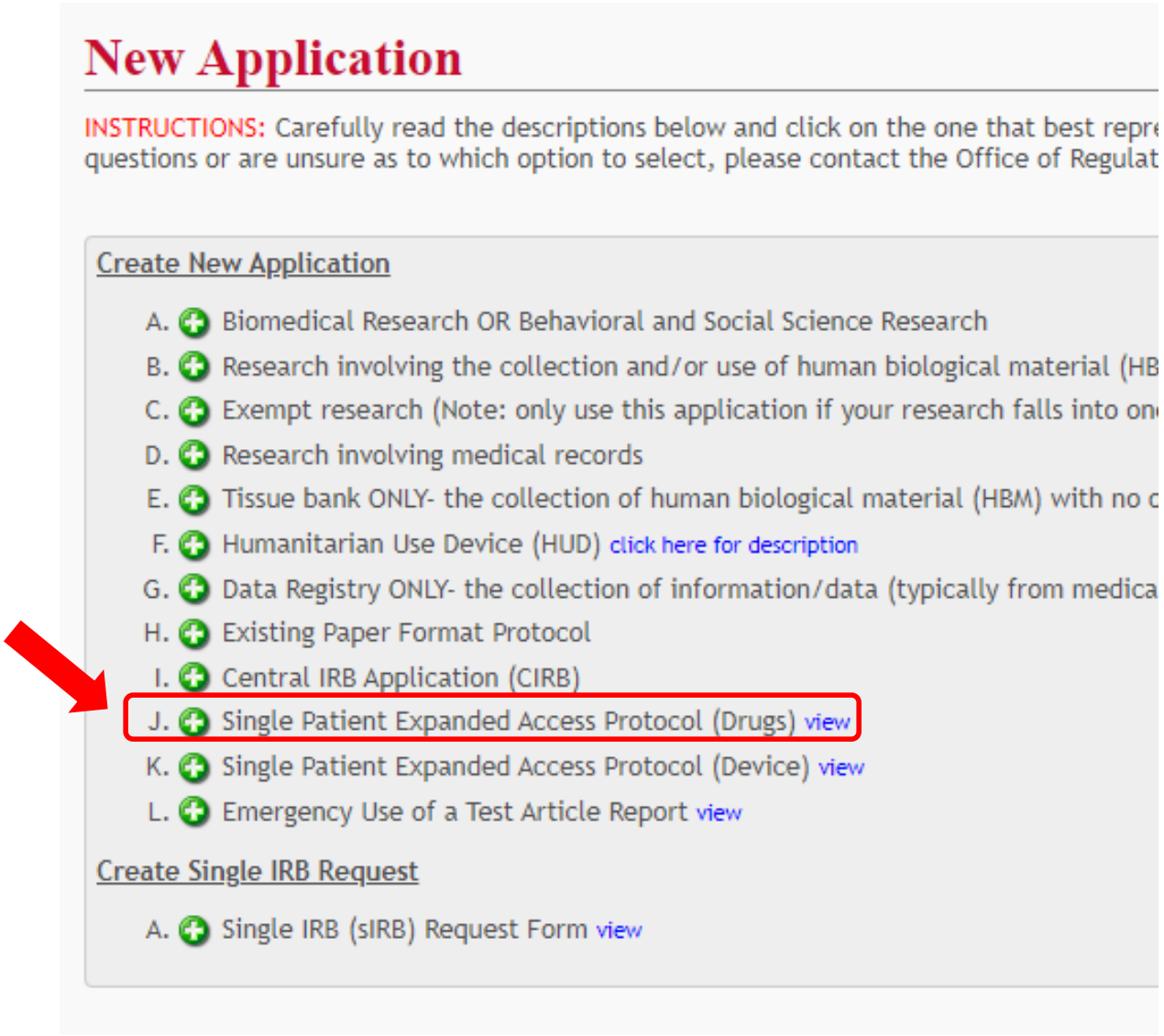
- *FDA allows waivers of the requirement for review and approval at a convened IRB meeting for individual patient expanded access INDs
  - IRB chairperson or designated IRB member provides concurrence
  - Only applies to individual patient EAPs

Process

- Contact IRB Office

Process

- Contact IRB Office
- Complete Single Patient Expanded Access Protocol in RSS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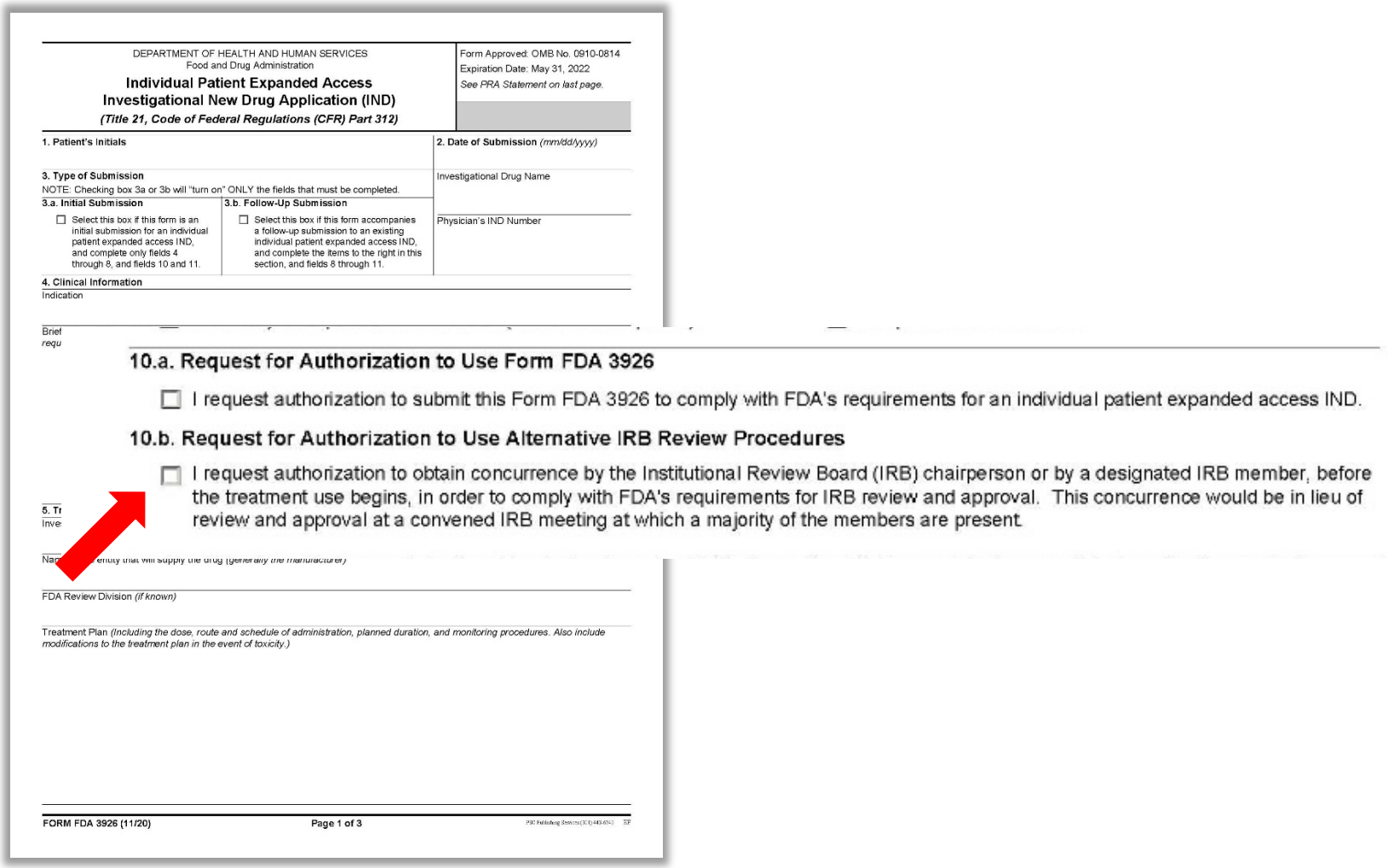
L. Emergency Use of a Test Article Report view
Create Single IRB Request
A. Single IRB (sIRB) Request Form view

Process

- Contact IRB Office
- Complete Single Patient Expanded Access Protocol in RSS
- Complete FDA form 3926
  - Check box 10b if requesting waiver of the requirement for review and approval at a convened IRB meeting

FDA 3926 (Individual Patient Expanded Access Investigational New Drug Application)



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Individual Patient Expanded Access Investigational New Drug Application (IND)

(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0814
Expiration Date: May 31, 2022
See PRA Statement on last page.

1. Patient's Initials

2. Date of Submission *(mm/dd/yyyy)*

3. Type of Submission

NOTE: Checking box 3a or 3b will "turn on" ONLY the fields that must be completed.

3.a. Initial Submission

☐ Select this box if this form is an initial submission for an individual patient expanded access IND, and complete only fields 4 through 8, and fields 10 and 11.

3.b. Follow-Up Submission

☐ Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 8 through 11.

Investigational Drug Name

Physician's IND Number

4. Clinical Information

Indication

Brief
requ

10.a. Request for Authorization to Use Form FDA 3926

☐ I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

10.b. Request for Authorization to Use Alternative IRB Review Procedures

☐ I request authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting at which a majority of the members are present.

5. Tr
Inve

Nam *entity that will supply the drug (generally the manufacturer)*

FDA Review Division *(if known)*

Treatment Plan *(Including the dose, route and schedule of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity.)*

FORM FDA 3926 (11/20) **Page 1 of 3**

Process

- Contact IRB Office
- Complete Single Patient Expanded Access Protocol in RSS
- Complete FDA form 3926
  - Check box 10b if requesting waiver of the requirement for review and approval at a convened IRB meeting
- Obtain written permission from the Sponsor (to use drug and to reference sponsor's IND)

Process

- Contact IRB Office
- Complete Single Patient Expanded Access Protocol in RSS
- Complete FDA form 3926
  - Check box 10b if requesting waiver of the requirement for review and approval at a convened IRB meeting
- Obtain written permission from the Sponsor (to use drug and to reference sponsor's IND)
- Await approval by convened IRB, or concurrence by IRB chair

Process

- Contact IRB Office
- Complete Single Patient Expanded Access Protocol in RSS
- Complete FDA form 3926
  - Check box 10b if requesting waiver of the requirement for review and approval at a convened IRB meeting
- Obtain written permission from the Sponsor (to use drug and to reference sponsor's IND)
- Await approval by convened IRB, or concurrence by IRB chair
- Obtain informed consent before using drug

Consent

- CF must include "a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental" (21 CFR 50.25(a)(1))
  - "given the compassionate nature of the request, consent documents should meet the requirements listed in 21 CFR 50.25, using plain language that is specifically aimed at 'patients' who expect direct benefit, as opposed to 'subjects' who may not expect direct benefit"

- https://www.fda.gov/news-events/public-health-focus/expanded-access

- Expanded Access to Investigational Drugs for Treatment Use — Questions and Answers Guidance for Industry (June 2016)
  - https://www.fda.gov/media/85675/download

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by Jim Unger

"I feel a lot better since I ran out of those pills you gave me."