IND Exemption: Case Scenarios

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Scenario No. 1

- Investigator plans to study anti-flu drug to treat flu symptoms in children under the age of 10
- Drug INFLUN is currently approved in the pediatric setting, given as an injection
- In the proposed study, INFLUN will be administered via nasal drops
- The Duke pharmacy will receive the INFLUN vials (for injection) and create the nasal drops for use in this study

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Scenario No. 1

- **Is this study eligible for an IND exemption?**

  Yes

- **What is off label in this case?**

  A change in the route of administration, potentially formulation, dosage. . .

- **What kind of documentation you would provide to the IRB and/or FDA?**

  Previously published data? Manufacturing information, information concerns surrounding contamination, consistency of drug amount…

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Scenario No. 2

- **Investigator plans to do a trial to assess the effectiveness of Vitamin D in the treatment of depression**
- **Vitamin D manufactured from Company X is legally marketed as a drug to treat osteoporosis**
- **Vitamin D manufactured by Company Y is legally marketed as a supplement**
- **The investigator is using Vitamin D capsules from Company Y**

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Scenario No. 2

- **Is this study eligible for an IND exemption?**

YES

Or

NO

Scenario No. 2

- **The study is not using a marketed version of Vitamin D capsules**

21 CFR 312.2(b)(1) - Must be the "investigation of a drug product that is lawfully marketed in the United States" 21 CFR 312.2(b)(1)

- **In case of supplements the need for an IND is determined by intent**

Structure/Function Study = no IND Required.

Therapeutic studies require INDs (treat, diagnose, cure, mitigate disease)

Scenario No. 3

- Drug A and Drug B are FDA approved for treatment of a rare type of colon cancer
- An investigator wants to add Drug C (an FDA approved drug) to the therapeutic cocktail based on some previously published studies involving breast cancer patients (the breast cancer study involved triple therapy with Drugs A, B & C)

Scenario No. 3

- Is this study eligible for an IND exemption?

  Yes

- How many things are off-label in this simple example?

Drugs A and B are approved to be give in the combination, but not approved to be given in a combination with Drug C. Drug C is neither approved to be given in the combo with A and B nor approved for that indication

- What kind of documentation you would provide to the IRB and/or FDA?

Any previously published data on the use of this combination? Any data on the use of drug C in this indication

Scenario No. 4

- Investigator plans to study structural and functional changes that occur in the eye after the exposure to ragweed
- Ragweed extract is an FDA approved drug for use in skin prick tests to diagnose allergies
- Investigator plans to use the extract in the eye to study the structural and functional changes after exposure

Scenario No. 4

- Is this study eligible for an IND exemption?

  Yes

- What is off label in this case?

  A change in the route of administration, dosage?

- What kind of documentation you would provide to the IRB and/or FDA?

  Previously published data?

IND Safety Report: Case Scenarios

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Scenario 1

Mr. Jones was participating in a phase II clinical trial for product ABC. At his second study visit, Mr. Jones developed elevations in SGOT (AST), SGPT (ALT) and GGT and is jaundice. Two days prior to the detection of the laboratory abnormalities, Mr. Jones felt nauseated, was fatigued and had a low-grade fever. Physical exam revealed tenderness in the RUQ. Within 24 hours of stopping the study drug, all of Mr. Jones symptoms completely resolved. The investigator characterized the event as possibly related to study drug.

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Scenario 1

From the Investigator Brochure of ABC:

"Elevations of liver enzymes are possibly related to the use of ABC, and were reported at twice the frequency in patients receiving ABC than in patients receiving placebo during initial phase I and phase I/II studies."

Scenario 1

Is this case Serious?

Is this case Expected or Unexpected?

Is this event Study Related?

How and when would you report this event to the FDA?

Scenario 2

A 70-year old woman is receiving Product U for late stage ovarian cancer as part of a Sponsor-Investigator initiated clinical trial (Product U is already an approved drug for other types of cancer). The investigator reported that the subject developed petechiae and had a platelet count of 6000 (normal range 140,000-340,000). She was hospitalized, determined to have an intracranial bleed and subsequently died. The investigator characterized the event as possibly related to the Product U.

Scenario 2

Labeling Information of Product U

The Product U package insert contains the following statements: "Fatalities associated with administration of Product U, although rare, have occurred due to severe reactions including Steven-Johnson Syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias."

The Product U package insert lists the following in the ADVERSE REACTIONS section: hematologic: agranulocytosis; aplastic anemia; thrombocytopenia.

Scenario 2

Is this case Serious?

Is this case Expected or Unexpected?

Is this event Study Related?

How and when would you report this event to the FDA?