# Clinical Trials at NASA

## WHAT MAKES A CLINICAL TRIAL & WHAT ARE THE REQUIREMENTS FOR INTERNATIONAL PARTNERS?

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**May 2024**

# A G E N D A

- What constitutes a Clinical Trial?
- Historical Context
- Clinical Trial Mandates & Regulations
- Clinicaltrials.gov
- Case Examples at NASA
- Identifying the why?
- What does this mean for International Partners?

# WHAT CONSTITUTES A CLINICAL TRIAL

- Clinical trials are **prospective**, organized, **systematic exposures** of patients **to an intervention** of some kind (drug, surgical procedure, dietary change).

- Clinical trials in the United States have evolved in pursuit of a larger therapeutic goal -- to see that physicians use the best possible therapies available.

# HISTORICAL CONTEXT: HOW WE GOT TO WHERE WE ARE NOW

## *1920-1940*

**Cooperative Investigations**

Medical researchers begin conducting cooperative investigations.

Aims Include:

- Remove errors attributed to individual observers
- Standardize evaluations of research on larger patient population

## *1937*

**1938 Food, Drug, & Cosmetic Act**

Various Drug Crises generate mistrust in the general public.

- 1937: Sulfanilamide Crisis: Over 100 people are killed by a product (poison) which is untested prior to marketing (antifreeze)

## *1962-1963*

**Drug Amendments & Investigational drug regulations**

1961: Thalidomide Crisis: severe birth defects & death in infants born to mothers prescribed drug during early pregnancy

Amendments posit:

- FDA would rely on scientific testing . New approvals based on proof of safety AND substantial evidence of product's efficacy in the clinical trial setting

## *1978*

**Society for Clinical Trials**

Organized to develop and discuss clinical trial design and the analysis of clinical trials in government as well as industry sponsored clinical trial research.

Clinical guidelines are developed, describing the study designs and expected data required for particular therapeutic classes.

## *1980's*

**AIDS Epidemic**

Reconsider essential requirements for a meaningful clinical trial.

- Sick patients push for access to drugs at earliest stages of development.
- 1988 Congress mandates that each AIDS drug IND be publicly disclosed in a computer-accessible database to facilitate access by patients with AIDS.

# MANDATES & REGULATIONS

## *FDAAA*

A **prospective** clinical study of **health outcome**s comparing an **intervention** with a device product/test article, subject to the FDA, against a control in human subjects.

## *ICMJE*

Any research project that **prospectively** assigns people or a group of people to an **intervention**, with or without concurrent comparison or control groups, to study the relationship between a **health-related intervention and a health outcome.**

## *NIH*

A research study in which one or more human subjects are **prospectively** assigned to one or more **interventions** (which may include placebo or other control) to **evaluate the effects** on those interventions on **health-related biomedical or behavioral outcomes.**

## *Revised Common Rule*

**Prospectively** assigns 1 or more human subjects to 1 or more **interventions** to ***evaluate*** the effects of the interventions on biomedical or behavioral outcomes

# F D A A A

**Criteria:**

- Meets the definition of an Applicable Clinical Trial
- Specific to FDA regulated products: evaluates at least 1 drug, biologic, or device regulated by the US FDA
    - **Excludes:** preclinical (phase 0), Phase 1, and feasibility studies


**Requirements:**

- Required language must be included in the consent that is approved by the IRB
- Research study must be registered on CT.gov
    - Supporting documentation such as the protocol is required
    - NASA Policy: prior to enrollment of first subject
    - Any modifications to the study must be updated on CT.gov
- Results must be reported on CT.gov

**Penalties:**

- Civil
- Monetary
- Criminal
    -

# I C M J E

**Criteria:**

- Meets the definition of a Clinical Trial
- Intent to publish in an ICMJE Journal

**Requirements:**

- Required language must be included in the consent that is approved by the IRB
- Research Study must be registered on CT.gov
  - NASA Policy: prior to enrollment of first subject
  - Any modifications to the study must be updated on CT.gov


**Penalties:**

- Publication Rejection

# I C M J E

**Criteria:**

- Meets the definition of a Clinical Trial
- Funded or supported by the NIH

**Requirements:**

- Required language must be included in the consent that is approved by the IRB
- Research Study must be registered on CT.gov
  - NASA Policy: prior to enrollment of first subject
  - Any modifications to the study must be updated on CT.gov
- Results must be reported to CT.gov


**Penalties:**

- Loss of Funding

| | FDAAA | NIH | ICMJE |
|---|---|---|---|
| **Mandate** | Regulation | Policy | Policy |
| **Registration Required** | Yes | Yes | Yes |
| **Registration Deadline** | Prior to enrollment of first subject | Prior to enrollment of first subject | Prior to enrollment of first subject |
| **Results Reporting Required** | Yes | Yes | No |
| **Dependent on Funding** | No | Yes | No |
| **Type of Intervention** | FDA-regulated products | All | All |
| **Study Phase** | Not preclinical (phase 0), Phase 1, feasibility | All | All |
| **Penalty** | Civil monetary and criminal | Loss of funding | Publication rejection |

**Chart available for review in ORA-705 Guidance Clinical Trials Document

# REVISED COMMON RULE

**Criteria:**

- Meets the definition of a clinical trial per 14CFR1230
- Supported by a Revised Common Rule Agency (such as NASA)

**Requirements:**

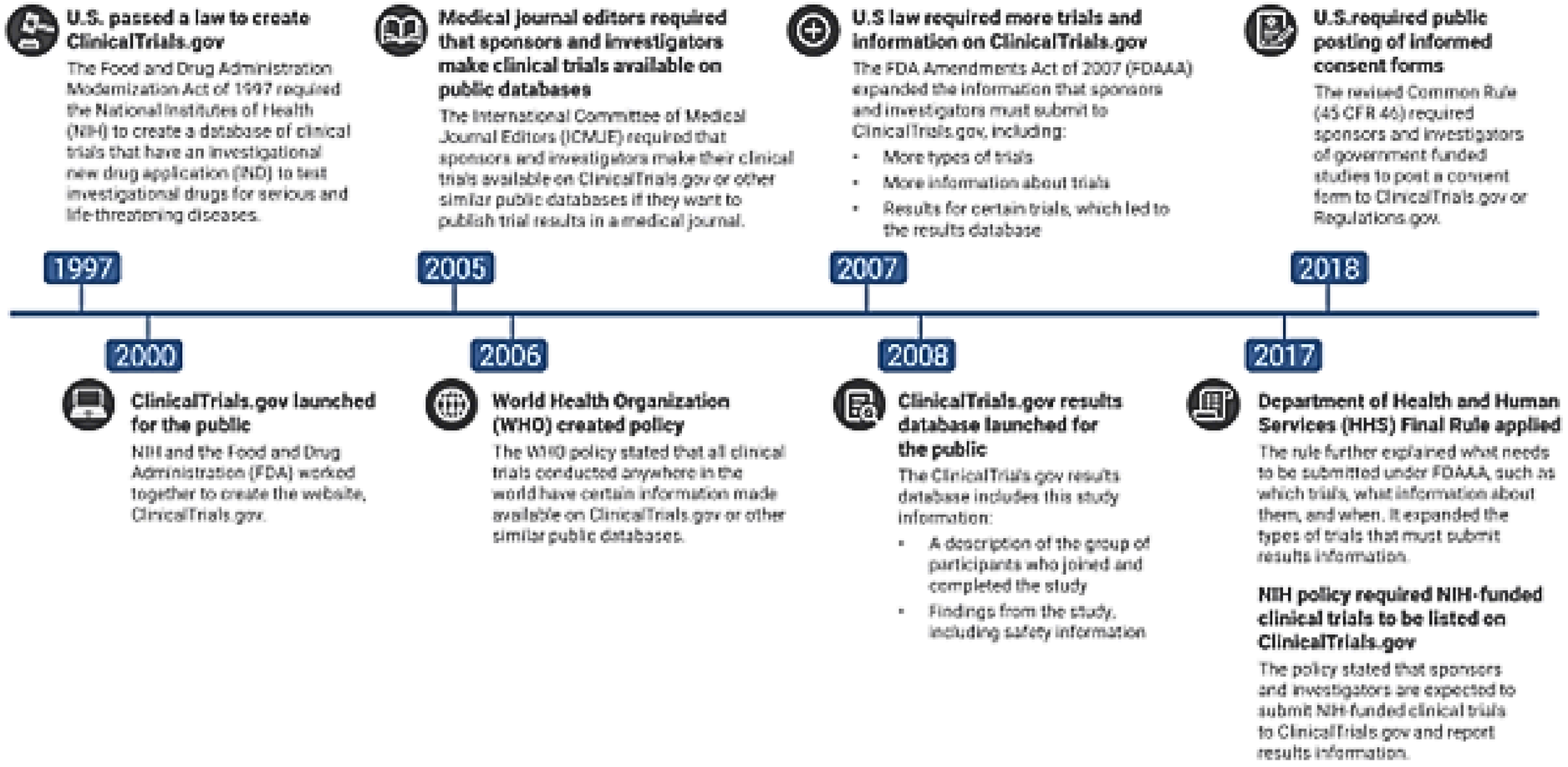
- Required language must be included in the consent that is approved by the IRB
- Must upload 1 unsigned informed consent form used to enroll participants on a publicly available **FEDERAL** website established as a repository for such information:
  - Clinicaltrials.gov
  - Regulations.gov

# WHAT IS CLINICALTRIALS.GOV?

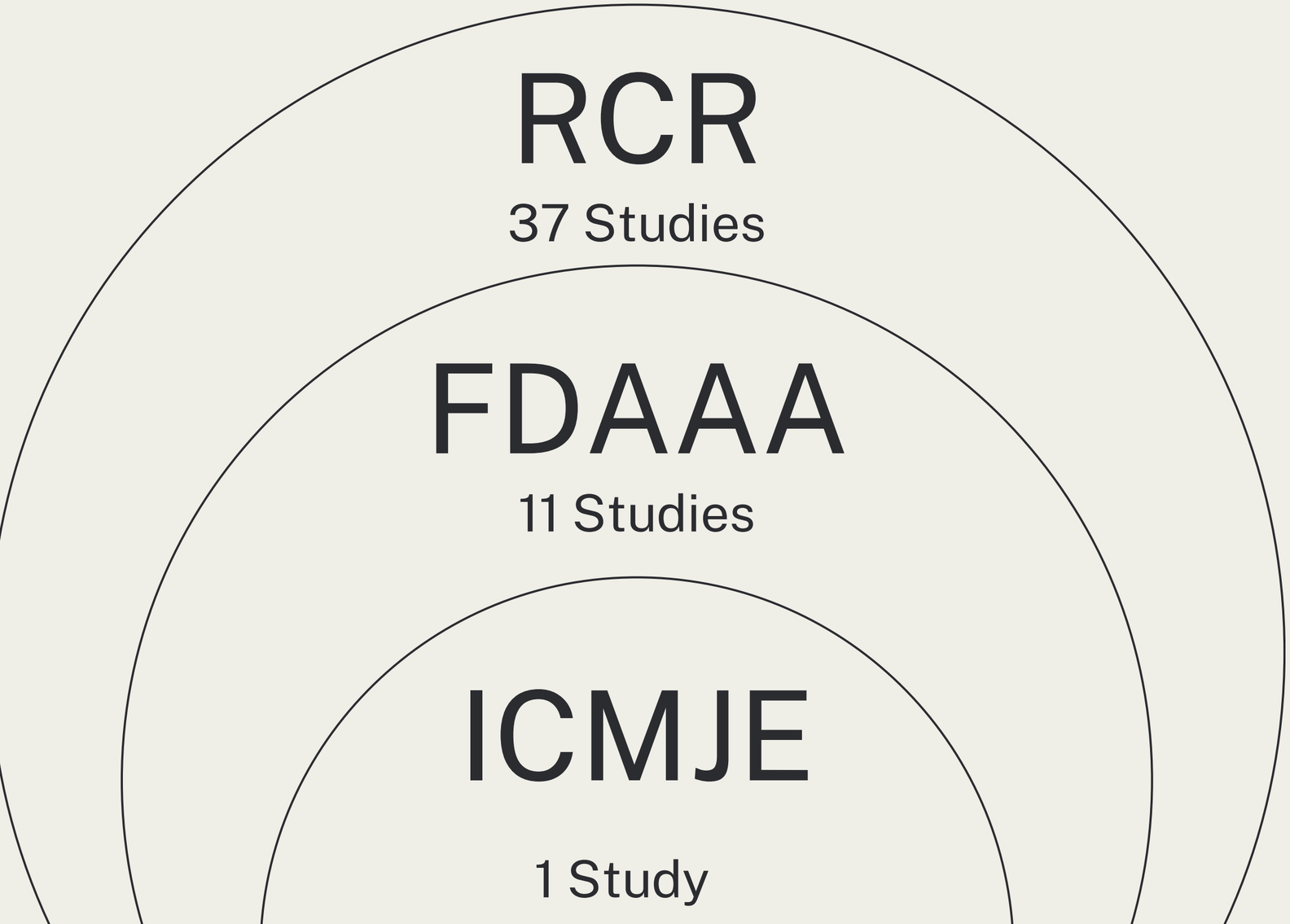
- Online database of clinical research studies and information about their results
- Purpose: to provide information about clinical research studies to the public, researchers, and healthcare professional
- Relies on sponsors or investigators to submit and update information about studies
- Up-to-date information on clinical research studies and their results
- Organized into study records, accessible to the general public, that includes:
  - study name, description, purpose, eligibility criteria, target enrollment numbers, description of the intervention, results, and contact information for study staff.

**Transparency/Library of Clinical Research/Publicly Accessible/ Up-to-Date Information**

# Major milestones related to ClinicalTrials.gov and how information in the database has changed over time



# TYPES OF CLINICAL TRIALS AT NASA




**RCR**

Revised Common Rule Clinical Trials

**FDAAA**

FDAAA Applicable Clinical Trial

**ICMJE**

International Committee of Medical Journal Editors

# CASE EXAMPLE#1

- Prospective Spaceflight study
- N=30
- Funding: NASA
- AIM: determine if partial gravity during parabolic flight will cause acute changes in vestibular, proprioceptive, and sensorimotor functions & test whether these changes will impact the performance of mission critical tasks such as standing, walking, and jumping.
- Study Design: Control vs. Intervention

Study that manipulates the **environment** to modify/examine **biomedical or behavioral space related outcomes** (e.g. hypobaric chamber, parabolic flight, bed rest) **funded by NASA**

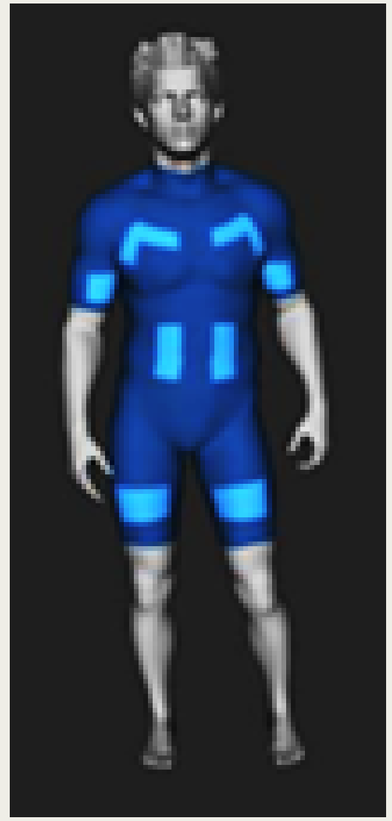
**Would meet the criteria for a Revised Common Rule definition of a clinical trial**

# CASE EXAMPLE#2

- Prospective Space Flight Study
- N= 8 Astronauts aboard ISS
- Funding= NASA
- AIM:  demonstrate efficacy of a suit that provides whole body electric muscle stimulation as alternative inflight exercise protocol for passive muscle tone/stiffness

Study **evaluates** the **safety or effectiveness** of an FDA-regulated drug, **device,** or biologic, as a countermeasure to prevent space-related health effects (muscle stiffness)

**FDAAA applicable clinical trial**



# WHY IS THIS IMPORTANT?

- Incomplete disclosure of research results impedes scientific process
- Transparency of clinical trial information increases trust between public and researchers
- Meets ethical obligation to human research participants
- Enhances patient access to enrollment in clinical trials
- Informs future research and research funding decisions
- Mitigates information bias (non-publication)
- Evaluates research integrity
- Prevents duplication of trials that are unsafe or ineffective interventions
- Provides access to data support evidence based medicine
- Relying only on publications is not adequate

# WHAT DOES THIS MEAN FOR INTERNATIONAL PARTNERS?

- US regulations regarding clinical trials are **still applicable** for International Partners when requesting the **use of NASA crew**
  - This is particularly important when conducting research **aboard the ISS**

- Clinical trials registration and posting requirements are the responsibility of the Sponsor or Principal Investigator

# Thank you!

If you have any questions or want to discuss your project, you are encouraged to reach out to the IRB Staff at **NASA-IRB@NASA.gov**