# Clinical Trials at NASA

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



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#### AGENDA

- 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 outcomes 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

#### FDAAA

#### **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

0

#### ICMJE

#### **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

#### ICMJE

#### **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

<sup>\*\*</sup>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



#### U.S. passed a law to create ClinicalTrials.gov

The Food and Drug Administration Modernization Act of 1997 required the National Institutes of Health (NIH) to create a database of clinical. trials that have an investigational new drug application (ND) to test investigational drugs for serious and life-threatening diseases.



#### Medical journal editors required that sponsors and investigators make clinical trials available on public databases

The International Committee of Medical Journal Editors (ICMJE) required that sponsors and investigators make their clinical trials available on ClinicalTrials gov or other similar public databases if they want to publish trial results in a medical journal.



#### U.S law required more trials and information on ClinicalTrials.gov

The FDA Amendments Act of 2007 (FDAAA) expanded the information that sponsors and investigators must submit to ClinicalTrials.gov, including:

- More types of trials
- More information about trials.
- Results for certain trials, which led to the results database



#### U.S.required public posting of informed consent forms

The revised Common Rule (45 CFR 46) required sponsors and investigators of government funded. studies to post a consent. form to ClinicalTrials.gov or Regulations.gov.









#### 2000



#### ClinicalTrials.gov launched for the public

NIH and the Food and Drug Administration (FDA) worked together to create the website, ClinicalTrials.gov.

#### 2006



#### World Health Organization (WHO) created policy

The WHO policy stated that all clinical trials conducted anywhere in the world have certain information made. available on ClinicalTrials.gov or other similar public databases.

#### 2008



#### ClinicalTrials.gov results database launched for the public

The ClinicalTrials.gov results database includes this study information:

- A description of the group of participants who joined and completed the study
- Findings from the study. including safety information

#### 2017



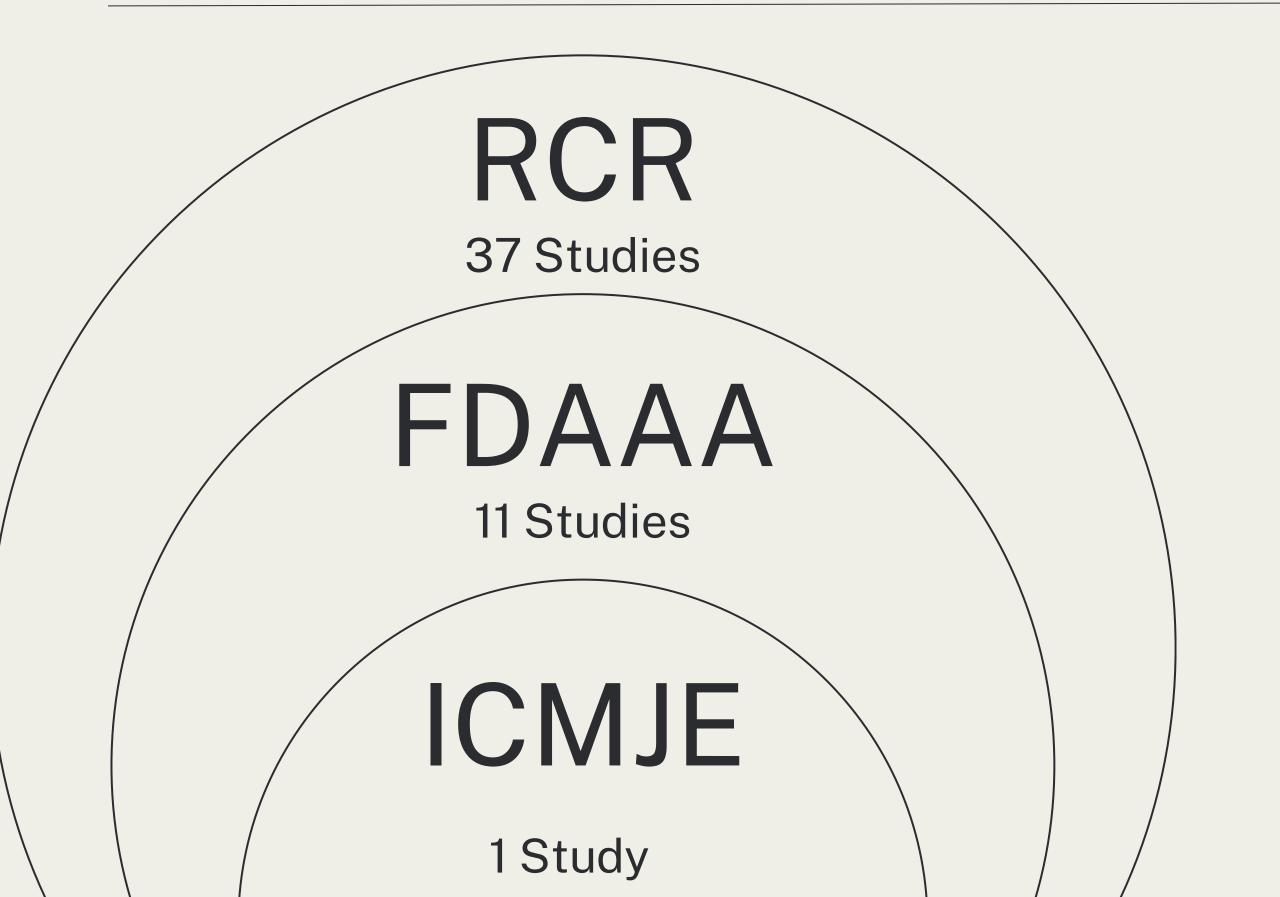
#### Department of Health and Human Services (HHS) Final Rule applied

The rule further explained what needs to be submitted under FDAAA, such as which trials, what information about them, and when. It expanded the types of trials that must submit. results information.

#### NIH policy required NIH-funded clinical trials to be listed on ClinicalTrials.gov

The policy stated that sponsors and investigators are expected to submit NH-funded clinical trials to Clinical Irials gov and report results information.

#### TYPES OF CLINICAL TRIALS AT NASA



#### RCR

Revised Common Rule Clinical Trials

#### **FDAAA**

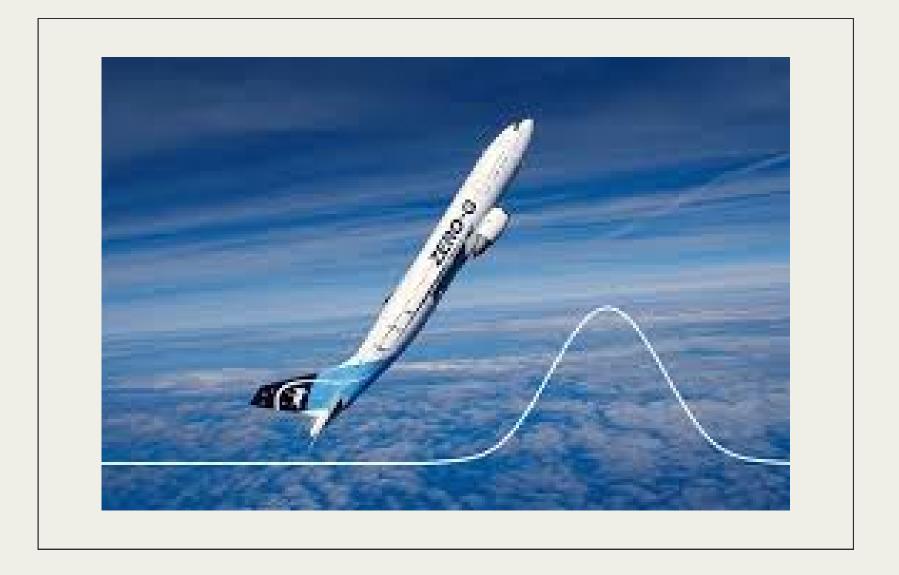
FDAAA Applicable Clinical Trial

#### **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