JUMP START

Energize your Research in Parenteral Nutrition

JUMPstart Virtual Meeting

Basic module JUMPstart 2021: Day 2 Presentation slides

January 31, 2021

Introduction

Dear JUMPstart participants,

We are happy to share with you the presentation slides for the Basic module. In this document, you will find the content presented in the live meeting on Sunday January 31. For your convenience, the slide numbers in this booklet correlate with those you will see in the live meeting.

Some slides (indicated by the  icon) will not be shown in the live session but are available for further information within this booklet.

Please feel free to use this document to take notes and refer back to.

Please do not share or reproduce any of the content within this booklet.

If you have any questions please contact: JUMPstart@fresenius-kabi.com.

Meeting agenda: Sunday, Jan 31, 2021, Part I

Time (GMT)	Session	Lead
13:05	Warming up: Any questions?	Scientific Committee
Part I: Down to the nitty gritty - Running a clinical study in detail II		
13:10	Who writes remains: CT documentation and data management	Prof. Ho-Seong Han
13:30	Discussion	
13:35	Who writes remains: CT documentation and data management	Prof. Olav Rooyackers
14:05	Discussion	
14:10	Planning a budget for a CT	Prof. Bob Martindale
14:35	Discussion	
14:45	**Break (20 minutes)**	

CT, clinical trial

Meeting agenda: Sunday, Jan 31, 2021, Part II

Time (GMT)	Session	Lead
15:05	Welcome back	Dr. Anke Wenn
15:10	**Bubble discussions**	All
Part II: On the finishing line - Publishing a clinical trial		
15:50	Skills and resources	Prof. Mette Berger
16:10	Publication strategies	Prof. Olav Rooyackers
16:30	Discussion	
16:40	Reflections from the Scientific Committee	Scientific Committee
16:50	Wrap up of the Basic module and next steps	Dr. Anke Wenn Prof. Mette Berger

Contents: Day 2

Part I: Down to the nitty gritty - Running a clinical study in detail II

Who writes remains: CT documentation and data management

Prof. Ho-Seong Han

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JUMPstart Training Program

Who writes, Remains

Prof. Ho-Seong Han, M.D., Ph.D

Basic Module: Running a clinical trial; Day 2, Part I: Down to the nitty gritty – running a clinical study in detail II

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Content

This segment of the training program covers:

- Important types of clinical trial documentation – Part 1

This extended version contains the slide set as presented by Prof. Ho-Seong Han and additional content marked with this icon:

Clinical trial documentation:
The Trial Master File (TMF)

Central file that contains **all essential documents** regarding the study for every clinical trial.

Trial Master File (TMF) = Investigator Site File (ISF) = Regulatory Binder (RB) (and many other names depending on the type of research, the country and the competent authority)

In **investigator-initiated trials**, the sponsor-investigator usually establishes only **one file (TMF) for collecting all study documents**.

In industry-sponsored trials, two files are maintained: one appropriate for the investigator and one for the sponsor.

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Clinical trial documentation:
Solid proof of clinical excellence

Documenting your study well builds a solid foundation for the clinical aspect of your treatment. Ultimately, a properly documented trial underscores reliably, validly and realistically your clinical efforts to help each and every patient.

Comprehensive list of documentation: ICH GCP E6(R2) Guideline, Section 8:

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf

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Clinical trial documentation:
Definition of documentation

According to ICH GCP:

Any kind of record that describes or keeps the **methods**, the **conduct/results**, the **factors influencing an intervention** as well as the **measures taken** in a clinical trial.

Formats: written, electronic, magnetic, optical, etc. This includes scans, x-rays, CT/MRI images, ECGs and other source documents from the patient chart.

The physician as a **sponsor-investigator** is **responsible** (with his/her signature as confirmation) **for reviewing** the information in all trial documents.

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Clinical trial documentation

We will focus on the most important aspects of your trial documents and what they need to contain:

Essential documents for your study*	
Clinical study protocol (CSP)	Informed consent form (ICF)
Case report form (CRF)	Adverse event form (AE form)
Concomitant medication form (Conmed form)	Various logs (subject screening/enrollment log, delegation log, drug accountability log)
Investigator brochure (IB)	Statements of insurance and financial conflicts of interest

*Depending on the study design and local regulatory requirements

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Clinical study protocol (CSP)

A protocol **describes the conduct of a clinical study** (i.e., inclusion and exclusion criteria, the endpoints, the methodology, design, objectives, and the statistical considerations). It also describes the safety management and reporting of the trial subjects and the integrity of the data collected.

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The following recommendations describe the best scenario of what a CSP should contain. Try to achieve as much as possible in the time you have available for the study. ***The better your documentation, the better your data quality*** *and overall administrative aspect of your trial.*

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1. General information

a. Protocol Title, Number, Date, and Version.

b. Name and address of the sponsor/CRO, if applicable.

c. Name and title of Principal Investigator, address and contact details of site unless the trial is conducted at multiple sites.

d. Name and address(es) of laboratories/technical departments or other institutions involved.

e. Protocol synopsis — The synopsis is a summary of your protocol: title, investigational site(s), study number, objectives, study design, inclusion/exclusion criteria, description of intervention, study duration, endpoints, sample size, and statistical analysis.

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2. Background Information and Scientific Rationale

a. **Rationale for and description of intervention**, eg. name and descriptions of the investigational product as well as the justification for the route of administration, dosage, dosage regimen, and treatment periods.

b. Statement of compliance with the protocol, GCP, and the applicable regulatory requirements.

c. Description of the population to be studied.

d. Summaries of **potential risks and benefits** and why the value of the information to be gained outweighs the risks involved.

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3. Trial Objectives and Purpose

a. Primary and secondary objectives of the study.

b. **Primary outcome measures (endpoints).** Normally only one primary variable, a clinically relevant, valid and reliable measure of the primary objective. At times this may involve composite endpoints.

c. Secondary outcome measures (endpoints). Supportive information related to the disease/research question.

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4. Trial Design I

a. Study type/design:
    a. e.g., double-blind, placebo controlled, open-label, randomized, retrospective…
    b. the phase of the trial,
    c. single or multiple centers,
    d. a schematic diagram of trial design,
    e. procedures,
    f. stages
b. The study populations (e.g., healthy participants, sick patients, inpatient/ outpatient), sample size, and expected duration of subject participation.
c. Detailed randomization and blinding description if applicable.

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4. Trial Design II

e. “Stopping rules” or “**discontinuation criteria**” for individual participants.

f. The study plan:

- illustrated by a **study flowchart**
- detailed **description of all study procedures and visits**

g. **Eligibility criteria:** Inclusion/Exclusion criteria, screening laboratory tests for safety (if applicable)

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CSP: Further Contents

5. Assessment of Safety: Adverse events, serious adverse events, expected and unexpected adverse reactions
6. Statistics: Sample size calculations, analyses plan
7. Administrative issues: Quality assurance
8. Ethics, regulatory and legal issues
9. Data handling and record keeping
10. Publication policy
11. Literature references

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Clinical study protocol (CSP) – Summary

The development of the protocol is very complex and often requires the **help of your study team** (incl. study coordinator, laboratory, pharmacy, statistician, data manager, nurses, doctors and other health care or technical staff).

The main sections of a protocol are:		
General and background information	Trial design, objectives and purpose	Selection and withdrawal of subjects
Treatment, schedules, visits	Assessment of efficacy and safety	Statistics
Direct access to source data/documents	Quality control and quality assurance	Ethics/CA approvals
Data handling and record keeping (data management	Financing and insurance	Publication policy

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Informed consent form (ICF)

- Most important document for the protection of human subjects in clinical trials
- Also protects the sponsor-investigator from legal consequences if the patient is harmed.

Two main parts: The signed document and the process of obtaining consent.

Ongoing process: Prior to any trial-related procedures AND during the trial.

A "laymen" summary of the trial: easily understandable and age appropriate.

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Informed consent form (ICF)

- ✓ Only effective after IRB/EC/CA approval
- ✓ Patient receives, reads, dates and signs the form
- ✓ Patient has to be given sufficient time to decide
- ✓ The sponsor-investigator has to sign it after the participant

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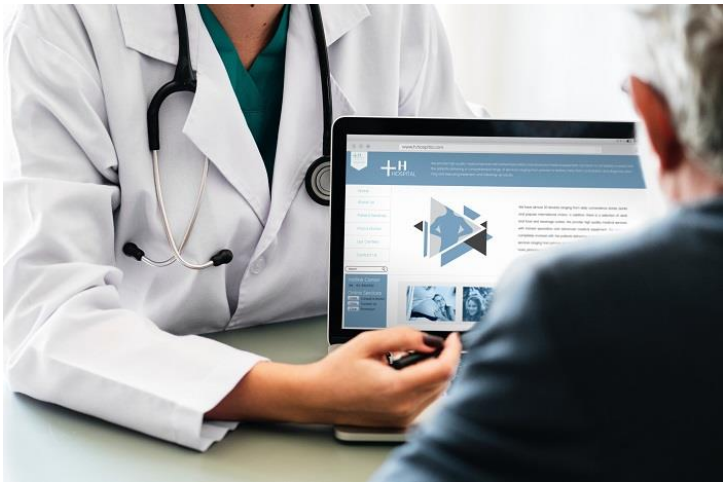
ICF Contents:
Information on the clinical trial

- Explanation that the clinical trial is part of research
- Course of events and study design, study duration
- Treatment during the trial
- Probability for randomized allocation to a study group
- Alternative treatments for the participant and their side effects
- Update of changes of the trial for patients



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ICF Contents:
Rights and duties of participants

- Voluntary participation and possibilities for refusal at any time (without any disadvantages for participant who dropped out)
- Open access for responsible monitors, auditors, EC/CA to every medical document regarding the trial including original documents
- Data protection, especially the personal data of the patients, has to be considered and in line with every countries' or region's laws
- Preservation of anonymization; documents which identify the participants have to be treated confidentially
- Contact person or institutions in case of harm

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ICF Contents:
Risks and benefits

- Compensation and insurances for the participant if he/she is harmed
- Foreseeable risks for participants as well as for embryo, fetus and nursed infants
- Expected benefits and the purpose of the trial; if there is no clinical benefit expected the participant has to know that as well
- Expense allowance and possible personal expenses for the participant
- Circumstances and reasons that can stop the participation or study

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Patient communication

a. The **sponsor-investigator** may delegate the task of administering and obtaining informed consent to a qualified individual; however, he or she is **ultimately responsible** for ensuring proper conduct

b. The PI/delegate discusses the trial's risks, benefits, and other aspects with the potential participant and, if required, the participant's legal representative, before the trial begins.

c. The PI gives the potential participant **ample time and opportunity to ask questions** about the trial and discuss it with relatives and family members.

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ICF Documentation

Details to be documented are as follows:

- Description of how consent was obtained—written or verbally.
- The **participant's level of comprehension**, that is, did the participant understand the main purpose of the study, procedures to be done, risks involved in participating and frequency and duration of visits?
- **Start time and end time** of consent process.
- **Questions asked by the participant and answers given**.

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Informed consent form (ICF) - summary

The Council for International Organisations for Medical Sciences (CIOMS) has one of the most advanced international guidelines regarding the informed consent process, which states:

"obtaining informed consent is a process that is begun when initial contact is made with a prospective subject and continues throughout the course of the study. By informing the prospective subjects, by repetition and explanation, by answering their questions as they arise, and by ensuring that each individual understands each procedure, investigators elicit their informed consent and in doing so ***manifest respect for their dignity and autonomy.*** *Each individual must be given as much time as is needed to reach a decision, including time for consultation with family. Informing the individual subject must not be simply a ritual recitation of the contents of a written document. Rather, the investigator must convey the information … in language that suits the individual's level of understanding … the investigator must then ensure that the prospective subject has adequately understood the information."*

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Case report form (CRF)

A Case Report Form (CRF) is a trial **data reporting document** used in a clinical study. In it, patient data is collected in a standardized format:

1. In accordance with the protocol
2. Complying with regulatory requirements
3. Allowing for efficient analysis
4. In an anonymized fashion (coded)

A CRF is a printed or electronic document that is created to capture defined clinical data from each patient separately and to transfer it to Data Management.

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Case report form (CRF)

The **study protocol** determines what data will be collected on the CRF:

- All data must be collected on the CRF if so specified in the protocol
- Data that will not be used for analysis should not appear on the CRF

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Case report form (CRF)

Paper forms:

- ✓ Study staff transcribing information recorded in the source documents
- ✓ Transferred to data entry personnel who enter the information into an electronic database.

eCRFs:

- ✓ Less errors
- ✓ Quality control measures
- ✓ Communicate data directly into the study database

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Case report form (CRF)

A CRF consists of many sub-forms that gather the patient's data from screening through every follow-up, all the way to the end of the study.

Design requirements for a proper CRF are:

1. Header
2. Principal section
3. Footer

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Paper CRF - sample

[redacted] TRIAL

[redacted] (HIST. CONTROL) – BASELINE

FORM 1D - INCLUSION AND EXCLUSION CRITERIA

Patient ID: X - Y Y Y - Z

Initials of person completing form: _ _ _ Date: _ _/_ _ _/_ _ _ _

A INCLUSION CRITERIA

These criteria were assessed by the investigator at the time of inclusion of the patient into the study.

A1 Was the patient PN-dependent and expected to require PN for at least 14 more days from inclusion?

Yes ☐
No ☐ *Ineligible*

A2 Did the patient have PN-associated liver disease as defined by at least two consecutive direct bilirubin values ≥ 2.0mg/dl three days at minimum apart?

Yes ☐
No ☐ *Ineligible*

A3 Did the patient receive standard therapies to prevent progression of liver disease: (including surgical treatment, cyclic PN, avoiding overfeeding, reduction/removal of copper & manganese from PN, advancement of enteral feeding and the use of Ursodiol)?

Yes ☐
No ☐ *Ineligible*

B EXCLUSION CRITERIA

B1 Did the patient have any other known causes of chronic liver disease such as: Hepatitis C, cystic fibrosis, biliary atresia, alpha anti-trypsin deficiency?

Yes ☐ *Ineligible*
No ☐

B2 Did the patient have multi-organ or renal failure?

Yes ☐ *Ineligible*
No ☐

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CRF:
Header requirements

- Study identification data (study name, number, logo, title or abbreviated title)
- **Patient identification** (unique patient code, site number)
- Guidance text including headline
- Optional: identification of data entry personnel via initials

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CRF:
Principal section requirements

- Informed consent obtained and its date
- Screening: All inclusion and exclusion criteria with individual check marks
- Baseline visit information such as demographics, physical exam data, etc. (age, weight, sex, gender, ethnicity, pregnancy status – all depending on the protocol)
- Medical history (comorbidity, concomitant and previous medication)
- Visits (data collected during each visit in the study)
- Trial medication and concomitant medication
- Adverse and serious adverse events
- Death or transplantation forms
- Specialized forms for documentation of your particular trial protocol

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eCRF - sample

[redacted]

Date	02.02.2018 - 11:55 (MEZ)	Pat-ID	aaa000	Completion status	completely filled, data entry complete
BCH patex	patient export BCH	Add-ID	1-011-8	Review status	data review (B)
Project	[redacted] (FINAL 1.9.5d)	Baseline	15.11.2005 (MEZ)	Query status	without query
Centre	Zentrum B[redacted]	Form family	FORM 1A	Comment status	--
		Form	FORM 1A - INCLUSION AND EXCLUSION CRITERIA (BCH)	SDV status	in progress

FORM 1A - INCLUSION AND EXCLUSION CRITERIA (BCH) (Print Document-No. 9 - 9)

A INCLUSION CRITERIA

A1 Was the patient PN-dependent and expected to require PN for at least 30 more days from inclusion?

- ○ not applicable
- ◉ Yes
- ○ No

A2 Did the patient have PN-associated liver disease as defined by at least two consecutive direct bilirubin values ? 2.0mg/dl three days at minimum apart??

- ○ not applicable
- ◉ Yes
- ○ No

A3 Did the patient receive standard therapies to prevent progression of liver disease: (including surgical treatment, cyclic PN, avoiding overfeeding, reduction/removal of copper & manganese from PN, advancement of enteral feeding and the use of Ursodiol)?

- ○ not applicable
- ◉ Yes
- ○ No

A4 Was an informed consent form signed?

- ○ not applicable
- ○ Yes
- ○ No
- ◉ NA (for historical controls)

A4a Date of informed consent:

[ ] dd.mm.yyyy

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CRF:
Designed to avoid mistakes

- Optically appealing**, clear and unambiguous** form
- Avoid possibilities for misinterpretations or confusion!
- Use **short and concise language**
- Train all staff well on the requirements of the CRF
- Imply **explicit queries**, clear instructions, prompts and controlling fields.
- Allow for the efficient and complete coding of data for processing and analysis.

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CRF:
Final check

- The CRF needs to be finalized (with versioning and **approvals**) before you start enrolling patients into the clinical trial.
- **Anonymization:** Ensure that on the CRF, personal data is not identifiable; use coded numbers (screening, randomization numbers) and initials.
- Before using your CRF, **run a sample** CRF on a sample patient and verify that you adhere to all aspects of the protocol.

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Case report form (CRF) - summary

The CRF is a trial data reporting document used in a clinical study to collect all relevant patient data in a standardized, anonymized format. The CRF will be designed according to protocol, comply with all regulatory and IRG requirements and allow for appropriate analysis of data.

The CRF may be a printed or electronic document that should mirror exactly all relevant source data of the patient. Appropriate CRFs consist of header, principal and footer sections.

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Session summary

- ✓ Coverage of important clinical trial documentation such as Clinical study protocol (CSP), Informed consent form (ICF) & Case report form (CRF).

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Who writes remains: CT documentation and data management

Prof. Olav Rooyakers

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JUMPstart Training Program

Clinical trial documentation, data management and data quality

Prof. Olav Rooyackers, Ph.D

Basic Module: Running a clinical trial; Day 2, Part I: Down to the nitty gritty – running a clinical study in detail II

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Agenda

This segment of the training program will cover:

- Important types of clinical trial documentation
- Data management
- Data quality

Some of the most important CRF sub forms used in clinical trails

1. Adverse event form
2. Concomitant medication form

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Adverse event form (AE form)

This form collects relevant information on any untoward medical occurrence in a patient or clinical trial subject who receives an IMP. The event does not necessarily have to have a causal relationship with the study drug.

An adverse event can therefore be any unfavorable and unintended event or sign (out of range lab value, etc.), e.g. symptom or disease temporally associated with the use of an IMP, even it is not related to the IMP. All events need to be documented on this form.

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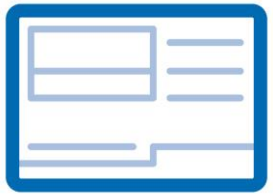
Adverse event form (AE form)



Adverse Event (AE): Any untoward medical occurrence during a clinical trial, not necessarily related to the investigational product.

Adverse Reaction (AR): An adverse medical occurrence related to the investigational product.

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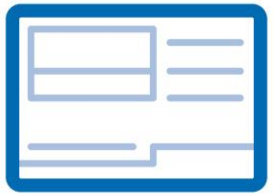
Adverse event form (AE form)



Serious Adverse Event (SAE) Criteria per ICH GCP are:

Any untoward medical occurrence that at any dose:

(1)results in **death**,

(2)is **life threatening** (patient was at immediate risk of death at the time of the event in the opinion of the PI or investigator),

(3)requires inpatient **hospitalization** (at least 24 h) **or** prolongation of existing hospitalization,

(4)results in **persisten**t or significant **disability/incapacity**,

(5)requires **intervention** (this is an FDA criterion) to prevent permanent impairment (e.g. emergency room treatment, etc.), or

(6)was **medically significant** (in the judgment of the reporting or company physician, the event was serious, although not meeting the above criteria, e.g. convulsion).

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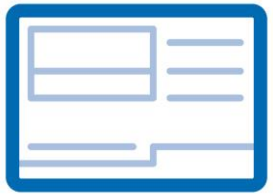
Adverse event form (AE form)



Ideally, the **AE form** is a very detailed form and reports on the following aspects.

1. **Term** of the event
2. **Start and end times** of the event
3. **Severity**
4. **Outcome** (did it resolve, did it resolve with sequelae, not resolve)
5. **Relatedness** (AE relation to the IMP – possibly, probably, etc.)
6. **Action taken** with the IMP (resume IMP, discontinue IMP, etc.)
7. **Seriousness** (is it an SAE?, if yes, what is the criterion that qualifies the event as an SAE)

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FORM B – ADVERSE EVENTS

Patient ID: X - Y Y Y - Z

Initials of person completing form: __ __ __

Date: __ __/__ __ __/__ __ __ __

B1a	B1b	B1c	B1d	B1e	B1f	B1g	B1h	B1i	B1j	B1k
AE num ber	**What is the AE term?**	**AE Start date? DD/MMM/YYYY**	**Is the adverse event still ongoin g?** 1 = Yes *(skip B1e)* 2 = No	**AE end date? DD/MMM/YYYY**	**Severity** 1 = Mild 2 = Moderate 3 = Severe 4 = Life-threat./ disabling 5 = Death (complete form 8)	**Related to study drug** 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	**Action Taken with Study Intervention (SI)**1 = None 2 = SI interrupted 3 = SI discontinued 4 = SI modified	**Outcome** 1 = Not resolved 2 = Resolved 3 = Resolved with sequelae 4 = Resolving 5 = Fatal (complete form 8) 6 = Unknown	**Is the AE serious?** 1 = Yes 2 = No (skip B1k)	**Seriousness criteria** 1 = death 2 = life-threatening 3 = inpatient hosp. or prolong. of existing hosp. 4 = persistent or significant disability/incapacity 5 = congenital anomaly/birth defect 6 = Other medically important condition
		__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __						
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Is this the last page of Form B? Yes ☐ No ☐ *If no, please complete another page of Form B*

Concomitant medication form (Conmed form)

Concomitant Medication is the term for:

medication taken by the subject during the course of a clinical trial, in addition to the investigational product(s).

Detailed and careful documentation of conmeds is critical to ensure the appropriate evaluation of the IMPs safety and drug interaction profile.

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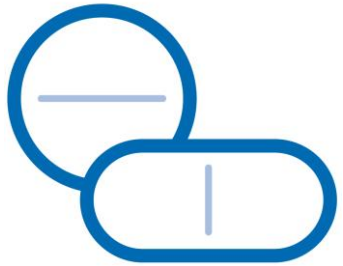
Concomitant medication form



1. **Name** (generic or trade)
2. **Dose**
3. **Unit** (ml, g, mg, etc.)
4. **Frequency** (once, q4d, tid, etc.)
5. **Route** (subcut., IM, IV, oral, etc.)
6. **Start date/time**
7. **End date/time**
8. **Ongoing or not**
9. **Prescribed or given**

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[redacted] (HIST. CONTROL) – CONTINUOUS ASSESSMENT
FORM C – CONCOMITANT MEDICATION

Patient ID: X - Y Y Y - Z

Initials of person completing form: __ __ __

Date: __ __/__ __ __/__ __ __ __

C1a	C1b	C1c	C1d	C1e	C1f	C1g	C1h	C1i	C1k
Conc Med Number	Medication name (Trade or generic name)	Dose	Unit	Frequency	Route	Start date (DD/MMM/YYYY)	Ongoing? 1 = Yes (skip C1i) 2 = No 3 = Unknown (skip C1i)	End date (DD/MMM/YYYY)	Source of con med information
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered
						__ __/__ __ __/__ __ __ __		__ __/__ __ __/__ __ __ __	☐ given ☐ delivered ☐ ordered

Is this the last page of Form C? Yes ☐ No ☐ *If no, please complete another page of Form C*

Some of the most important logs used in clinical trails

1. Subject enrolment / screening log
2. Delegation log
3. Drug accountability log

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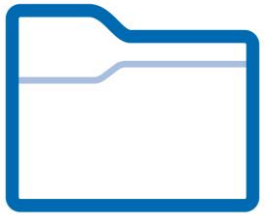
Subject enrolment / screening log



- **Screening log**: detailing all screened subjects

- **Enrolment log**: add a section on enrolment or separate

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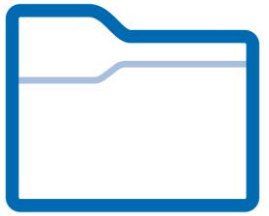
Delegation log



- **All assigned duties and responsibilities in the clinical trial**
- The PI or sponsor-investigator allocates
- Includes everyone’s signature and initials and their dates of start and end of activity in the trial

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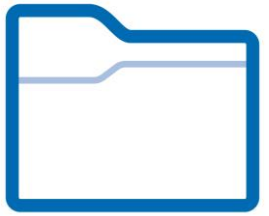
Drug accountability log



Drug accountability is the documentation of the:

1. Investigational medicinal product (IMP) with expiration date, lot number, etc.
2. Administered dose, amount, and lot of the IMP per patient
3. Unused or lost amount of IMP per patient
4. Dispensing, destruction and redemption of the IMPs is documented in the drug accountability log

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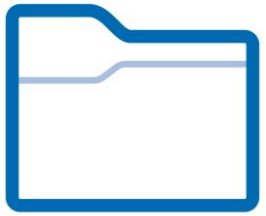
Drug accountability log



The drug accountability log should include the following:

- Name of the sponsor-investigator
- Protocol title, number and version
- Name of the pharmaceutical product
- Date
- Amount
- Manufacturer
- Dose, form and strength of the IMP
- Lot number
- Study site number
- Signature of the study team member responsible for administration or dispensing

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Investigator brochure (IB)

1. The IB is a **summary of information** regarding an investigational product obtained during preclinical and clinical trials.

2. The IB provides the investigator with **details necessary to manage** a clinical trial and study participants.

3. It provides the investigator **information regarding possible risks** and adverse reactions, and of specific precautions that may be needed.

4. The IB should also provide information regarding the recognition and **treatment of overdose** and the possible treatment thereof.

5. The manufacturer is responsible to **update the IB**. It should be reviewed annually and/or whenever new and important information becomes available.

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Investigator brochure (IB)

Main sections of an IB:

1. **Title page** (manufacturer's/Sponsor's name, the identity of the product, an edition number and date)
2. **List of abbreviations.**
3. **Contents.**
4. **Summary**
5. **Introduction** (chemical name, all active components, pharmacological class, the rationale for performing further research with the investigational product, and anticipated indications for its use)
6. **Physical, chemical, and pharmaceutical properties** (the handling, storage, and preparation of IMP needed, prior to administration)
7. **Nonclinical studies:**
8. **Effects in humans:**
9. **Summary of data and guidance for the investigators (**therapeutic indications, contraindications, warnings, and precautions for use)

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Statements of insurance and financial conflicts of interest

All participants and players in a clinical trial need to be covered and protected by insurance.

The investigator and his/her team make clear that all of their efforts in the studies are not influenced by any conflicts.

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Data management and data quality

Data management is one of the most critical parts of any clinical trial – it ensures the validity and reliability of your data to allow for accurate and appropriate reporting. It forms the basis of your data's quality.

It covers all aspects from CRF design to data transfer for statistical analyses.

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Data management and data quality

1. Pivotal studies used for new drug applications to regulatory authorities often require the applicants to implement Good Clinical Data Management Practice guidelines (GCDMP). These guidelines allow for the strict handling of your trial's data to ensure quality, reliability and validity of data and its interpretation.
2. Investigator-initiated trials are often run by a clinical study team that does not have separate, full time data managers to handle their studies' data.

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Data management and data quality

1. **Protocol** Design
2. **Case report form** design
3. **Database** design (in most IITs, this is done through spreadsheets)
4. **Data collection** (on paper CRFs)
5. **Data entry** (from paper CRF to eCRF or spreadsheet)
6. **Data cleaning, verification and dataset locked** (This is usually done by a data manager with specialized skills and the monitoring team)
7. **Statistical analysis** (DM transfers data to statistician)
8. **Repor**t writing / publication

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Data management and data quality

The **data manager**:

- conducts quality control (QC)
- identifies ongoing data quality issues
- is responsible for processing and validating clinical study date

Clinical **monitor:**

- an independent reviewer of data
- provided by a sponsor, by the institution or the IRB.
- will compare source data to CRF data (source data verification (SDV))
- assessment of the trial's documentation adherence to GCP and local regulatory requirements

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Data management and data quality

To **ensure your data's quality**:

- Design the CRF in a way that follows the flow of the patient and his/her visits and study schedule.
- Allow for time to review data validity:
  - Out of range values
  - Nonsensical data points (e.g.: adult weight: 6.0 kg)
  - Wrong entries (lab value entered in medication field)
- If using an eCRF/database all these checks will be performed automatically after programming
- Use monitoring to improve data quality

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Session summary

- ✓ Coverage of most important clinical trial documentation
- ✓ Discussion of relevant data management aspects
- ✓ Illustration of the central quality measures in a trial

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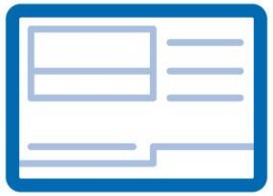
Adverse event form (AE form)



Serious Adverse Reaction (SAR): A SAE that is related to the investigational product.

Suspected Unexpected Serious Adverse Reaction (SUSAR): An (S)AE, which is suspected to be related to the investigational product and it is not specified in the IB/SmPC as expected.

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Statements of insurance and financial conflicts of interest

- The sponsor-investigator, the clinical trial staff and trial subjects must be insured
- Should be approved by IRB/EC

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Statements of insurance and financial conflicts of interest

Financial disclosure of the PI:

a document required by regulatory authorities and most IRBs to clarify any financial interest on the part of the investigator and co-investigators, in the drug manufacturer's organization, investigational product or other financial concern which might unduly influence their participation in a clinical trial.

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Planning a budget for a CT

Prof. Bob Martindale

FRESENIUS KABI
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JUMPstart Training Program

Running a trial in detail
Running the budget for a clinical trial

Prof. Bob Martindale MD PhD

Agenda

This segment of the program will cover:

- **Elements of a clinical trial budget**
  - **Institutional**
    - **Investigator initiated trials (IIT)**
  - **Governmental**
- **Helpful hints in what to consider when planning costs for a trial**
- **Sources of funding**

Building a Budget

What is allowable cost

Budget justifications

Split budgets

Personnel

Fringe benefits (OPE)

Equipment

> $3000 capital equipment

Travel

Patient care costs

nursing, dietician etc

Trainee

Core / Shared resources

Animal charges

Outgoing sub awards

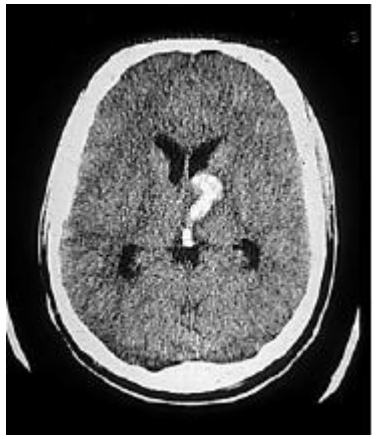
Indirect cost (F and A)

Cost sharing

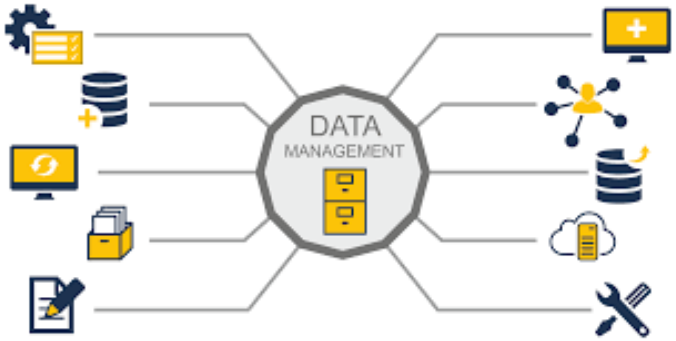
Major cost centers in a budget

The people

Use of technology



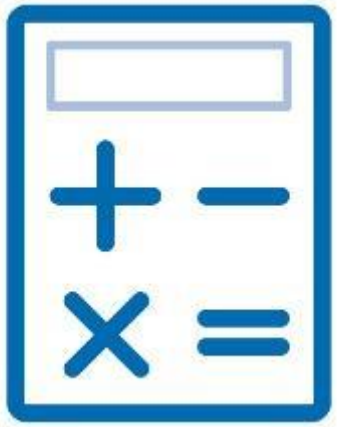
Study related care, study intervention cost



Statistical analysis and data management

Travel, meetings, publication costs

The elements of a clinical trial budget



- **Budgets can become very complex**
- **Get help early**
  - **Find those with history of budget experience**
    - **Experience PIs, Coordinators,**
  - **Department or institution finance, grant sections**
- **cost estimates, contracts, trial budgets and internal charges from other departments**
- **Involve entire clinical team in budget planning**
- **Government institutions have meticulous accountants who understand clinical study costs**
  - **Don’t undercut your study to “look good”**
  - **Don’t pad the budget**

The elements of a clinical trial budget

<u>Getting started:</u>

Secure funding

Understand the process (complexity) of clinical study

IRB approval – study --- presentation --- publication

PI is responsible for all parts of the study budget

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Where to Search for Funding

Newton's List - Newton's List seeks to facilitate international science cooperation by providing a forum for grant seekers and funders. The site is a free resource open to individuals searching for international funding and organizations looking to market their grants to an international audience. Established in 2013 and co-sponsored by CRDF Global and the U.S. National Science Foundation (NSF), Newton's List is a a user-driven aggregate of current international funding opportunities for students and researchers working in natural and social science fields.

Grants.gov - Grants.gov lists all current discretionary funding opportunities from 26 agencies of the United States government, including the National Institutes of Health, the National Science Foundation, the Department of Energy, and many others -- in other words, all the most important public funders of research in the United States. Grants.gov is free and does not require a subscription.

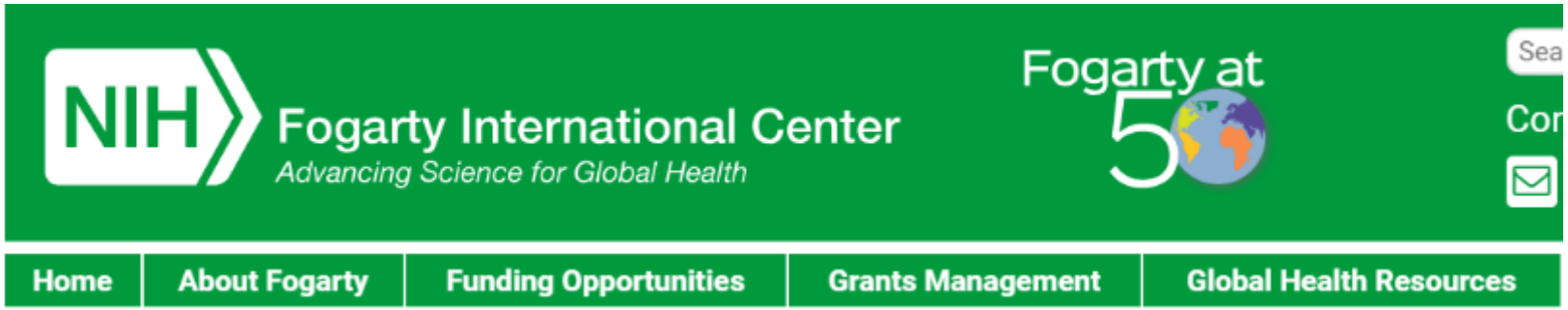
The National Institutes of Health (NIH) Office of Extramural Research - The largest funder of biomedical research in the world, NIH funds research in just about every area that's remotely related to human health and disease. This page includes extensive information about NIH grants, as well as a place to search NIH funding programs. NIH also has an **advanced search page**, which offers a wide range of search options. The NIH Web site is free and does not require a subscription.

The National Science Foundation (NSF) - An independent federal agency, the U.S. National Science Foundation funds approximately 20 percent of all federally supported basic research conducted at America's colleges and universities. This is the place to search for NSF funding programs. The NSF Web site is free and does not require a subscription.

Philanthropy

Growing source of funding globally

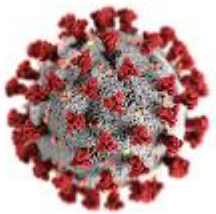

European Commission
CORDIS
Community Research and Development Information Service
European Commission > CORDIS > Search > Results page


NIH
Fogarty International Center
Advancing Science for Global Health
Fogarty at 50
Sea
Cor
Home
About Fogarty
Funding Opportunities
Grants Management
Global Health Resources


CULTIVATED
PLANT-BASED
The Good Food Institute
RESEARCH GRANTS


Funding opportunities for Nutrition for Precision Health, powered by the All of Us Research Program to be published in January 2021


International Health Care Funding Report
2020
IAA AAI
SOCIETY OF ACTUARIES



How to Get Funding: NIH Free Web Site

Get valuable insight into the process for finding, applying for, and securing funding.

- **Special Feature: Grant Writing for Tight Times**

Faced with falling grant-approval rates, researchers need to work harder and smarter to get their projects funded.

  - **The NIH R01 Tool Kit**
  - **Getting to the Top of a Big Pile**
  - **A Guide to NSF Success**

- **Article Series: How Not to Kill a Grant Application**
  - **Part 1: Murder Most Foul**
  - **Part 2: Abstract Killers**
  - **Part 3: So What?**
  - **Part 4: Lost at Sea**
  - **Part 5: The Facts of the Case**
  - **Part 6: Developing Your Research Plan**
- **Writing a Research Plan**
- **NSF Grant Reviewer Tells All**
- **Giving it 110 % (Percent Effort)**
- **Dealing with Peer Review**

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Sources of funding

1. **Investigator initiated trials (IIT)**

    a) your institution commonly has money for IIT

    b) industry commonly will have funds for IIT

        usually testing a product

        IIT grants usually noted on company websites

2. **Common sources for IIT**

    a)Grants

        to institution vs individual

    Foundations, professional societies

    companies

Sources of funding

2. **Grants**

There are two main pathways for grant requests:

a. **National or international grant agencies**

   a. **<u>EU:</u> H2020, IMI**

   b. **<u>US:</u> NIH, FDA**

   c. **<u>China:</u> MoST, NFSC, CAS, etc.**

b. **Industry**

c. **Foundations**

Budget must reflect the total scope of the study

You need to know

- **How many sites are needed to recruit patients over what period of time?**
  cautious with being overly optimistic

- **How many patients are needed to answer your primary question?**
- **What are the per patient costs in terms of technology (imaging, labs, etc.), treatments (drugs, devices), and personnel time to screen, enroll, measure outcomes, follow subjects, and data entry?**

- **Who is running/coordinating the trial and what are their effort/costs/expenses?**

- **Who is providing statistical analysis and managing and monitoring data and what are their effort/costs/expenses?**

- **What are the travel and communication costs to train trial staff and sites?**

- **What additional costs of technologic measurements image analysis, labs, etc?**

- **Are you using consultants/advisors and how much do they cost?**

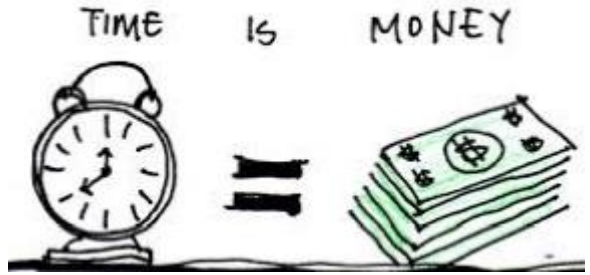
Every task and data point collected cost money

- **Less is more – minimizing data points makes the trial easier and decreases budget**
  - **carefully consider each collection point**
- **Budget for additional sites if likely to be needed**
- **Try to use standard of care (SOC) labs/imaging whenever possible**
    - **SOC should be well described**

Never underestimate time required and number of sites to recruit numbers required to complete study

- **Extending study often exceeds budgeted finances**
  - **Example 5 yr data collection become 6 or 7 yrs**
- **NIH trial awards are now based on milestone-based and study will be stopped (money withdrawn) if recruitments don't meet targets**
- **Pay study coordinators based on time worked vs set payments**
  - **This way if recruitments are slower than expected $ still available to complete study**

Estimates of OHSU costs for personnel involved in study



MD- $500 per hour

Study Coordinator – $200 per hour

Nursing – Nursing departments sets fee

Pharmacy – set fees depending time commitment

Don’t forget fringe benefits, vacation, sick days etc

2080 working hours per year – calculate based on this example: 1% = 20.8 hours annually etc

Effort / Hours conversions

Total work hours annually	effort	Annual hours	monthly hours	weekly hours
2080	**1%**	20.8	1.73	0.43
2080	**2%**	41.6	3.47	0.87
2080	**3%**	62.4	5.20	1.30
2080	**4%**	83.2	6.93	1.73
2080	**5%**	104	8.67	2.17
2080	**6%**	124.8	10.40	2.60
2080	**7%**	145.6	12.13	3.03
2080	**8%**	166.4	13.87	3.47
2080	**9%**	187.2	15.60	3.90
2080	**10%**	208	17.33	4.33
2080	**11%**	228.8	19.07	4.77
2080	**12%**	249.6	20.80	5.20
2080	**13%**	270.4	22.53	5.63
2080	**14%**	291.2	24.27	6.07
2080	**15%**	312	26.00	6.50
2080	**16%**	332.8	27.73	6.93
2080	**17%**	353.6	29.47	7.37
2080	**18%**	374.4	31.20	7.80
2080	**19%**	395.2	32.93	8.23
2080	**20%**	416	34.67	8.67
2080	**21%**	436.8	36.40	9.10
2080	**22%**	457.6	38.13	9.53

Example of NIH personnel budget sheet

Program Director/Principal Investigator (Last, First, Middle): Strong, Doctor

DETAILED BUDGET FOR INITIAL BUDGET PERIOD DIRECT COSTS ONLY	FROM 07/01/2017	THROUGH 06/30/2018

List PERSONNEL *(Applicant organization only)*
Use Cal, Acad, or Summer to Enter Months Devoted to Project Enter Dollar Amounts Requested *(omit cents)* for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Dr. Strong	PD/PI	.12			357,000	3,570	526	4,096
TBN	Research Resident	8.95			59,900	44,692	12,290	56,982
TBN	Biostatistician	.25			73,000	1,533	383	1,916
TBN	Research Coordinator	.24			33.023	661	59	720
SUBTOTALS →						50,455	13,259	63,714

CONSULTANT COSTS	
EQUIPMENT *(Itemize)* **-80 Freezer**	7,500
SUPPLIES *(Itemize by category)* **Specimen Collection Kits- $25/ ea., 50 patients enrolling = $25 X 50**	1,250
TRAVEL **Travel for the PI to attend a national meeting to present study findings**	1,500
INPATIENT CARE COSTS	
OUTPATIENT CARE COSTS	
ALTERATIONS AND RENOVATIONS *(Itemize by category)*	
OTHER EXPENSES *(Itemize by category)*	
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*	$ 74,264
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	40,103
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD	$ 114,367

PHS 398 (Rev. 03/16 Approved Through 10/31/2018)
OMB No. 0925-0001 Page

The planning of a clinical trial budget

- ✓ **Estimate costs of clinical procedures, imaging, lab analyses, storage, refrigeration, transport, shipping etc. (standard clinical charges versus discounted 'research' rates)**
- ✓ **Indirect costs: usually around of 25–30%, these must be negotiated for each individual site with the financial supporter of your study**
  - ✓ **The indirects pays electricity, house keeping, heat, water, sewer etc**
  - ✓ **NIH pays from 40% to 51%**
- ✓ **Institution start op fees**
  - ✓ **Dependent on funding source industry / government / IIT**

ITT = Investigator initiated trial

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Sources of funding

How do I assess the appropriate range of costs for a particular service?

1. **<u>Institutions:</u> finance departments usually provide detailed costing for all internal services necessary to perform the study. This includes procedures, lab tests, hospital stays, medication, etc. Also, larger institutions / university hospitals may have clinical research offices that support the planning and execution of studies.**

2. **<u>Governmental benchmarks:</u> when assessing personnel cost for particular staff like post-doctoral students, junior researchers, residents, medical-technical staff, etc., use benchmarks provided by governmental agencies or national granting institutions. They usually publish a guide for personnel costs for FTE (full-time equivalents) per annum.**

Project Title:	
PI:	Robert Martindale
Project Dates:	
Agency:	Nature Research Awards
Submission Date:	November 30, 2018

Joie Eckert:
We reduced from 20% to 5% which is about 2.17 hours per week or 104 hours annually.

Personnel Name	Title	Months	Fringe Rate	Effort Yr 1	YEAR 1	Grand Totals
Martindale	PI	0.12	22%	1%	$ 5,596	$ 5,596
Kyla Siemens	Coordinator	0.60	40%	5%	$ 2,964	$ 2,964
Subtotal Personnel					**$ 8,561**	**$ 8,561**
Non-Personnel						
Materials & Supplies	**cost**	**# subjects**		**# days/ units**		
Probiotics	$5.00	40		4	$ 800	$ 800
Collection kits	$25.00	40		5	$ 5,000	$ 5,000
Shipping fees	$50.00			2	$ 100	$ 100
Subtotal Non-Personnel					**$ 5,900**	**$ 5,900**
University of Oregon						
Subcontract Direct Costs*					$ 80,000	$ 80,000
Subtotal Direct Costs					**$ 94,461**	**$ 94,461**
Subcontract Indirect Costs*			used as multiplier for sub		$ 8,000	$ 8,000
Total Subcontract					$ 88,000	$ 88,000
TOTAL DIRECT COSTS					$ 102,461	$ 102,461
Modified total direct costs (*excludes Tuition, Fees, Equipment & Subcontrac					$ 102,461	$ 102,461
Indirect Costs	rate			10%	$ 10,246	$ 10,246
TOTAL					**$ 112,707**	**$ 112,707**

Schedule of visits drives the per patient budget

Study Visits	Screening	Enrollment and Randomization	Baseline Visit	Visit 2	Visit 3	Final Visit
Informed Consent	X					
Medical History	X					
Physical Exam	X					
NIHSSS		X		X	X	X
Vital Signs		X		X	X	X
Laboratory assessment -Serum Chemistry /hematology	X					X
Study drug or device Administration			X			
Adverse events			X	X	X	X

The planning of a clinical trial budget

- ✓ **Fees for space – how many rooms do I need to use and for how long? Space for archiving and storage of documents**
- ✓ **Site 'start-up' expenses including training and IRB preparation**
- ✓ **Pharmacy fees**
- ✓ **Phlebotomy fees, supplies, sample prep, imaging**
  - ✓ **SOC is key here; SOC vs study requirements**
- ✓ **Local publicity/advertising/posters**
- ✓ **Participant transportation and parking**
- ✓ **Potential unscheduled visits for SAE**
- ✓ **Data safety monitoring (DSMB)**
  - ✓ **External vs internal – IRB has requirements**

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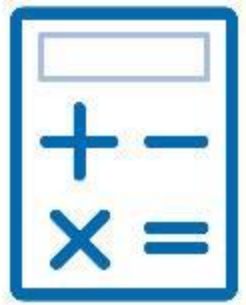
The planning of a clinical trial budget: commonly overlooked expenses



- ✓ **Site inspection**
- ✓ **Regular status updates/reports for the funding agency (private or public)**
- ✓ **Travel coordination for various meetings (DSMB, site visits, inspections, training, etc.)**
- ✓ **Administrative costs for maintaining current IRB certification/regulatory authority approval**
- ✓ **Patient insurance**
  - ✓ **Who pays for complications of study ?**

What to avoid when planning a clinical trial budget

Governmental agencies frown upon

- **Enrollment incentives**
- **Finders or referral fees**
- **Paperwork work completion fees**

Summary – preparing a budget:

- **Start early**
- **Talk to knowledgeable and experienced PI and coordinators**
- **Be as sure as possible on numbers needed**
- **Add technology only when needed ($)**
- **Overestimates are better than underestimates on budget**
- **Most successfully funded studies have these things in common:**
  - **answer a clinically relevant question**
  - **straightforward, simple design**
  - **clear budget**
- **Keep deadlines in mind throughout budget process**
- **Caution of being overly optimistic on recruitment timelines**

References and literature

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Chinese Ministry of Science and Technology http://www.most.gov.cn/eng/

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A Comprehensive and Practical Guide to Clinical Trials; 1st Edition; Editors: Delva Shamley Brenda Wright eBook ISBN: 9780128047309; Published Date: 11th June 2017

Department of Health and Human Services; Office of Human Research Protection. Available from http://www.hhs.gov/ohrp/about-ohrp/index.html#

Part II: On the finishing line - Publishing a clinical trial

Skills and resources

Prof. Mette Berger

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JUMPstart Training Program

A teamwork approach: skills and resources

Prof. Hon. Mette Berger, M.D., Ph.D

Basic Module: Publishing a clinical trial; Day 2, Part II: On the finishing line

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Agenda

This segment of the training program will cover:

- Necessary skills in a clinical trial team
- Resources required for successful studies
- Training as the key to success

Skills, resources and necessary training in a multidisciplinary research team

All team members of the clinical trial team need to:

- *Be experienced in each important aspect of planning, running and reporting of a trial.*
- *Be aware about their specific pre-defined roles.*
- *Training is the key to sharing knowledge and a standardized work flow.*
- *It takes many resources and players to execute a successful clinical trial.*

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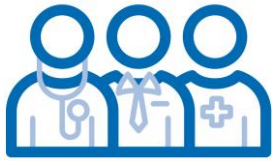
Skills - clinical research team



All trials involving humans, personal data or information, or biological samples must comply with adequate **ethical, clinical and methodological standards**.

The rights, safety, and well-being of research participants need to be protected.

This is increasingly important in the context of "globalization of clinical trials," where medical research is carried out by commercial and non-commercial actors in a variety of settings in high-, middle-, and low-income countries, with increasingly complex challenges arising particularly in international collaborative research.

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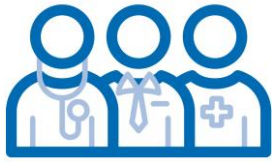
Skills - clinical research team



Clinical research teams can rely on guidance and expertise from domains beyond medical and scientific skills (international guidelines, etc).

But this is insufficient.

Study teams need to be well trained in GCP guidelines and this training needs to be recurrent and documented.

Clinical study staff must be able to adequately and timely deal with contracts, administrative issues, efficient planning and project management, training and strive to work well in cross-functional teams.

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Skills - clinical research team

What skills do I need to be part of a clinical trial team?

Essential skills for clinical research	
Full understanding of GCP	Basic understanding of clinical study phases
Documentation requirements for trials	Interaction with IRB, EC and regulators
Specialized knowledge of your area of responsibility (medicine, coordination, statistics, etc.)	Overall understanding of what and who it takes to perform a clinical study successfully
Understanding that clinical trials are complex and interconnected projects led by cross-functional teams	Everything you aims at generating high quality data enabling appropriate and scientifically sound reporting

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Sponsor-investigator - PI:

In an IIT, it is the sponsor-investigator (or PI) who takes the ultimate responsibility for the trial.

He/she is responsible for a continual risk/benefit assessment and, furthermore, is the one who is able to stop or interrupt the trial if he/she cannot longer take the responsibility for continuation due to e.g. safety reasons.

The sponsor-investigator is responsible for a protocol-compliant trial and might decide to terminate or interrupt the trial due to specific concerns.

Sponsor-investigator of the clinical research team

The sponsor-investigator is also responsible for the:

- IMP
- Indication
- Study management
- Handling of information/data
- Compliance with the study protocol
- Randomization method
- Handling of SAEs and SUSARs
- Communication with ECs, IRBs and regulatory authorities
- Medical care of the participants before, during and after the trial

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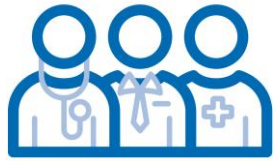
Skills - clinical research team



The main actors of a clinical trial need to be experienced in their field to execute the trial well and train new or inexperienced staff in their roles.

In addition, cross-functional training should be established to allow for an understanding of my colleagues' roles:

- physicians need to understand principles of data quality and documentation requirements
- Biometricians benefit from understanding how data was generated in the trial by the clinical team
- Study coordinators excel when they understand the intricacies of each aspect of the trial to anticipate delays and obstacles

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Resources of the clinical research team

A research team includes many players:

Study nurses, laboratory staff, pharmacy staff, study coordinators, physicians (co- and sub-investigators), archivist, Institutional Review Board (IRB) personnel, attorneys, biometricians, and many more.

In addition to personnel, there a several resources that are crucial to the successful running of a clinical trial:

Trial site infrastructure in general, the pharmacy, the labs, the technical standards and equipment maintenance, the IRB processes, the cooperation between medical and surgical departments, the business office including legal affairs and accounting.

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Resources of the clinical research team

Basic resources ensure the fitness of a trial site for clinical studies and include:

- enough staff to tend to study participants
- plenty of room to perform trial related activities
- short distances
- controlled logistics to labs and analytical service providers to ensure appropriate handling of laboratory or tissue specimen
- effective communication channels with all relevant decision makers
- up-to-date and well-maintained equipment
- access to emergency crash carts during active clinical trials
- permanent availability of on-call staff to ensure around the clock patient care when needed

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The key to a well-balanced clinical trial team is ***continuous training***

and ***effective***

and ***concise communication****.*

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Training of the clinical research team

Training is a permanent issue before, during and after a trial.

There are internal and external trainings. Internal training consists of staff orientation, GCP training, SOP training, occupational safety training, first-aid/life-support and IRB/Ethics Committee (EC) process training.

External training includes the investigator meeting, the site initiation visit and meeting, protocol-specific training, specific GCP training, and all on-line training.

The Principal Investigator (PI, or sponsor-investigator) is responsible for adequate protocol training of all staff. Tasks may delegated to adequately trained, qualified staff, but responsibility may not be delegated.

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The training of the clinical research team

Internal Training

Orientation: all new clinical staff should have an orientation. This will familiarize staff with the team, site, processes and policies, confidentiality, HR, access control, etc.

The orientation program should be documented and signed by all new staff upon completion.

Safety: usually you will find many aspects of safety covered in SOPs or in the quality policies/procedures.

Part of safety training would be the handling of human tissues and specimen, basic/advanced life support training, etc.

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Training of the clinical research team

Standard operating procedures (SOPs): trial sites usually have generic hospital-issued SOPs regarding procedures and processes that will cover most trials.

In investigator-initiated trials, SOPs are usually protocol specific. Some sites use manuals of operations (MOOs).

If you have external support for a study, policies and SOPs may be provided to aid in executing the study.

SOP training must be completed prior to the start of the clinical trial and signed by all members of the study team.

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Training of the clinical research team

External Training

1. Start-Up (investigator meeting)

a. In company sponsored trials, this meeting is organized and presented by the sponsor.

b. In IITs, this meeting will be the PI's responsibility and it is often combined with the initiation meeting.

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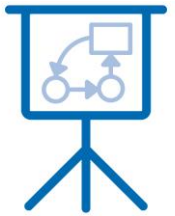
Training of the clinical research team



c. Investigator initiation meetings should be arranged after regulatory and IRB approvals are available.

d. During this meeting, the study protocol will be discussed in detail.

e. The entire study team participating in the clinical trial should be available to partake in the training.

   If not all members of the trial team are available, representatives from the relevant departments may be sent.

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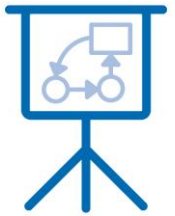
Training of the clinical research team



f. This is the best opportunity for the PI, the study coordinator, the study nurses, the data manager, the biometrician and all other relevant study team members to identify possible challenges regarding the protocol and conduct of the trial.

   It also provides the best platform to ask questions and address any uncertainties regarding the protocol, study procedures, laboratory procedures, statistical analysis, data capturing, etc.

f. Ensure that you are familiar with the content of the protocol prior to the meeting.

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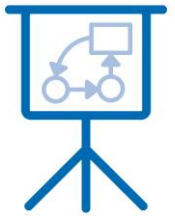
Training of the clinical research team



h. The main metrics of the trial are discussed: timelines, visit schedules, recruitment strategies and screening, etc.

i. A document will be issued certifying attendance and understanding of all relevant information pertaining to the trial.

j. A print-out of the presentation slides will be provided to the team.

The certificate of attendance is then filed along with all other training records in the study site file.

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The sponsor-investigator of the clinical research team

The sponsor-investigator keeps everyone up-to-date. This communication is most effective when it is concise, clear and documented.

The sponsor-investigator authenticates with a signature that he/she takes note of any new documents.

If new staff join the study team or existing staff leave, the IRB/EC must immediately be notified, the delegation and study staff log updated, and the CVs added to the investigator site file or trial master file.

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Session summary

- ✓ Coverage of most important clinical trial skills
- ✓ Discussion of relevant resources needed
- ✓ Illustration of the central training needs

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Conclusion

Clinical research has become professional

- Too many trials have been conducted in vain due to poor design
- Ethical issues have marred some studies
- Research training is specific

Clinical research is a teamwork

Humility and Honesty belong to the training package

M.M. Berger January 2021

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Publication strategies

Prof. Olav Rooyackers

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JUMPstart Training Program

Out in the open: publication strategies

Prof. Olav Rooyackers, Ph.D

Basic Module: Running a clinical trial; Day 2, Part II: On the finishing line – publishing a clinical trial

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Agenda

This segment of the training program will cover:

- Publication strategies
- Journal selection

Publication strategies

- Starts with the protocol
- Ethical requirement to share the results
- Data that forms the basis for the analyses may be requested along with the manuscript

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Publication strategies

There are several **guidelines** available that recommend the appropriate steps to ethical reporting and publication:

1. International Society for Medical Publication Professionals (ISMPP) https://www.ismpp.org/
2. Good Publication Practice (GPP)
3. International Committee of Medical Journal Editors http://www.icmje.org/icmje-recommendations.pdf
4. The CONSORT statement

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Publication strategies

The new **GPP3** guide covers the following topics and provides updates to already existing items of significance:

Integrity	**Accountability**	**Transparency**
Completeness	**Responsibility**	**Data sharing**

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Publication strategies

What do the GPP3 recommendations cover?

1. The design and results of all clinical trials should be reported in a **complete, accurate, balanced, transparent, and timely** manner.

2. Reporting and publication processes should **follow applicable laws** (e.g. FDA Amendments Act of 2007, EU law) and **guidelines** (e.g. ICMJE recommendations).

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Publication strategies

3. **Journal and congress requirements** should be followed, especially ethical guidelines on originality and avoiding redundancy (duplicate publication).

4. Publication planning and development should be a **collaboration among all persons involved** (clinicians, statisticians, researchers, and publication professionals, including medical writers) and reflect the collaborative nature of research and the range of skills required to conduct, analyze, interpret, and report research findings.

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Publication strategies

5. The **rights, roles, requirements, and responsibilities of all contributors** (authors and nonauthors) should be confirmed in writing, ideally at the start of the research and, in all cases, before publication preparation begins.

6. All authors should have **access to relevant aggregated study data** and other information (for example, the study protocol) required to understand and report research findings.

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Publication strategies

7. The **authors** should take responsibility for the way in which research findings are **presented and published**, be fully involved at **all stages** of publication, and be willing to take **public responsibility for all aspects** of the work.

8. Author lists and contributorship statements should **accurately reflect all substantial intellectual contributions** to the research, data analyses, and publication or presentation development. Relevant contributions from persons who did not qualify as authors should also be disclosed.

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Publication strategies

9. The **role of the sponsor or supporter** in the design, execution, analysis, reporting, and funding (if applicable) of the research should be fully disclosed in all publications and presentations of the findings.

10. Any involvement by **persons or organizations with an interest (financial or nonfinancial**) in the findings should also be disclosed. All authors and contributors should disclose any relationships or potential competing interests relating to the research and its publication or presentation.

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Publication strategies

EQUATOR Network reporting guidelines for main study types

Type of study	Guideline	Additional
Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	
Economic evaluations	CHEERS	

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Publication strategies

What defines an author (according to ICMJE)?

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; **AND**

2. Drafting the work or revising it critically for important intellectual content; **AND**

3. Final approval of the version to be published; **AND**

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The contributors to the manuscript that do not fulfill all 4 criteria shall be acknowledged.

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Remember:

Register your clinical trial!

Choose a **primary register** of the WHO International Clinical Trials Registry Platform (ICTRP)

(www.who.int/ictrp/network/primary/en/index.html or www.ClinicalTrials.gov to register your trial)

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Trial registries

Registering your trial is a requirement before the first patient may be recruited into your study, according to the Declaration of Helsinki – here is a useful link for primary registries under the WHO umbrella:

http://www.who.int/ictrp/network/primary/en/

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Journal selection

How do I find my target journal?

1. Selecting the journal by **type of publication**
    a. Original work, review, case report, etc.
    b. Area of science (internal medicine, surgery, hybrid ([e.g. vascular medicine/interventional radiology etc.])
2. Selecting the journal based on **impact factor or position**
    a. highest impact factor OR other factors
    b. “TOP” journals

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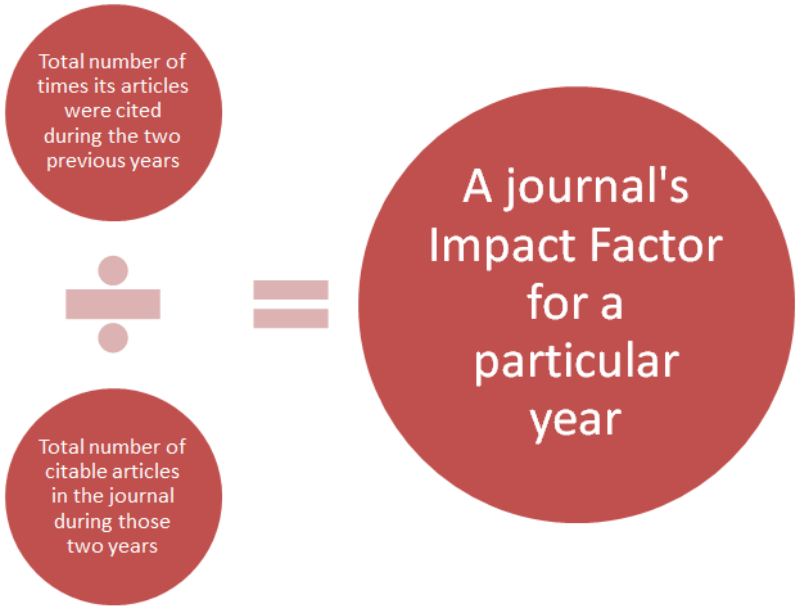
Journal selection

The **impact factor (IF)** of a journal is a measure describing metrically the yearly average number of citations in comparison to recent articles published in that journal:



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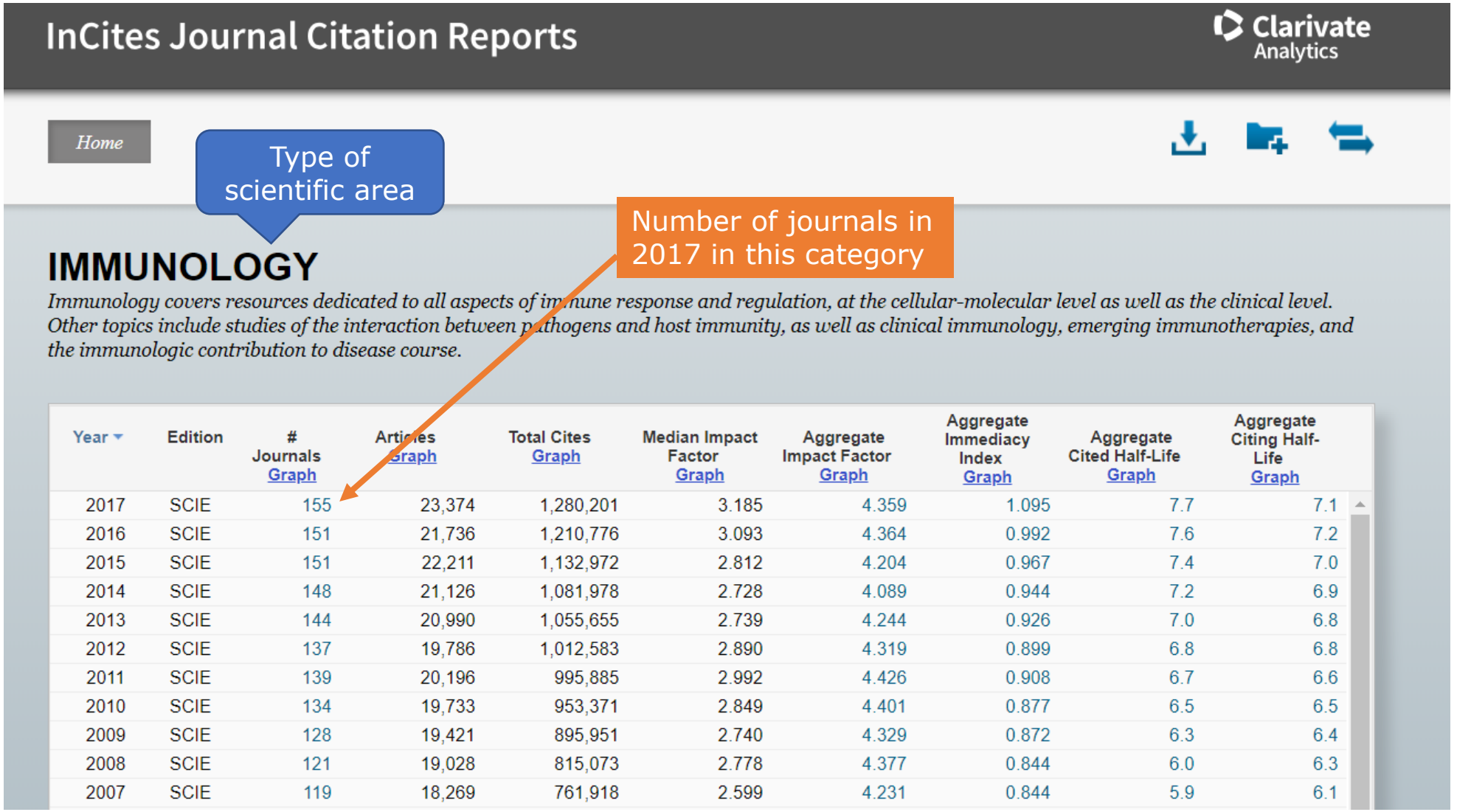

Year	Edition	# Journals Graph	Articles Graph	Total Cites Graph	Median Impact Factor Graph	Aggregate Impact Factor Graph	Aggregate Immediacy Index Graph	Aggregate Cited Half-Life Graph	Aggregate Citing Half-Life Graph
2017	SCIE	155	23,374	1,280,201	3.185	4.359	1.095	7.7	7.1
2016	SCIE	151	21,736	1,210,776	3.093	4.364	0.992	7.6	7.2
2015	SCIE	151	22,211	1,132,972	2.812	4.204	0.967	7.4	7.0
2014	SCIE	148	21,126	1,081,978	2.728	4.089	0.944	7.2	6.9
2013	SCIE	144	20,990	1,055,655	2.739	4.244	0.926	7.0	6.8
2012	SCIE	137	19,786	1,012,583	2.890	4.319	0.899	6.8	6.8
2011	SCIE	139	20,196	995,885	2.992	4.426	0.908	6.7	6.6
2010	SCIE	134	19,733	953,371	2.849	4.401	0.877	6.5	6.5
2009	SCIE	128	19,421	895,951	2.740	4.329	0.872	6.3	6.4
2008	SCIE	121	19,028	815,073	2.778	4.377	0.844	6.0	6.3
2007	SCIE	119	18,269	761,918	2.599	4.231	0.844	5.9	6.1

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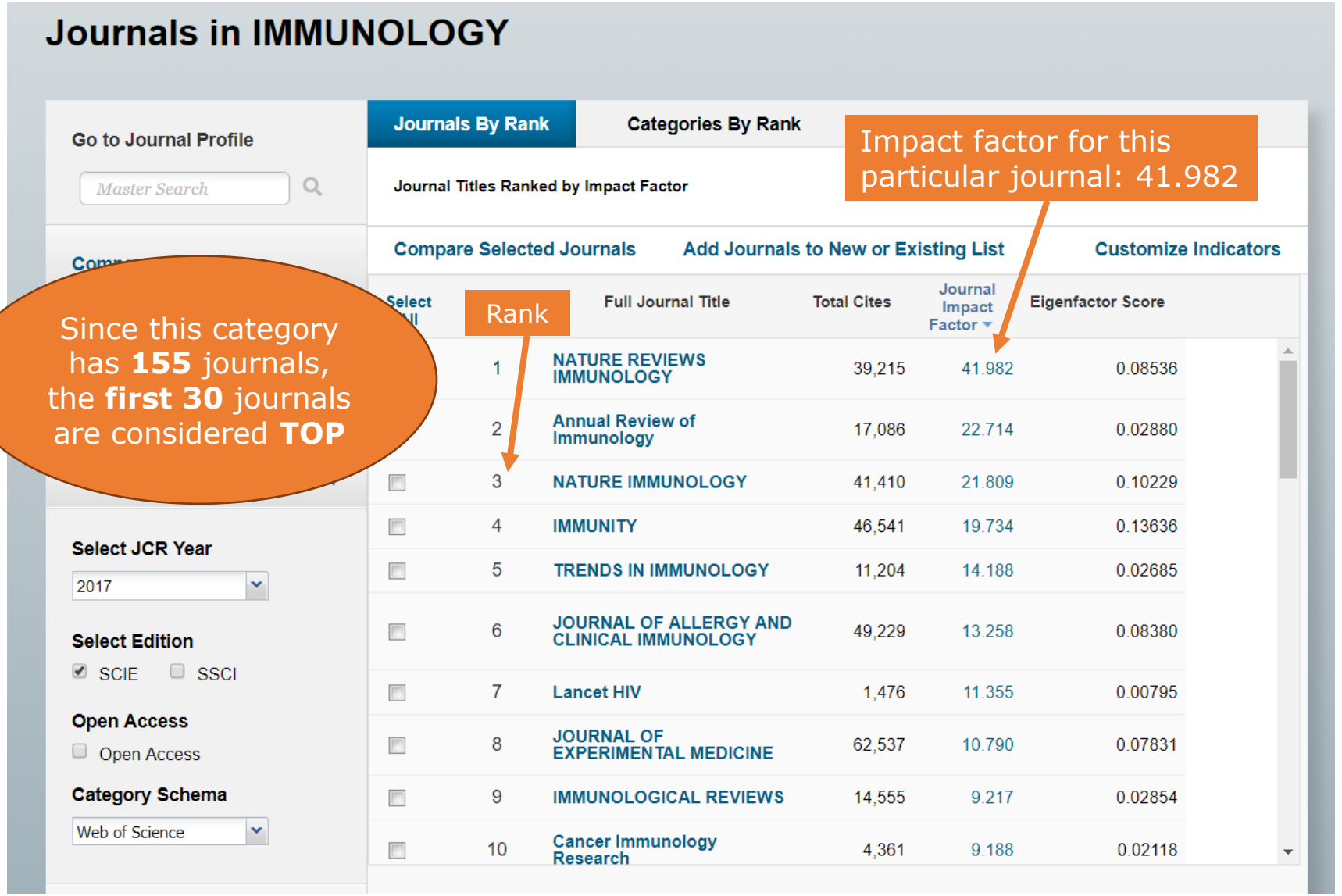

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Session summary

- ✓ Publication strategies
  - ✓ Use a publication plan, especially in large consorts
  - ✓ Register your study
- ✓ Journal selection

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Publication strategies

Your **publication plan** should:

- ✓ ensure timely presentation of data
- ✓ ensure that both positive and negative results are published
- ✓ ensure that novel methods are published before clinical data
- ✓ identify scientific and clinical needs for subsequent publications (subgroup analyses, pooled data analyses, or systematic reviews)
- ✓ avoid duplicate publication
- ✓ establish the publication team
- ✓ define authors and non-authoring contributors

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