Clinical Trials Handbook

Design and conduct forms, worksheets, and checklists

Curtis L Meinert

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Acknowledgements

Thanks to Betty Collison, Jill Meinert, and Lea Drye for reading copy and providing helpful comments. But primary thanks is to the groups I have worked with over the years designing and conducting clinical trials. Do enough trials and you come to realize the issues in the organization and operation are the same even though the questions are different. Without doubt, the early experiences in the University Group Diabetes Program[14] and the Coronary Drug Project[4] were formative. But, also important was the classroom teaching of budding trialists and trying to impress upon them with the reality that trials will not succeed without organization and structure to ensure methods and procedures are followed.

Preface

To be sure, every trial is different, but just as surely they are all the same. Specifics differ, but the basics of design, organization, and operation are the same – the same whether the trial is single center or multicenter, the same regardless of how funded, the same regardless of where done, and the same regardless of who is studied.

This reality is the basis for this handbook. The collection of tables, worksheets, and checklists is intended for use by designers and conductors of clinical trials. The focus is on randomized trials having parallel treatment designs with persons as the observation unit, but many of the issues in design and conduct are the same for other designs as well.

In a linear world, there would be a prescribed order for the use of forms, worksheets, and checklists in this handbook, but the world of trials is not linear. The activities in designing, organizing, and operating a trial are, at best, only crudely linear. Obviously, there is some ordering in that there is no starting without a design, without money, or without some modicum of organization to initiate operations, but that is about it for order. Even the activities of design and funding are not ordered in that the main activities of design can come before or after funding depending on how the trial is initiated and funded.

The best that can be done is to rely on a crude ordering of activities in that basic design, organizational, and operational issues have to be resolved upstream of other activities. For example, regardless of whether basic design precedes or comes after funding, there is no starting until there is an established treatment protocol and specification of the outcome of interest, and there is no enrollment until IRB approval.

Design is an ongoing process over the course of a trial. Hence, forms in this package related to design, even if completed early in the course of the trial, merit review and updating over the course of the trial. There are aspects of design, even if "set" early on, that need to be reviewed and modified as the trial proceeds.

Likewise, issues of organization are omnipresent from start to finish. The issues change but never cease to exist. Hence, design forms relating to organization need updating over the course of the trial.

Trials, whether single center or multicenter, national or multinational, are corporate activities and hence there has to be "buy-in" by investigators as to design, organization, and operating procedures. Hence, completed forms, regardless of who completes them, require leadership review and buy-in if they are to be of value in conducting the trial. Key specifications reflected in forms should be signed-off by study leaders and periodically reviewed by them over the course of the trial.

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Explanatory notes and conventions

This handbook is a companion to one entitled *Clinical Trials Handbook: Design and conduct* published by Wiley (summer 2012).

The language conventions herein are similar to those in *Clinical Trials Dictionary: Terminology and usage recommendations*[10]. Definitions are from that dictionary and a 2nd edition published by Wiley (summer 2012).

The default language is that of **clinical trials**. The designation for a person enrolled in a trial is **patient**. Medically neutral terms, such as person, human being, or individual are used when the connotation of illness is inappropriate.

The term "treatment" is used throughout to refer to the experimental variable of trials. The different treatments represented in a trial are referred to as **study treatments**. The treatments may be **test treatments** or **control treatments**. The group of persons assigned to receive a particular study treatment is referred to as a **treatment group**.

Forms, worksheets, and checklists are arranged by topic, as represented in the table of contents.

The date on the left below end lines of documents indicates the last revision date. The version number on that same line for forms, checklists, and worksheets is used to indicate the version of posted documents. The number to the right of the decimal point indicates minor changes to previous postings. The number to the left of the decimal point indicates major revisions.

Planning and execution aids

No one sets out to do a half-baked trial. That being so, how come we end up with so many half-baked trials? Lots of reasons, but a major one is lack of planning and inadequate organizational structure.

The hard part of planning is planning. The second hardest part is getting people to follow plans.

Largely, people are inclined to put off until tomorrow that which can be put off. We have a propensity to do that when it comes to planning. That propensity is reinforced by the fact that trials are deceptively simple. State a question, randomize a few patients, treat and follow them for outcomes of interest, analyze the results, write them up, publish them, and move on.

If only it were that easy. The reality is that planning is time consuming and easily put off in favor of the more immediate.

Planning, even if exquisite, is useless if no one pays attention to the plan. For example, it does no good to devise policy on paper writing and authorship if nobody pays attention to the policy. Planning is useless unless there is buy-in by investigators on plans and policy.

The forms, checklist, and worksheets herein are offered as aids in planning and monitoring activities in trials. The majority of them are intended for completion early in the course of planning before the start of enrollment. But even if completed early, many of them should be reviewed and updated as the trial proceeds to the extent that the conditions and requirements change as the trial proceeds.

Abbreviations and designations

A

ADAPT	Alzheimer's Disease Anti-inflammatory Prevention Trial[1]
ADE	adverse drug experience
ADR	adverse drug reaction
AE	adverse event
ARC	advisory-review committee
ARTEMC	advisory-review and treatment effects monitoring committee

B

Bl	baseline
BlV	baseline visit

C

CC	coordinating center
CDP	Coronary Drug Project[4]
Cl	clinic
CL	central laboratory
CO	chair's office
CONSORT	Consolidated Standards of Reporting Trials[2]
CPIB	ethyl alpha parachlorophenoxy-isobutyrate
CRF	case report form
CRO	contract research organization
CV	curriculum vitae; cardiovascular
CV	clinic visit

D

DNA	deoxyribonucleic acid
DMC	data monitoring committee
DSMB	data safety monitoring board
DSMC	data and safety monitoring committee
DT4	dextrothyroxine

E

EC	executive committee
ECG	electrocardiogram
EDC	electronic data capture
ESG	estrogen

F

FDA	Food and Drug Administration
fr	from
FTE	full-time equivalent
Fu, FU	followup
FuV	followup visit

G

GLT	Glaucoma Laser Trial[7]

H

HIPAA	Health Insurance Portability and Accountability Act
HPT	Hypertension Prevention Trial[8]

I

ID, Id	identification
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	institutional review board
ITT	intention-to-treat

L

LV	letter visit

M

MPS	Macular Photocoagulation Studies[9]
MRFIT	Multiple Risk Factor Intervention Trial[11]

N

NETT	National Emphysema Treatment Trial[13]
NICA	nicotinic acid
NIH	National Institutes of Health
NLM	National Library of Medicine

O

OMB	Office of Management and Budget
ORI	Office of Research Integrity

P

PAA	per assignment analysis
PC	personal computer
PI	principal investigator
PO	project office; project officer
PPA	per protocol analysis
PPM	policy and procedure memoranda

Q

QA	quality assurance
QC	quality control

R

RC	reading center
RFA	request for application
RFP	request for proposal
rt	related term

S

SC	steering committee
Scr	screening
ScrV	screening visit
SO	study officer; study officers
syn	synonym

T

TV	telephone visit
TEM	treatment effects monitoring
TEMC	treatment effects monitoring committee
trt, Trt	treatment
TrtV	treatment visit

U

UGDP	University Group Diabetes Program[14]