Clinical Trials Handbook

Design and conduct forms, worksheets, and checklists

Curtis L Meinert

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Contents

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]

Clinical Trials Handbook

Design and conduct forms, worksheets, and checklists

1 Funding tables, worksheets, and checklists

Table 1.1 Questions when deciding whether to respond to an RFA or RFP (QuesRFP.Tab)

When: When considering whether to respond to an RFA or RFP after issue

Who: The person responding

Purpose: To understand what is involved in doing what is proposed and in helping to decide whether one should respond

Answer questions "yes" or "no" by checking ($_{y}$) or ($_{n}$). Any "no" answer should be pause for concern. Three or more "nos" should be sufficient for you to stand down from replying.

Definitions

request for application (RFA) - A document prepared and distributed by a sponsoring agency to solicit applications pertaining to an area of work detailed in the request; especially such a document prepared and distributed by an agency of the federal government and in which said work is to be supported by grants. rt: request for proposal ***Usage note***: From the NIH perspective, both RFAs and RFPs are used as vehicles for identifying and selecting investigators and centers in trials. As a general rule, investigators have more control over the activity proposed under the NIH RFA mode of initiation and grant support than under the NIH RFP mode of initiation and contract support. The emphasis in an RFA is on a scientific question or issue. The focus in an RFP is on a defined task and on deliverables related to that task.

request for proposal (RFP) - A document prepared and distributed by a sponsoring agency to solicit proposals for execution of a specified task, especially such a document prepared and distributed by an agency of the federal government and in which said work is to be supported by contracts. rt: request for application ***Usage note***: Not to be confused with request for application.

A. Identifying information

1. RFA/RFP name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—___—____

B. General questions

Career goals

- Is the role proposed compatible with your goals and interests? . . . . . ($_{y}$) ($_{n}$)
- Do you have sufficient time for the work? . . . . . ($_{y}$) ($_{n}$)
- Do you enjoy multicenter collaboration? . . . . . ($_{y}$) ($_{n}$)
- Will there be opportunities for writing and authoring papers in the project? . . . . . ($_{y}$) ($_{n}$)
- Do you function well in committee settings and are you willing to accept the dictates of committees and sponsors in the execution of the study? . . . . . ($_{y}$) ($_{n}$)

Table 1.1 Questions when deciding whether to respond to an RFA or RFP

Environment

- Are stipulations in the RFA or RFP compatible with policies of your institution? . . (y) (n)
- Are personnel recruitment practices, pay scales, and promotion criteria of your institution compatible with those needed for the work proposed? . . . . . (y) (n)
- Is the business office of your institution capable of administering the funding if awarded?
- Is the work compatible with the goals of your department? . . . . . (y) (n)
- Are colleagues in your institution likely to view your activities in the work in a favorable light?
- Will you be able to obtain the necessary signatures from administrative personnel in your institution to submit a response? . . . . . (y) (n)
- Will you have the active support of your chief if you are funded? . . . . . (y) (n)
- Will there be adequate space and facilities to do the work if you are funded? . . . . . (y) (n)
- Do you believe you will be able to acquire the people needed for the project? . . . . (y) (n)

C. Specific questions concerning the RFA or RFP

- Is the problem posed worthy of investigation? . . . . . (y) (n)
- Are you willing to be a party to randomizing persons to the treatments proposed for study?
- Is there sufficient time to prepare an adequate response? . . . . . (y) (n)
- Is the project likely to achieve its stated aims? . . . . . (y) (n)
- Does the project have a realistic timetable and, if not, do you believe the sponsor is willing to modify it? . . . . . (y) (n)
- Does the sponsoring agency desire scientific input in the way the work is designed and carried out? . . . . . (y) (n)
- Will there be adequate time for development of the study protocol and data forms before the study is launched? . . . . . (y) (n)
- Are staffing guidelines realistic? . . . . . (y) (n)
- Are funding levels realistic? . . . . . (y) (n)
- Are the duties of the project officer compatible with your role in the trial? . . . . . (y) (n)
- Is the reporting schedule for progress summaries during the trial reasonable? . . . . . (y) (n)
- Are the policy and procedures proposed for treatment effects monitoring and data sharing acceptable? . . . . . (y) (n)
- Will investigators have autonomy in paper writing and publication? . . . . . (y) (n)

Table 1.2 Proposed budget by center (BudSum.Tab)

When: As a prelude to submission of an investigator-initiated multicenter proposal

Who: The study chair or director of the coordinating center

Purpose: To summarize funding requested by type of center and essential functions and to provide summary tables for inclusion in the funding request

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

4. Dollar cost by center (direct costs)

		Yr 1	Yr 2	Yr 3	Yr 4	Yr 5	Total
4.a.	Clinics						
4.b.	Coord center						
4.c.	Other centers						
4.d.	**Total direct**						

5. Fractional costs of total direct cost by center

5.a.	Clinics Item 4.a ÷ 4.d						
5.b.	Coord center Item 4.b ÷ 4.d						
5.c.	Other centers Item 4.c ÷ 4.d						
5.d.	**Total**	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**

6. Total personnel costs (direct costs: salaries + fringe benefits)

6.a.	Clinics						
6.b.	Coord center						
6.c.	Other centers						
6.d.	**Total**						

Table 1.2 Budget summary tables

	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5	Total
7. Fraction of budget devoted to personnel costs						
7.a. Clinics Items 6.a ÷ 4.a						
7.b. Coord center Items 6.b ÷ 4.b						
7.c. Other centers Items 6.c ÷ 4.c						

Table 1.3 Budget analysis (BudAnal.Tab)

When: As a prelude to submission of an investigator-initiated multicenter proposal

Who: The study chair or director of the coordinating center

Purpose: To assess the adequacy of allocation of funding

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—_____

B. Budget analysis

4. Years of support requested as represented in Table 1.2 . . . . . _____

5. Funds requested (direct costs only)
   - 5.a. Clinics (fr Table 1.2, item 4.a) . . . . . _____
   - 5.b. Coordinating center (fr Table 1.2, item 4.b) . . . . . _____
   - 5.c. Other centers (fr Table 1.2, item 4.c) . . . . . _____
   - 5.d. **Total** (fr Table 1.2, item 5.d) . . . . . _____

6. Projected sample size (fr WS 1.1, item 5) . . . . . _____

7. Cost per person enrolled
   - 7.a. Clinic (item 5.a ÷ item 6) . . . . . _____
   - 7.b. Coordinating center (item 5.b ÷ item 6) . . . . . _____
   - 7.c. Other centers (item 5.c ÷ item 6) . . . . . _____
   - 7.d. **Total** (item 5.d ÷ item 6) . . . . . _____

8. Unit of followup time (check one)
   - ( ) Day
   - ( ) Week
   - ( ) Month
   - ( ) Year

Table 1.3 Budget analysis

( ) Other (specify)

_____

9. Projected person units of followup time (expected median length of followup per person enrolled x projected sample size) . . . . . _____

10. Cost per person unit of followup time

    10.a. Clinic (item 5.a ÷ item 9) . . . . . _____

    10.b. Coordinating center (item 5.b ÷ item 9) . . . . . _____

    10.c. Other centers (item 5.c ÷ item 9) . . . . . _____

    10.d. **Total** (item 5.d ÷ item 9) . . . . . _____

11. Expected number of data collection visits (fr item 13; WS 1.1)

    . . . . . _____

12. Cost per data collection visit

    12.a. Clinic (item 5.a ÷ item 11) . . . . . _____

    12.b. Coordinating center (item 5.b ÷ item 11) . . . . . _____

    12.c. Other centers (item 5.c ÷ item 11) . . . . . _____

    12.d. **Total** (item 5.d ÷ item 11) . . . . . _____

13. Personnel cost (fr item 6, Table 1.2)

    13.a. Clinic . . . . . _____

    13.b. Coordinating center . . . . . _____

    13.c. Other centers . . . . . _____

    13.d. **Total** . . . . . _____

14. Proportion of cost devoted to personnel

    14.a. Clinic (item 13.a ÷ item 5.a) . . . . . _____

    14.b. Coordinating center (item 13.b ÷ item 5.b) . . . . . _____

Table 1.3 Budget analysis

14.c. Other centers (item 13.c ÷ item 5.b) . . . . . _____

14.d. **Total** (item 13.d ÷ item 5.d) . . . . . _____

C. Budget assessment

15. Is the allocation of funding, as represented in Table 1.2, consistent with the effort required?
    ( ) Yes
    ( ) No; adjustments are necessary.

16. If clinics are to be paid by person enrolled or completed data collection visits per person, is the amount to be paid consistent with FTE requirements as detailed in Budget Checklist (CL 1.1)?
    ( ) Yes
    ( ) No; level of funding inadequate for effort required

17. Is percentage of funds devoted to data center activities less than 10%?
    ( ) Yes; level of funding likely inadequate
    ( ) No

WS 1.1 Budget worksheet (Budget.WS)

When: Preparing a funding initiative

Who: A senior investigator

Purpose: To provide a set of reminders for construction of budget in a funding request

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Specifications

4. Treatment groups

   Test-assigned groups . . . . . _____

   Control-assigned groups . . . . . _____

   Total number of treatment groups . . . . . _____

5. Sample size goals

   Number per test-assigned group . . . . . _____

   Number per control-assigned group . . . . . _____

   Total planned sample size . . . . . _____

6. Proposed timetable

   Start up . . . . . _____ Mos

   Enrollment and treatment . . . . . _____ Mos

   Treatment and followup . . . . . _____ Mos

   Close out of data collection . . . . . _____ Mos

   Wind up . . . . . _____ Mos

   Total anticipated time . . . . . _____ Mos

7. Close out design

   ( ) Anniversary (specify period of followup) . . . . . _____ Mos

   ( ) Common close date (specify range of followup)

   Min: _____ Mos Max: _____ Mos

8. Trial type (check all that apply)
   ( ) Treatment
   ( ) Prevention

   ( ) Phase I/II
   ( ) Phase III
   ( ) Phase IV

   ( ) Parallel treatment design
   ( ) Crossover design

C. Screening and enrollment

9. Primary method of recruitment
   ( ) Referral
   ( ) Screening
   ( ) Record review
   ( ) Mailings
   ( ) Other (specify)

   _____

10. Expected screening rate per person enrolled
    ( ) > 10 to 1
    ( ) 7 - 10 to 1
    ( ) 6 - 4 to 1
    ( ) 3 to 1
    ( ) < 3 to 1

D. Data collection schedule

11. Screening and baseline data collection visits

    Expected number of screenees per enrollee . . . . . _____

12. Treatment and followup data collection visits

    Expected number per person enrolled . . . . . _____

13. Total number of expected visits per person enrolled (sum of values in items 11 and 12)

. . . . . _____

14. Total number of expected data collection visits (item 5 x item 13) . . . . . _____

E. Number of study centers

Clinics . . . . . _____

Coordinating centers . . . . . _____

Other centers . . . . . _____

Total number of centers . . . . . _____

WS 1.2 Funding specification worksheet (FundMode.WS)

When: Early in the design phase of the trial and prior to the start of enrollment

Who: Study chair and director of the coordinating center, independent of one another to reveal areas of confusion or uncertainty

Purpose: For multicenter trials to make clear the mode of funding and mechanism of funding for the various centers in the trial

Definitions

direct funding - A mode of funding in which money flows to the point of use directly from a sponsor.

indirect funding - A mode of funding in which money flows to the point of use from an intermediary of a sponsor, e.g., with centers in a multicenter trial funded via another center in the trial as in consortium funding.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Funding sources and vehicles

4. Number of funding sources?

( ) One (specify)

_____

( ) Two or more (specify; list in descending order by amount)

_____

_____

_____

5. Primary funding vehicles for clinics and coordinating center

Clinics

( ) Grant
( ) Cooperative agreement
( ) Contract
( ) Fixed amount per person enrolled (specify amount) . . . . . $ _____

( ) Fixed amount per completed visit (specify amount) . . . . . $ _____

( ) Other _____

Coordinating center

( ) Grant
( ) Cooperative agreement
( ) Contract
( ) Other _____

C. Funding route

6. Route of money from funding agency to clinics

( ) Direct, i.e., direct from funding agency to individual clinics
( ) Indirect, i.e., via an intermediary to clinics (e.g., to the coordinating center from the funding agency and then from the coordinating center to clinics); indicate the intermediary

_____

( ) Mixed; some direct and other indirect (explain)

_____

_____

7. Route of money from funding agency to data center/coordinating center

( ) Direct
( ) Indirect (specify)

_____

8. Other study centers?

( ) No
( ) Yes

If yes, list and indicate whether direct or indirect funding by writing D or I in the space at the right

Center

_____ . . . . . ___

_____ . . . . . ___

_____ . . . . . ___

_____ . . . . . ___

9. Funding awards

Number direct from funding agency to centers . . . . . _____

Number indirect . . . . . _____

Total number . . . . . _____

D. Funding agreement and period of funding

10. Funding agreements

Clinics (check all that apply)

( ) Fixed cost
( ) Cost reimbursement
( ) Per person enrolled
( ) Per person with complete followup
( ) Other (specify)

_____

Coordinating center (check one)

( ) Fixed cost
( ) Cost reimbursement
( ) Other (specify)

_____

11. Period of funding

( ) ≤ 2 years
( ) 3 years
( ) 4 years
( ) 5 years
( ) > 5 years

CL 1.1 Budget checklist (Bud.CL)

When: Preparing a funding initiative

Who: A senior investigator

Purpose: To provide a set of reminders for construction of budget in a funding request

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __-___-____

B. Personnel

4. Full time equivalent personnel (check all that apply and indicate aggregate number of FTEs for 1st year of funding, middle year of funding, and end year of funding)

Note

Contrary to expectation personnel support remains relatively flat over the course of the trial including for the coordinating center. Duties may change but personnel support remains fairly constant.

	1st yr FTEs	Middle yr FTEs	End yr FTEs
( ) Center directors			
( ) Deputy directors			
( ) Study physicians			
( ) Clinic coordinators			
( ) Laboratory technicians			
( ) Biostatisticians			
( ) Programmers			
( ) Data coordinators			

	1st yr FTEs	Middle yr FTEs	End yr FTEs
( ) Data entry personnel	_____	_____	_____
( ) Research/administrative assistants	_____	_____	_____
( ) Other support personnel	_____	_____	_____
Total FTEs	_____	_____	_____

5. Estimated personnel cost

5.a. Median salary of study personnel . . . . . $ _____

5.b. Median fringe benefit cost as percentage of median salary . . . . . _____ %

5.c. Total median salary expense (item 5.a + (item 5.a x item 5.b)) . . . . . $ _____

5.d. Inflation factor relative to 1st yr

Middle yr . . . . . _____ %

End yr . . . . . _____ %

5.e . Total personnel cost

1st yr (item 5.c x 1st year total FTEs in item 4) . . . . . $ _____

Middle yr (item 5.c x middle year total FTEs x middle yr inflation factor) . $ _____

End yr (item 5.c x end year total FTEs x end yr inflation factor) . . . . . $ _____

6. Consultants (persons paid on a retainer or fee-for-service basis; typically not associated with any center in the trial)

( ) To provide expert advice in the diagnosis, classification, or treatment of patients in the trial . . . . . $ _____

( ) To perform a specialty function, such as reading ECGs, biopsy material, etc. $ _____

( ) To provide expert advice to a resource center in the trial, such as to the data coordinating center for data analysis . . . . . $ _____

( ) To serve as an expert advisor to the study leadership or sponsor of the trial $ _____

( ) To serve as voting members of the treatment effects monitoring committee . $ _____

7. Other personnel (list)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

C. Equipment (purchase or lease)

8. Study clinics

( ) General office equipment* . . . . . $ _____

( ) Furniture for examining and waiting rooms* . . . . . $ _____

( ) Dedicated equipment needed for data collection, e.g., fundus photography camera or spirometer; justification should indicate why existing equipment will not meet the needs of the study; requests for standard equipment, regarded as essential to any clinic setting not generally approved . . . . . $ _____

( ) Other (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

9. Data center/coordinating center

( ) General office equipment* . . . . . $ _____

( ) Computing equipment for receiving, processing, and analyzing data . . . . . $ _____

( ) Computing software packages for database management and analyses . . . . $ _____

( ) Mailing equipment . . . . . $ _____

( ) Machines for assembling and binding reports . . . . . $ _____

( ) Paper shredders . . . . . $ _____

( ) Other (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

D. Supplies

10. Clinics

( ) Office supplies (paper, pencils, notebooks, file folders, postage, photocopy supplies, telephone line charges, etc.) . . . . . $ _____

( ) Drugs, syringes, laboratory reagents and supplies, patient information brochures, postage for patient mailings, etc. . . . . $ _____

( ) Other (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

11. Data center/coordinating center

( ) Office supplies (paper, pencils, notebooks, file folders, postage, photocopy supplies, telephone line charges, etc.) . . . . . $ _____

( ) Computer supplies, printer supplies, electronic storage mediums, etc. . . . . $ _____

( ) Other (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

E. Travel

12. Clinic

( ) Local (Mileage charges for study related travel to a study site, for patient recruitment, for home visits, etc.) . . . . . $ _____

( ) Study related (Travel and living expenses for meetings of research group and study committees) . . . . . $ _____

( ) Other (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

13. Data center/coordinating center
    ( ) Local (Mileage charges for local travel) . . . . . $ _____

    ( ) Study related (Travel and living expenses for meetings of research group and study committees) . . . . . $ _____

    ( ) Travel and living expenses for study site visits . . . . . $ _____

    ( ) Other (specify)

    _____ . . . . . $ _____

    _____ . . . . . $ _____

    _____ . . . . . $ _____

14. Meetings of treatment effects monitoring committee
    ( ) Travel and living expenses for TEMC members . . . . . $ _____

    ( ) Travel of data center personnel to meetings of the TEMC . . . . . $ _____

15. Other travel
    ( ) National (Travel and living expenses incurred in conjunction with study meetings, site visits, and for study-related professional meetings) . . . . . $ _____

    ( ) International (Travel and living expenses for study and related activities and for selected professional meetings related to the needs and goals of the study) . . . . . $ _____

F. Patient care costs*

16. Pay for study-related procedures not covered by 3rd party payers . . . . . $ _____

17. Other expenses (specify)

    _____ . . . . . $ _____

    _____ . . . . . $ _____

    _____ . . . . . $ _____

G. Alterations and renovations*

( ) Renovations of a clinic area . . . . . $ _____

( ) Renovations to accommodate special items of equipment needed in the trial . $ _____

( ) Other expenses (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

H. Consortium/contractual costs

Funds to cover payments to individuals or groups outside the investigator's institution who have formal agreements to perform specified functions in the trial . . . . . $ _____

I. Other expenses

( ) Patient travel to and from clinic . . . . . $ _____

( ) Equipment maintenance charges . . . . . $ _____

( ) Telephone installation and monthly usage charges . . . . . $ _____

( ) Copying and reproduction charges . . . . . $ _____

( ) Data entry charges . . . . . $ _____

( ) Study insurance . . . . . $ _____

( ) Books and journals . . . . . $ _____

( ) Journal page and reprint charges . . . . . $ _____

( ) Charges for printing and distributing study forms, manuals, etc. . . . . $ _____

( ) Fee-for-service charges, such as for laboratory determinations, reading ECGs, etc., if not covered under a consultant or contractual agreement . . . . . $ _____

( ) Space rental . . . . . $ _____

( ) Moving charges . . . . . $ _____

( ) Indirect costs or associated contractual services included in item 8 . . . . . $ _____

( ) Purchase of study drug . . . . . $ _____

( ) Packaging and distribution of study drug . . . . . $ _____

( ) Other expenses (specify)

_____ . . . . . $ _____

_____ . . . . . $ _____

_____ . . . . . $ _____

* Generally not allowed

2 Design tables, worksheets and checklists

Table 2.1 Protocol content and suggested features (ProtDoc.Tab)

The study protocol is the foundation of the trial. It is the first document produced and is likely revised several times over the course of the trial. It drives all other documents and publications in the trial. It serves as the basis for IRB submissions and as the road map for the trial.

Outside cover
Title (e.g., Protocol for the XYZ Trial)
Version number
Version date

Inside cover
Title
Version number
Version date
Print date
Document custodian

Table of contents (with page nos.)

History page (cumulative summary of changes from all previous versions)

Body of document
Print font: 11 or 12 point
Page orientation: Portrait
Margins (1" left, right, top, and bottom)
Page numbering: Continuous; upper right hand corner

References

Appendices
Glossary
Consent form
Design summary
etc.

Sample table of contents for ADAPT[1] (version 1.4; 19 Nov 2002; http://jhuccs1.us/adapt/documents.htm)

Table 2.1. Protocol content and suggested features

Table 2.2 Suggestions for development of study handbooks and manuals of operations (HandBk.Tab)

A. General

- Identify major topics or functions for which handbooks/manuals are required (e.g., clinic operations, data intake and processing, laboratory procedures, etc.)
- Develop draft table of contents for each required handbook/manual and submit for review and comment by the leadership group of the trial before development
- Develop methods and procedures for data collection with input from key study personnel, including clinicians, statisticians, clinic coordinators, laboratory technicians, and the like
- Strive to ensure that written material contained in handbooks/manuals is concise and devoid of complex sentences and esoteric language
- Test the adequacy of each handbook/manual by having it reviewed by individuals who will use it
- Release for use only after it has been reviewed and approved by study leadership

B. Organization

- Each handbook/manual should have a unique official name
- The name of the handbook/manual, date of release, version or edition number, and name of the individual or group responsible for its distribution should be indicated on the title page of the document
- Include a detailed table of contents, along with a listing of tables and figures in the document
- Include a subject index and glossary
- Chapters in manuals should be divided into numbered subsections; the accompanying numbers and titles should appear in the table of contents of the document
- Left-hand page margins should be wide enough to keep text from being obscured or lost when pages are photocopied or bound (e.g., at least 1" for standard 8½" x 11" pages assembled in loose-leaf notebooks or pressure binders)
- Right-hand page margins should be wide enough to allow room for user notes (e.g., at least 0.75" for standard 8½ x 11" pages). The same is true of top and bottom margins
- Boldface or other fonts should be used to identify key phrases, definitions, and important procedural statements
- Pages should be numbered sequentially from beginning to the end of a document; avoid numbering by chapter or section
- Page numbers should appear in the same location throughout the document regardless of page orientation (preferably upper right-hand corner)

C. Suggested maintenance aids

- Responsibility for review and revision of handbook/manual should be assigned to a specific individual or group
- A specific individual should be given responsibility for keeping track of revisions made to a handbook/manual and for making certain users of the handbook/manual are supplied with updates as they are produced
- Each new version of a handbook/manual should be identified with a version date and should indicate the date and version number of the document it replaces
- Large documents that are subject to frequent updates should be kept in loose-leaf binders to facilitate page replacements and to simplify photo-reproduction of pages in the document

Table 2.2 Study handbooks and manuals of operations

- Individual pages that are updated and inserted in an existing version of a document as replacements should include the revision date in the top or bottom right-hand corner of the pages

Table 2.3 Sample size specification table (SampSize.Tab)

When: After the design is set

Who: Study statistician

Purpose: To set down details of the sample size design

Definitions

class of trial - Class in regard to the nature of treatment effect to be detected as specified in sample size or power calculations for the trial: superiority trial, equivalence trial, noninferiority trial, and inferiority trial.

primary treatment group comparison - 1. The treatment group comparison of primary importance to the trial as specified in the study protocol and as used in sample size calculations. 2. One of several such comparisons in a trial involving multiple treatment groups, e.g., r-1 comparisons in a trial involving t treatment groups (t-1 test treatment groups and one control treatment) in which each of the t-1 treatments are compared against the control treatment.

treatment group - The group of persons assigned to receive a specified treatment in a trial

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—_____

B. Basic design features

4. Sample size design
   ( ) Fixed
   ( ) Sequential
   ( ) Open
   ( ) Closed

5. Treatment structure
   ( ) Parallel
   ( ) Crossover

Table 2.3 Sample size specification table

6. Number of treatment groups (including the control or comparison treatment group)
   ( ) Two
   ( ) ≥ three

   Number of primary treatment group comparisons . . . . . Number ___

   Specify primary treatment group comparisons

   _____

7. Primary outcome measure
   ( ) Change
   ( ) Event
      ( ) Death
      ( ) Cause specific death
      ( ) Disease
      ( ) Re-occurrence of disease
      ( ) Worsening of disease
      ( ) Other (specify)

      _____

   ( ) Other (specify)

   _____

8. Planned length of treatment and followup

   Anniversary closeout . . . . . Length _____ mos

   Common closing date . . . . . Length: Min _____ mos Max _____ mos

9. Planned length of followup same as planned length of treatment?
   ( ) Yes
   ( ) No

   Length of treatment . . . . . _____ mos

   Length of followup after treatment . . . . . Min _____ mos Max _____ mos

C. Sample size

10. Class of trial
   ( ) Superiority trial
   ( ) Equivalence trial
   ( ) Noninferiority trial
   ( ) Inferiority trial

Table 2.3 Sample size specification table

11. Sample size design
    ( ) Open sequential sample size design

    ( ) Closed sequential sample size design
    Minimum sample size . . . . . _____

    Maximum sample size . . . . . _____

    ( ) Fixed sample size design
    Total . . . . . _____

    Sample size per treatment group . . . . . _____

12. Sample size cited in item 11 is the result of (check one):
    ( ) Pragmatics (answer items 13 and 14)
    ( ) Sample size calculation

13. What is the driving pragmatic constraint:
    ( ) Money
    ( ) Availability of suitable people for study
    ( ) Other (specify)

    _____

14. Power with proposed sample size (provide a table of power values for different treatment differences)

    Power table here

15. Basis for sample size calculation; list details below, including the type I and II levels of error protection, the size of the difference to be detected, and the formula used for the calculation

    Specifications here

Table 2.4 Outcome specification table (Outcome.Tab)

When: During the design phase of the trial

Who: Study leaders

Purpose: To designate the primary outcome measure for use in the trial

Definitions

design variable - The variable used for determining sample size in planning a trial. Usually synonymous with primary outcome but need not be.

designed subgroup comparison - A subgroup comparison specified in the study protocol, especially one based on a sample size calculation when the trial was designed.

outcome measure - [trials] An observation variable recorded for a treatment unit at one or more time points after enrollment for the purpose of assessing the effect of a study treatment. 2. A measurement or observation used to measure the effect of an experimental variable. syn: **outcome variable**

primary outcome measure - That measure, among two or more in a trial, considered to be of primary importance in its design (e.g., the one used for the sample size calculation) or analysis; may be a continuous measure or an event depending on the trial.

secondary outcome measure - 1. A measure of relevance to a secondary objective of a trial. 2. A measure specified in the study protocol as secondary. 3. A measure specified as secondary in a study publication.

subgroup comparison - A comparison of treatment groups within a specified subgroup of people to assess treatment effect; subgroup typically defined by disease state or history on entry or by entry baseline or demographic characteristics.

surrogate outcome measure - An outcome measure used as a substitute for some other outcome. In trials, usually one that is known to be or presumed to be predictive of a clinical event and that, when used as a basis for designing a trial, leads to an estimated sample size or duration of followup that is less than that required for detecting a meaningful difference using the clinical event as an outcome measure.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

Table 2.4 Outcome specification table

B. Primary outcome measure

4. Design variable
   ( ) Identical to primary outcome measure
   ( ) Different then the primary outcome measure (specify design variable)

   _____

5. Primary outcome measure (check one)
   ( ) All cause mortality
   ( ) Death due to a specific cause
   ( ) Clinical event
   ( ) Cause specific death or related nonfatal event
   ( ) Change measure
   ( ) Composite measure (specify)

   _____

   ( ) Surrogate measure (specify)

   _____

6. Clinical relevance of the outcome measure
   ( ) High
   ( ) Intermediate
   ( ) Marginal

7. Scientific rationale for choice of primary outcome measure (check one)
   ( ) Previous trials suggesting effect
   ( ) Evidence of effect from observational studies
   ( ) Deductive

8. Is the measure a surrogate measure?
   ( ) No
   ( ) Yes, indicate what the measure is a surrogate for and the scientific basis to supporting its use as a surrogate

   _____

   _____

   _____

Table 2.4 Outcome specification table

9. Is the outcome measure specified as primary in the study protocol?
   ( ) No (explain)

   _____

   ( ) Yes

C. Other outcome measures

10. Secondary outcome measures mentioned in the study protocol?
    ( ) No
    ( ) Yes; list

    _____

    _____

11. Safety outcome measures? (list)

    _____

    _____

D. Subgroup comparisons

12. Treatment comparisons by demographic or baseline entry characteristics mentioned in the study protocol?
    ( ) No
    ( ) Yes, answer items 13 and 14

13. Comparisons mentioned (check all that apply)
    ( ) Treatment group by gender
    ( ) Treatment group by age at entry
    ( ) Treatment group by ethnic origin
    ( ) Treatment group by disease state
    ( ) Other (specify)

    _____

14. Are any of the comparisons indicated in item 13 designed?
    ( ) No
    ( ) Yes (specify)

    _____

Table 2.5 Treatment specification table (Trt.Tab)

When: In the design phase of a trial

Who: Study leaders

Purpose: To specify the treatment design for the trial

Definitions

factorial treatment design - A type of treatment design in which one treatment (factor) is crossed (full or partial) with another treatment (factor). For example, a 2 x 2 factorial design in a trial with a parallel treatment design to evaluate the usefulness of counseling to reduce sodium intake and caloric intake in relation to blood pressure control; in its simplest form with just two levels for each factor (counseling or no counseling) yields four counseling regimens: AB, **A**B, A**B**, and **AB**, where **A** represents counseling for sodium reduction and A denotes absence of such counseling, and where **B** represents counseling for caloric restriction and B denotes absence of such counseling.

complete factorial - 1. A factorial design in which each treatment appears in combination with every other treatment; e.g., the treatment combinations AB, **A**B, A**B**, and **AB** in a parallel treatment trial involving test treatments **A** and **B** and matching placebos A and B. 2. A design in which a specified subset of treatments appear in combination with every other treatment in that subset; e.g., the treatment combinations represented above as part of a larger set involving treatments **C** and **D** not appearing in combination with **A** or **B** or their matching placebos.

incomplete factorial - 1. A factorial design in which only some of the combinations of factors, conditions, or treatments possible in a complete factorial appear, are used, or are administered; e.g., the combinations **A**B, **AB**, and AB in a trial involving the treatments **A** and **B** and matching placebos, A and B, respectively. 2. Any factorial arrangement that is incomplete, even if complete for a defined subset of the factors, conditions, or treatments represented, e.g., an arrangement in which the combinations **A**B, **AB**, A**B**, and AB are represented but in a trial involving a third treatment, **C**, not used in combination with **A**, A, **B**, or B.

treatment design - The portion of the study design that specifies the treatments to be evaluated, the nature of the treatment structure, the treatment assignment design, and the way in which the treatments are to be administered.

treatment modality, **treatment mode** - The method or agent used to treat, ameliorate, or prevent disease or to improve health; in regard to a test treatment in a trial, the general class of method or agent by which effect is to be achieved, e.g., via surgery, medical treatment, radiation, electrotherapy, drug, biologic, device, diet modification, dietary supplement, counseling, or etc.

treatment structure - The interrelation of treatment groups represented in a trial; parallel treatment structure, crossover treatment structure, factorial treatment structure.

Table 2.5 Treatment specification table

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __-__-____

B. Treatment design

4. Test treatment groups
   Number . . . . . ____

   Test trt group 1 _____

   Test trt group 2 _____

   Test trt group 3 _____

   Test trt group 4 _____

5. Control/comparison treatment groups
   Number . . . . . ____

   Ctrl/comparison group 1 _____

   Ctrl/comparison group 2 _____

6. Treatment structure
   ( ) Crossover
      ( ) Complete
      ( ) Incomplete
   ( ) Parallel
      ( ) Uncrossed
      ( ) Crossed
         ( ) Complete factorial structure
         ( ) Incomplete factorial structure

7. Method of treatment assignment (check one)
   ( ) Randomization
   ( ) Other
      ( ) Systematic; order seen, day of the week, morning-afternoon
      ( ) Other (specify)

      _____

Table 2.5 Treatment specification table

8. Unit of assignment
   - ( ) Person
   - ( ) Part of person (e.g., eyes in an eye trial; specify)

     _____
   - ( ) Aggregate of persons
     - ( ) Household
     - ( ) Hospital ward
     - ( ) Census tract
     - ( ) Other (specify) _____

9. System of assignment?
   - ( ) Random
     - ( ) Simple
     - ( ) Restricted
   - ( ) Haphazard
   - ( ) Systematic/alternation
   - ( ) Deterministic
   - ( ) Deterministic with random component
   - ( ) Other (specify)

     _____

10. Assignment ratio?
    - ( ) Fixed
      - ( ) Uniform
      - ( ) Nonuniform (specify) . . . . . _____
    - ( ) Adaptive
      - ( ) Baseline (specify variable(s) used for adaptation)

        _____
      - ( ) Outcome (specify outcome used for adaptation)

        _____
      - ( ) Play-the-winner (specify outcome)

        _____
      - ( ) Other (specify)

        _____

Table 2.5 Treatment specification table

11. Treatment modalities represented in items 4 and 5 (check all that apply)
    ( ) Drug
    ( ) Vaccine
    ( ) Biologic
    ( ) Device
    ( ) Surgery
    ( ) Radiation
    ( ) Dietary regimen/diet supplement
    ( ) Exercise
    ( ) Educational/training regimen
    ( ) Placebo/sham
    ( ) Other (specify)

    _____

C. Treatment administration

12. Treatment masking
    ( ) None
    ( ) Single masked
        ( ) Patient masked
        ( ) Physician masked

    ( ) Double masked

13. Treatment application schedule
    ( ) Single application (specify point of application relative to point of treatment assignment and dosage)

    _____

    ( ) Multiple applications
        ( ) Daily to end of followup (specify dosage schedule; if double-masked drug trial specify pills per day)

        _____

        ( ) Other (specify schedule and dosage)

        _____

D. Other administrative and operational issues

14. Do any of the test treatments represented in item 4 require an IND or IDE?
    ( ) No
    ( ) Yes (specify holder of the IND or IDE)

    _____

Table 2.5 Treatment specification table

15. Are any of the test treatments represented in item 4 drugs, biologics, or devices?
    ( ) No
    ( ) Yes (specify suppliers)

    _____

    _____

16. Is the trial a double-masked drug trial?
    ( ) No
    ( ) Yes
    Who is the supplier of matching placebos
    ( ) The same as the supplier of the test treatments
    ( ) Other (specify)

    _____

WS 2.1 Terminology worksheet (Defns.WS)

When: Early in the course of design, prior to the development of key study documents

Who: Key leadership personnel; typically, in the case of a multicenter trial, personnel in the coordinating center

Purpose: To establish terminology conventions for use in development of key study documents

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Generic terms (language conventions to be used in study documents and publications)

4. Person screened for enrollment into the trial
   ( ) Screenee
   ( ) Study candidate
   ( ) Other specify _____

5. Person enrolled in the trial
   ( ) Study patient (typical in treatment trials)
   ( ) Study participant (typical in trials involving study of healthy people or in settings where there is a desire to avoid medical connotations)
   ( ) Study subject
   ( ) Other (specify)

   _____

6. Collective name for body of persons enrolled in trial
   ( ) Study population
   ( ) Other (specify)

   _____

7. Experimental variable (i.e., the variable represented in the assignment process for the trial)
   ( ) Treatment/study treatment
   ( ) Intervention/study intervention
   ( ) Regimen/study regimen
   ( ) Arm/study arm
   ( ) Other (specify)

8. Name used for designating any one of study groups created by the assignment process regardless of whether test or control treatment
   ( ) Treatment group (recommended)
   ( ) Study group
   ( ) Other (specify)

   _____

9. Name used when referring to any of the study groups except the group receiving the control or comparison treatment
   ( ) Test-assigned group
   ( ) Test treated-assigned group
   ( ) Test treatment group
   ( ) Study group (not recommended)
   ( ) Other (specify)

   _____

10. Name used when referring to the control or comparison treatment in the trial
    ( ) Control-assigned group
    ( ) Control group
    ( ) Comparison-assigned group
    ( ) Comparison group
    ( ) Other (specify)

    _____

11. If control treatment is a placebo, name of person assigned to that treatment
    ( ) Placebo-assigned patient/participant
    ( ) Placebo patient/participant (avoid)
    ( ) Other (specify)

    _____

12. If the control treatment is a placebo, name of group assigned to that treatment
    ( ) Placebo-assigned group
    ( ) Placebo control-assigned group
    ( ) Placebo control group
    ( ) Placebo group (avoid)
    ( ) Other (specify)

    _____

13. Generic name for any outcome measure
    ( ) Outcome measure
    ( ) Event (avoid)
    ( ) Endpoint (avoid)
    ( ) Other (specify)

    _____

14. Generic name for observation variable
    ( ) Variable
    ( ) Parameter (avoid)
    ( ) Other (specify)

    _____

15. Name of study head?
    ( ) Principal investigator
    ( ) Study chair
    ( ) Other (specify)

    _____

16. Generic name of place where study persons are enrolled and followed?
    ( ) Study clinic
    ( ) Field site
    ( ) Other (specify)

    _____

17. Generic name of entire research team
    ( ) Research group
    ( ) Study group (not recommended)
    ( ) Other (specify)

    _____

18. For multicenter trial define:
    Center/study center (Recommended: An operational unit in the structure of a trial responsible for performing specified functions in one or more stages of the trial; e.g., a clinical center or resource center.)

    _____

    _____

Resource center (Recommended: Any center providing expertise and support in a differentiated study structure; in multicenter trials, usually any of the following: data coordinating center, treatment coordinating center, coordinating center, and project office; may also include data center, central laboratory, reading center, and quality control center if heads represented in the leadership structure of the trial are located in that center.)

_____

_____

19. Generic name for heads of centers:
    ( ) Center director
    ( ) Other (specify)

    _____

20. Name of the key leadership body (typically steering committee)

    _____

21. Give the name of the body responsible for treatment effects monitoring
    ( ) Data and safety monitoring committee (DSMC)
    ( ) Data and safety monitoring board (DSMB)
    ( ) Data monitoring committee (DMC)
    ( ) Policy data monitoring board (PDMB)
    ( ) Treatment effects monitoring committee (TEMC)
    ( ) Other (specify)

    _____

22. Name of site/center responsible for data processing and analysis
    ( ) Data center
    ( ) Biostatistics center
    ( ) Data coordinating center
    ( ) Coordinating center
    ( ) Other (specify)

    _____

C. Definitions

23. The point defining the end of the baseline period of observation and the start of the treatment and followup period of observation (Recommended: The point at which a person is assigned to treatment)

    _____

24. The point at which a person is counted as enrolled in the trial (Recommended: The point at which assignment is revealed to clinic personnel)

    _____

25. The point at which a person is counted as a dropout (Recommended: When the person misses a specified number of followup visits or when a person actively withdraws from followup)

    _____

26. Scheduled followup visit
    ( ) A followup visit specified in the study protocol to be done within a specified time window
    ( ) Other (specify)

    _____

27. Unscheduled followup visit (aka interim visit)
    ( ) A followup visit that is not part of the followup data collection protocol
    ( ) Other (specify)

    _____

28. Missed clinic visit (Recommended: A clinic visit, as per the schedule specified in the study protocol, that was not made within the permissible time window for the visit)

    _____

29. Lost to followup (Recommended: Typically a dropout for observations that require clinic visits)

    _____

30. Consent (Recommended: Signed dated consent on IRB-approved consent form)

    _____

31. Baseline data (Recommended: Data collected after consent for screening through to the point of treatment assignment as marked by the point at which treatment assignment is revealed to clinic personnel)

    _____

32. Baseline period (Recommended: From first screening visit up to the point of treatment assignment)

    _____

33. Followup (Recommended: A process involving periodic contact with persons enrolled in a trial for the purpose of administering the assigned treatment(s), observing the effects of treatment(s), modifying the course of treatment(s), or for collecting required followup data.)

---

34. Randomized (Recommended: The condition of having been assigned to a treatment via a random process; normally considered to have occurred when the treatment assignment is revealed to any member of the clinic staff, e.g., when an envelope containing the treatment assignment is opened at the clinic.)

---

35. Time window (Recommended: The time interval for performing a specified activity or procedure. In trials and other followup studies, usually the window for performing a specified examination or type of data collection, such as for a baseline or followup visit.)

---

36. Intention to treat (Recommended: A philosophy in which there is an intent to account for all persons enrolled in a trial and to perform analyses by assigned treatment, regardless of observed course of treatment.)

---

37. Subgroup (A subpart or subset of a study population distinguished by a characteristic or set of characteristics, especially, in the case of trials, such a subpart or subset as distinguished by one or more baseline characteristics.)

---

38. Stopping rule (A rule for determining when to terminate or alter the treatment protocol of a trial based on the observed treatment difference for an outcome of interest; usually some function of a p-value produced by a designated test statistic evaluated at specified points in the course of the trial.)

---

39. Stopping guidelines (A guide as to size or type of treatment differences that may cause treatment effects monitors to recommend stopping or altering a trial. Not to be used interchangeably with stopping rule. Use stopping guideline instead of stopping rule if the rule is used simply as a guide as to when a stop or alteration may be indicated.)

---

40. Multiple look (Treatment comparisons made at two or more time points over the course of a trial; especially when done in relation to treatment effects monitoring and where they may lead to alteration of the treatment protocol.)

    _____

41. Protocol violation (A protocol departure considered to be serious, e.g., administration of the wrong treatment or enrollment of an ineligible person.)

    _____

42. Terms avoided (check all that apply)
    ( ) Treatment failure (presumptive)
    ( ) Informed consent (wishful thinking in the absence of information to indicate consent is truly informed)
    ( ) Endpoint (often interpreted by clinic staff to be synonymous with cessation of followup; not the case except where the "endpoint" is death)
    ( ) Placebo patient (no such person; use placebo-assigned)
    ( ) Drop-in (a person who receives a study treatment different than the one assigned in a trial; use inconsistent with analysis by original treatment assignment)
    ( ) Other (specify)

    _____

    _____

    _____

D. Abbreviations and labels

43. Abbreviations to be used in study documents and publications

Clinic (Recommended: Cl) . . . . . _____

Screening (Recommended: Scr) . . . . . _____

Screening visit (Recommended: ScrV) . . . . . _____

Baseline (Recommended: Bl) . . . . . _____

Baseline visit (Recommended: BlV) . . . . . _____

Followup (Recommended: Fu) . . . . . _____

Followup visit (Recommended: FuV) . . . . . _____

Treatment (Recommended: Trt) . . . . . _____

Treatment visit (Recommended: TrtV) . . . . . _____

44. Labels for treatment groups in treatment effects monitoring reports and publications

Test trt 1 . . . . . _____

Test trt 2 . . . . . _____

Test trt 3 . . . . . _____

Test trt 4 . . . . . _____

Test trt 5 . . . . . _____

Test trt 6 . . . . . _____

Control trt 1 . . . . . _____

Control trt 2 . . . . . _____

45. In multicenter trials, the letter codes for clinics to be displayed in performance monitoring reports

Clinic #	Location	Code
Cl 1		
Cl 2		
Cl 3		
Cl 4		
Cl 5		
Cl 6		
Cl 7		
Cl 8		
Cl 9		
Cl 10		

46. Other labels

Prime leadership committee . . . . . _____

Data center . . . . . _____

Monitoring committee . . . . . _____

WS 2.2 Name and acronym worksheet (BigName.WS)

When: On initiation of funding for a study or on creation of a multistudy structure

Who: Study chair or director of coordinating center with sign-off by study officers and steering committee

Purpose: To choose a study name or an umbrella name and a related acronym or acrostic

Related form: WS 17

Definitions

umbrella name - A name chosen to characterize a collection of studies as preformed under a common corporate structure, e.g., as represented in a study network

study name - A name chosen to characterize a particular study

Reminders and recommendations

Name

- Choose in favor of brevity, crispness, and succinctness
- Avoid redundant terms like "controlled" in "randomized controlled trial" and unnecessary descriptors like "clinical" in "clinical trial"
- Avoid catchy or "cute" names
- Avoid restrictive terms likely to render a name obsolete by subsequent expansion to activities not covered by the name
- Choose in favor of neutral, nonpromotional, names
- For umbrella names consider in conjunction with likely names of particular studies; avoid likely redundancies or contradictory terms when used in conjunction with the name of a specific study
- Keep other likely uses in mind, as in funding applications, publications, presentations, and other written references
- Avoid use of contrived, unprintable, characters
- Avoid choosing to create a desired or "cute" acronym
- Avoid names producing undesirable or vulgar acronyms (Reminder: A meaningless sequence of letters in one language can have meaning in another)
- Be cautious of regional geographical descriptors such as U.S. or Europe that require change if the activity eventually expands beyond the limit represented by the descriptor
- Avoid ill-defined regional terms such as "National" and "International"
- Once chosen, avoid variations of name

Acronym

- Useful for shorthand nomenclature in study documents and publications
- Ideally, choose to be of six or fewer characters
- Include base term in study name, e.g., "trial" as in NETT – National Emphysema Treatment Trial
- Include "network" or other like terms in umbrella name
- Avoid choosing name simply to produce pronounceable acronym

- Be wary of pronounceable acronym, e.g., MRFIT (Multiple Risk Factor Intervention Trial); converted by critics to Ms Fit because trial included only males
- Avoid variations
- Keep likely contractions of name and acronym in mind when choosing

A. Identifying information

1. Form completed by: _____

2. Date completed (day-month-year) . . . . . __—___—____

3. Form completed for (check one):
   ( ) Study name
   ( ) Umbrella name

B. Specifications

4. Maximum number of words, exclusive of articles and connectors . . . . . _____

5. Maximum number of characters, including spaces and punctuation . . . . . _____

6. Base descriptor for activities represented under the name
   ( ) Study(ies)
   ( ) Project(s)
   ( ) Program(s)
   ( ) Other (specify)

   _____

C. Descriptors and modifiers

7. Generic descriptors (check all that apply)
   ( ) Clinical
   ( ) Cooperative
   ( ) Multicenter
   ( ) National
   ( ) International
   ( ) Randomized
   ( ) Controlled
   ( ) Mask; blind
   ( ) Prospective
   ( ) Retrospective
   ( ) Surveillance
   ( ) Followup
   ( ) Other (specify)

   _____

8. Disease descriptor in name?
   ( ) No
   ( ) Yes (specify below)

   _____

9. Population descriptors in name?
   ( ) No
   ( ) Yes
      ( ) Age (e.g., infants, children, adults, elderly) _____
      ( ) Gender (male, men, boys; female, women, girls) _____
      ( ) Race/ethnic origin _____
      ( ) Other _____

10. State indicators in name (e.g., pregnant, healthy, normal, diseased, abnormal, etc.)?
    ( ) No
    ( ) Yes (specify)

    _____

11. Other descriptor terms in name?
    ( ) No
    ( ) Yes (specify)

    _____

D. Candidate names and acronyms

12. Candidate names

    a. _____

    b. _____

    c. _____

    d. _____

13. Candidate acronyms

    a. . . . . _____

    b. . . . . _____

    c. . . . . _____

    d. . . . . _____

E. Official name and acronym

14. Proposed official name

    _____

    Number of characters . . . . . ____

    Number of words, excluding articles and connectors . . . . . ____

15. Proposed official acronym . . . . . _____

16. Name of approving study body: _____

17. Date of approval: . . . . . __ __—__ __ __—__ __ __ __

WS 2.3 Study logo worksheet (Logo.WS)

When: Early in the stage of the study

Who: Study chair or director of coordinating center with sign-off by study officers and steering committee

Purpose: To provide a printable brand for identifying documents from the study

Related form: WS 2.2

Reminders and recommendations

- Useful for branding study documents such as handbooks, manuals, data reports, study forms and letterheads
- If in colors, choose colors easily seen and distinguishable under adverse light conditions; choose and arrange colors so that content remains intelligible when reproduced in black and white
- Reject logos that are easily degraded when copied or that become unreadable when copied several times on different machines and under different intensity settings

A. Identifying information

1. Study name: _____

2. Completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Specifications and desired characteristics

4. Content:
   ( ) Study acronym or acrostic included?
   ( ) Study name?
   ( ) Slogan or motto?

   _____

   ( ) Figures, objects, special characters, or symbols?

   _____

   ( ) Other

   _____

5. Characteristics:
   ( ) Black and white?
   ( ) Colored? (list colors)

   _____

   ( ) Still readable when photocopied?
   ( ) Word processor importable?
   ( ) Other

   _____

6. Uses
   ( ) Letterhead
   ( ) Headers or footers of forms
   ( ) Covers of manuals, handbooks, and study reports
   ( ) Consent documents
   ( ) Materials given to study participants during the study
   ( ) Other

   _____

C. Candidate logos

Sample A

Sample B

Sample C

D. Official logo

E. Sign-off

7. Name of accepting body: _____

8. Date of acceptance: . . . . . __ __—__ __ __—__ __ __ __

WS 2.4 Data sharing worksheet (DataGive.WS)

When: Complete in design phase of trial; review and update over the course of the trial

Who: Director of data center

Purpose: To enumerate data sharing expectations and responsibilities

Definitions

deidentified data - Data stripped of personal identifiers; data contained in a limited dataset.[6]

De-identification, as spelled out in HIPAA,[5] involves deleting for persons studied, their relatives, household members, and employers:

- Names
- Any geocodes that identify an individual household such as street address or Post Office Box Number
- Telephone numbers
- Fax numbers
- Electronic mail addresses
- Social Security Numbers
- Medical record numbers
- Health plan beneficiary identifiers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Medical device identifiers and serial numbers
- Web universal resource locators (URL)
- Internet Protocol (IP) address numbers
- Biometric identifiers, including finger and voice prints
- Full face photographic images

Datasets must also be devoid of:

- Geographic subdivisions designations smaller than a state (i.e., county, city, town, precinct)
- 5 or 9 digit ZIP codes (1st three digits allowable in most cases)
- All elements of dates (except year) directly related to an individual, including dates of birth or death, dates of health care services or health care claims (deidentified datasets cannot contain birth dates; file may contain the individual's age expressed in years, months, days, or hours, as appropriate, except for individuals aged 90 or above; such persons to be identified simply as being 90 or above)
- Any other unique identifying number, characteristic, or code that could be used to identify the individual (supplier of data may affix codes to allow user to associate data with persons, provided codes cannot be used to re-identify persons)

identified data - Data identifiable to a person by Id number or other personal identifiers.

WS 2.4 Data sharing worksheet

A. Identifying information

1. Form completed by: _____

2. Date completed (day-month-year) . . . . . __—___—_____

3. Types of data sharing planned (check all that apply)
   ( ) Data sharing within the investigator group (**Section B**)
   ( ) Data sharing external to the investigator group
   ( ) Voluntary external data sharing (**Section C**)
   ( ) Mandated external data sharing (**Section D**)

B. Internal data sharing (Data sharing within the investigator group)

4. Internal data sharing planned?
   ( ) Yes
   ( ) No (explain; internal sharing is the norm)

   _____

   _____

5. Mode of sharing during study (check all that apply)?
   ( ) None planned (explain)

   _____

   ( ) On demand via access to study database
   ( ) Via request to data center

   ( ) Other (specify) _____

6. Mode of sharing on completion of study (check all that apply)?

   ( ) None planned (explain)

   _____

   ( ) Finished dataset supplied to investigators via data center
      ( ) Supplied identified
      ( ) Supplied deidentified

   ( ) Other (specify)

   _____

7. Signed agreement by investigators receiving data to not identify persons studied and to not copy or provide data to persons outside the investigator group?
   ( ) Yes
   ( ) No (explain)

_____

C. Voluntary external data sharing (Data sharing with persons external to the investigator group and in which study investigators determine whether to share; typically external voluntary sharing carries conditions including the right of investigators to review uses prior to presentation or publication; data may be provided identified or deidentified depending on agreement.)

8. Voluntary data sharing planned?
   ( ) Yes
   Mode
   ( ) Passive (by request; no announcement of willingness to entertain requests for sharing)
   ( ) Active (by announcement of willingness to share on study website or in study publications)
   ( ) No

9. Procedure for reviewing requests (check all that apply)?
   ( ) Study chair/PI
   ( ) Study officers
   ( ) Steering committee
   ( ) Study officers & steering committee
   ( ) Other (specify)

_____

10. Sharing of interim treatment results?
    ( ) No (the norm)
    ( ) Yes (explain)

_____

11. Entertainment of external requests for analyses?
    ( ) No
    ( ) Yes
    ( ) Via analyses done by study data center without cost to requestor
    ( ) Via analyses by study data center with costs covered by requestor
    ( ) By requestor via data provided by the study data center
    ( ) Other (specify)

_____

12. Entertainment of external requests for study datasets?
    ( ) No
    ( ) Yes
        ( ) Supplied deidentified without use restriction
        ( ) Supplied deidentified with use restriction
        ( ) Supplied identified with use restriction
        ( ) Other (specify)

        _____

    Cost of preparation
    ( ) Supplied without cost to requestor
    ( ) Cost of preparation covered by requestor
    ( ) Other (specify)

        _____

D. Mandated external data sharing (Data sharing external to the investigator group mandated by the sponsoring agency and in which requests for data are answered by providing requestors deidentified data typically without investigator approval or constraints on use.)

13. Work scope of funding award includes provisions for mandated external data sharing?
    ( ) Yes
    ( ) No

14. Consent form includes mention of intent to provide access to deidentified data by people outside the investigator group?
    ( ) Yes
    ( ) No

15. Is the planned sample size per treatment group sufficiently large to make de-identification possible with minimal risk of probabilistic identification?
    ( ) Yes
    ( ) No

16. Reconciliations
    If Item 13 is answered Yes and Item 14 is answered No, explain the inconsistency

    _____

WS 2.4 Data sharing worksheet

Note

If Item 15 is answered No and Item 13 is answered Yes, revise work scope to exclude mandatory external data sharing or inform funding agency of unwillingness to engage in unrestricted release of study datasets

17. Mode of mandatory external data sharing
    - ( ) Submit datasets to sponsor to deal with requests for datasets
    - ( ) Submit datasets to 3rd party custodian to deal with requests for datasets
    - ( ) Study data center to serve as custodian
    - ( ) Other (specify)

    _____

18. Mode of announcing availability of datasets for external sharing (check all that apply)
    - ( ) Study website
    - ( ) Study publications
    - ( ) Other (specify)

    _____

19. Types of datasets to be made available to persons external to the investigator group (check all that apply)
    - ( ) Datasets corresponding to datasets used in publications
    - ( ) Finished dataset containing all study data, whether or not used in previous publications
    - ( ) Other (specify)

    _____

20. Time when deidentified data to be made (check all that apply)
    - ( ) In relation to individual study publications (e.g., by announcing availability of dataset supporting a publication in the publication)
    - ( ) Finished dataset compiled after the end of data collection and after editing and "cleanup" even if the investigator group is still working on publications
    - ( ) Finished dataset after cessation of paper writing activities by the investigator group
    - ( ) Finished dataset as supplied by data center in final year of support even if investigator group still working on publications
    - ( ) Other (specify)

    _____

CL 2.1 Treatment design synopsis checklist (TrtDesig.CL) (per Coronary Drug Project)[4]

When: After the trial is designed

Who: Senior people in the coordinating center

Purpose: To provide a synopsis of study design for use in study documents and in producing study publications

1. Trial type
- (x) Superiority
- ( ) Equivalence
- ( ) Inferiority
- ( ) Demonstration
- ( ) Other

2. Trial phase
- ( ) 1
- ( ) 2
- ( ) 3
- (x) 4
- ( ) Other

3. Purpose
- (x) Prevention
  - ( ) Primary
  - (x) Secondary
- ( ) Treatment
- ( ) Other

4. Test treatment(s)

Estrogen (ESG) mixed conjugated equine estrogen; two estrogen treatment groups: one receiving a dosage of 2.5mg/day and another receiving 5.0mg/day; Premarin®

Colfibrate (CPIB) ethyl alpha parachlorophenoxy-isobutyrate; Atromid-S®

Dextrothyroxine (DT4); Choloxin®

Nicotinic acid (NICA)

5. Primary outcome measure
- ( ) Event
  - (x) Death, any cause; 5 yr mortality
  - ( ) Death, specific cause
  - ( ) Morbid clinical event
  - ( ) Other
- ( ) Change measure
- ( ) Other

6. Treatment groups

Test treatment groups
- ( ) 1
- ( ) 2
- ( ) 3
- (x) 4 or more

Control treatment groups
- (x) 1
- ( ) 2
- ( ) 3 or more

Total number of treatment groups
- ( ) 2
- ( ) 3
- ( ) 4
- (x) 5 or more

7. Control treatment(s)
- ( ) Observation only
- (x) Matching placebo
- ( ) Sham procedure
- ( ) Standard medical care
- ( ) Other

8. Treatment structure
- (x) Parallel
  - ( ) Full factorial structure
  - ( ) Partial factorial structure
  - (x) Independent (uncrossed)
- ( ) Crossover
- ( ) Other

9. Treatment assignment design
- (x) Randomized
- ( ) Systematic
- ( ) Physician judgment
- ( ) Patient choice
- ( ) Other

10. Assignment unit
- ( ) Geographical area
- ( ) Household
- (x) Person
- ( ) Person part
- ( ) Other

11. Assignment ratio
- ( ) Uniform (same across treatment groups)
- (x) Non-uniform (specify); 1 to 2.5, per treatment group relative to control treatment, i.e., 1:1:1:1:1:2.5

12. Treatment administration
- ( ) Unmasked
  - ( ) Fully unmasked
  - ( ) Partially unmasked
- (x) Masked
  - ( ) Single-masked
  - (x) Fully double-masked
  - ( ) Partial double-masked

13. Treatment modalities
- (x) Drugs
  - ( ) Pills
  - ( ) Injections
  - ( ) Implants
  - ( ) Other
- ( ) Medical device
- ( ) Surgery
- ( ) Radiation
- ( ) Dietary
- ( ) Behavior modification
- ( ) Other

14. Bias control procedures
- (x) Concealment of assignments until issue
- (x) Masked treatment administration
- (x) Shielding of investigators from interim results
- (x) Independent treatment effects monitoring
- ( ) Other

15. Sample size requirement
- ( ) Not stated
- (x) Specified

16. Sample size rationale
- (x) Calculated
- ( ) Pragmatic
- ( ) Unspecified

17. Variance control procedures
- (x) Randomization
- (x) Stratification; clinic and two risk groups
- (x) Blocking of assignments
- ( ) Other

18. Primary treatment comparison in trials with more than one test-treated group

(x) Simple, i.e., comparison of individual test-treated groups vs control-treated group

( ) Complex: Simple comparison plus:

- ( ) Test-treated group compared with other test-treated groups
- ( ) Combinations of test-treated groups compared with control-treated group
- ( ) Other

3 Treatment assignment tables, worksheets, and checklists

Table 3.1 Variance control design (VarCtrl.Tab)

When: During design phase of the trial

Who: Coordinating center personnel

Purpose: To specify the variance control features of the study design

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Variance control strategies (check all that apply)

( ) Training of study personnel
( ) Stratified randomization
( ) Blocked randomization
( ) Matched paired design
( ) Crossover treatment design
( ) Patient as own control (e.g., as in designs where a person part such as eye is the randomization unit)
( ) Replicate measures (specify measures)

_____

( ) Adjudicated reading procedures (specify readings to be adjudicated)

_____

( ) Written study protocol
( ) Written study handbooks and manuals of operation
( ) Tested data collection forms
( ) Double data entry
( ) Large sample size
( ) Long period of followup
( ) Other (specify)

_____

Table 3.2 Bias control design (BiasCtrl.Tab)

When: When the trial is being planned

Who: Study chair and director of coordinating center

Purpose: To aid in designing the trial

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Bias control design features (check all that apply)

( ) Randomization
( ) Concealment of treatment assignments
( ) Masked treatment administration
( ) Masked data collection
( ) Masked readings
( ) Bias robust outcome measure
( ) Primary analysis by assigned treatment
( ) Adherence to intention to treat analysis principles
( ) Publication of results regardless of outcome
( ) Other (specify)

_____

C. Bias detection procedures (check all that apply)

( ) Audit of treatment assignment process for departures
( ) Counts of missing visits by treatment group
( ) Counts of people not on treatment by treatment group
( ) Counts of dropouts by treatment group
( ) Counts of persons lost to followup by treatment group
( ) Other (specify)

_____

WS 3.1 Assignment specification worksheet (TrtAss.WS)

When: Early in the design phase of the trial

Who: Persons in the center responsible for issuing assignments

Purpose: To set forth the primary features of the randomization design

Definitions

adaptive treatment assignment - Any method of treatment assignment in which the treatment assignment ratio changes as a function of previous assignments, baseline data, or observed outcomes. Types include: baseline adaptive treatment assignment, biased coin treatment assignment, minimization, minimum likelihood treatment assignment, number adaptive treatment assignment, outcome adaptive treatment assignment, play-the-winner treatment assignment, and urn model treatment assignment

audit trail - The sequence of transactions linking two events or actions. In treatment assignment, the sequence of transactions relating to the issue of treatment assignments, in particular those recorded that can be used at any time to check the veracity of the treatment assignment process.

bin number drug system - A system in randomized trials in which treatment assignment is indicated by bin number (see Coronary Drug Project for example involving 30 bins[4]); typically a system in which more than one person receives medication from the same bin; system easier to implement and manage than unique medication number system and typically more medication conserving; downside relates to potential for collateral unmasking if a bin number is unmasked.

block - A grouping of treatment assignments administered or to be administered in the order listed; especially a grouping of assignments in a parallel treatment design that satisfy the assignment ratio.

blocked randomization - Randomization constrained to force the assignment ratio to be satisfied when a block is filled.

complete randomization - Randomization not constrained by restrictions; simple randomization.

concealment - The process and structure for preventing disclosure of treatment assignments to patients and clinic personnel until patients have been judged eligible for enrollment, have consented, and have indicated a willingness to accept whatever treatment is assigned.

envelope treatment assignment - A system in which assignments are contained in sealed envelopes for repose at the site of use; typically numbered and supplied with instructions to use and open in the order supplied.

fixed treatment assignment - Any method of treatment assignment involving a fixed treatment assignment ratio.

haphazard treatment assignment - A treatment assignment that is made in a nonrandom, arbitrary fashion not according to any apparent plan or design.

masked treatment assignment - Any scheme in which communication of treatment assignment to clinic personnel is masked as necessary in single- or double-masked trials.

med Id number drug system - A drug dispensing system in which assigned treatment is indicated by a med number, e.g., a system in which patient Id number corresponds to med Id; dispensing system more difficult and expensive to implement and manage and less medication conserving than the bin number dispensing system, but immune to collateral unmasking because of unique numbering scheme.

open treatment assignment - 1. Treatment assignment resulting from an open treatment assignment schedule, e.g., as from a schedule posted in the clinic. 2. uncontrolled treatment assignment

random treatment assignment - 1. Treatment assignment determined by randomization. 2. The treatment assignment for a person as determined by randomization.

restricted randomization - Randomization involving restrictions, such as in blocked randomization.

stratification - An active ongoing process of placing patients into strata as a prelude to randomization. Stratification is done to control variation, but to be useful, the variable has to be related to the outcome of interest. Blocking is done to ensure that the assignment ratio is satisfied at points in time over the course of enrollment; stratification is done to ensure the comparability of the treatment groups with regard to the stratification variable(s). Stratification merely ensures the mix of people with regard to the stratification variable is the same across treatment groups.

stratification variable - A variable used to classify treatment units into strata in relation to treatment assignment.

treatment assignment ratio - The ratio of assignments for the different study treatment groups relative to the control group in the trial, e.g., 2:2:2:2:2:5 for a trial with five test-assigned groups and a single control-assigned group involving 2.5 times as many assignments as to any of the test-assigned groups.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Treatments groups and assignment

4. Test treatment groups
   Number . . . . . ____

Test trt group 1 _____

Test trt group 2 _____

Test trt group 3 _____

Test trt group 4 _____

5. Control/comparison treatment groups
   Number . . . . . _____

   Ctrl/comparison group 1 _____

   Ctrl/comparison group 2 _____

6. Specified assignment ratio
   ( ) Uniform
   ( ) Nonuniform (specify)

   _____

7. Unit of randomization
   ( ) Person
   ( ) Part of person (e.g., eyes in an eye trial; specify) _____
   ( ) Aggregate of persons
      ( ) Household
      ( ) Hospital ward
      ( ) Census tract
      ( ) Other (specify)

      _____

8. Assignment ratio?
   ( ) Fixed
   ( ) Adaptive
      ( ) Baseline (specify variable(s) used for adaptation)

      _____

      ( ) Outcome (specify outcome used for adaptation)

      _____

( ) Play-the-winner (specify outcome)

_____

( ) Other (specify)

_____

9. System of assignment?
   ( ) Random
      ( ) Simple randomization
      ( ) Restricted randomization
   ( ) Pseudo random
   ( ) Haphazard
   ( ) Systematic/alternation
   ( ) Deterministic
   ( ) Deterministic with random component
   ( ) Other (specify)

_____

10. Multiple clinics?
    ( ) No
    ( ) Yes
    Number of clinics . . . . . ___
    Randomization by clinic?
    ( ) No
    ( ) Yes
    If yes,
    ( ) Same assignment ratio for all clinics
    ( ) Different assignment ratios depending on clinic (describe differences)

_____

_____

11. Stratification?
    ( ) No
    ( ) Yes (check any that apply)
    ( ) Clinic . . . . . Number of clinics: ___

    ( ) Disease state/history . . . . . Number levels: ___

    ( ) Age . . . . . Number age groups: ___

    ( ) Gender 2

( ) Ethnic origin . . . . . Number groups: ___

( ) Other (specify)

_____ . . . . . Number levels: ___

_____ . . . . . Number levels: ___

12. Number of assignment strata (product of numbers entered in item 11) . . . . . ___

13. Blocked randomization?
    ( ) No (skip to item 16)
    ( ) Yes

14. Smallest possible block size (sum of integers from item 6, e.g., 2 for uniform assignment in a two treatment trial) . . . . . ___

15. Blocking design
    ( ) Fixed block size across strata (specify size) . . . . . ___

    ( ) Variable block size across strata (specify sizes) . . . . . _____
    Method of arranging blocks within strata
    ( ) Randomly ordered
    ( ) Other (specify) _____

C. Administration and management of assignments

16. When is person counted as randomized?
    ( ) When assignment becomes known to clinic personnel
    ( ) Other (specify)

    _____

17. Control of issue of assignments
    ( ) Uncontrolled
        ( ) Self-administered envelope scheme (e.g., accomplished by placing sealed numbered envelopes at clinic to be opened in order when person judged eligible and has consented)
        ( ) On demand by computer or via call to assignment center without checks on eligibility as condition for release
        ( ) Other (specify)

        _____

    ( ) Controlled
        ( ) Computer generated after requestors keys eligibility data and absent excluding conditions

( ) Telephone request to assignment center; issue after oral check of eligibility data
( ) Other (specify)

_____

18. Method of concealment
    ( ) None (open assignment lists)
    ( ) Trust (e.g., as required in self-administered envelope treatment assignment scheme)
    ( ) Enforced
        ( ) Computer controlled
        ( ) Other (specify)

_____

19. Communication of assignment to clinic
    ( ) Unmasked (e.g., by conveying Surg or Med in a surgery vs medical treatment trial)
    ( ) Masked (e.g., by conveying Med Id or Bin number in a masked drug trial)
    ( ) Other (specify)

_____

20. Audit trail of assignments?
    ( ) Computer issued with indelible audit trail of time and date of issue and of the assignment issued
    ( ) Issued by mail with record of when envelope containing assignment mailed
    ( ) Issued by telephone with record of time and date of call and of treatment assignment issued
    ( ) Self-administered envelope system with record of when envelope is opened
    ( ) Other (specify)

_____

D. Masked treatment assignment

21. Level of masking
    ( ) Full double-masked; patients and all clinic personnel masked to treatment assignments
    ( ) Partial double-masked
        ( ) Some treatments not double-masked
        ( ) Treatments double-masked to patients and treaters but not to all clinic personnel
    ( ) Single-masked
        ( ) Patient masked, treater not masked
        ( ) Treater masked, patient not masked
    ( ) Other (specify)

_____

22. Treatment modalities represented by test treatments
    - ( ) Drug
    - ( ) Vaccine
    - ( ) Biologic
    - ( ) Device
    - ( ) Surgery
    - ( ) Radiation
    - ( ) Dietary regimen/diet supplement
    - ( ) Exercise
    - ( ) Educational/training regimen
    - ( ) Other (specify)

    _____

23. Treatment modalities represented by control/comparison treatments
    - ( ) Matching placebo
    - ( ) Sham procedure
    - ( ) Mock treatment
    - ( ) Other (specify)

    _____

24. Treatment application schedule
    - ( ) Single application
    - ( ) Multiple applications

      Schedule of applications
      - ( ) Daily for a specified number of days
      - ( ) Daily for the duration of the trial
      - ( ) Other (specify)

      _____

E. Masked drug treatments

25. Packaging and labeling of drug
    - ( ) Packaged and labeled by a central pharmacy for shipment to clinics
    - ( ) Prepared and labeled by local pharmacies
    - ( ) Other (specify)

    _____

26. Method of identifying drug
    - ( ) Via med Id
    - ( ) Via bin number

( ) Other (specify)

_____

27. Provisions for unmasking
    ( ) 1-800 24-hr telephone
    ( ) Open sealed tear-off label revealing content stored at clinics
    ( ) Other (specify)

_____

WS 3.2 Eligibility overrides (Override.WS)

When: Early in the design phase of the trial

Who: Persons in the center responsible for issuing assignments

Purpose: To set forth policy on enrollment overrides

Definitions

enrollment override - [trials] A decision to proceed with enrollment of a person into a trial even though the person is not eligible for enrollment according to the study protocol; usually with the approval of the study sponsor or study chair. Note: Overrides are protocol violations and, hence, should be reported to IRBs as violations.

protocol violation - 1. A protocol departure considered to be serious, e.g., administration of the wrong treatment or enrollment of an ineligible person. 2. protocol override 3. Any protocol departure whether or not considered to be serious.

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __-___-____

B. Policy on enrollment overrides

4. Study policy on enrollment overrides (check one)
   ( ) Proscribed
   ( ) Proscribed for safety exclusions; allowed for exclusions not related to safety
   ( ) Allowed on a per case basis
   ( ) Other (specify)

   _____

5. Is the policy indicated in item 4 written?
   ( ) No (explain)

   _____

   ( ) Yes (check all that apply)
      ( ) Contained a study Policy and Procedures Memoranda
      ( ) Contained in the study protocol
      ( ) Contained in a study handbook or manual of operations

( ) Other (specify)

_____

C. Override procedures

6. If an override is to occur, who does the override (check one)?
   ( ) Coordinating center personnel
   ( ) Clinic personnel via online assignment system
   ( ) Other (specify)

   _____

7. Does the override procedure require entering false information to get the assignment?
   ( ) No
   ( ) Yes: STOP: Data falsification is scientific misconduct

8. If overrides are allowed with the approval of the study chair or study sponsor, is the coordinating center made aware of the override before the person is enrolled?
   ( ) No (communication linkage should be created since there is no way to monitor adherence to the enrollment protocol in communication structures where those decisions are made without knowledge of the coordinating center)
   ( ) Yes, by being a party to the decision
   ( ) Yes, by being copied on correspondence authorizing the override
   ( ) Other (specify)

   _____

D. Override prevention procedures

9. If overrides are proscribed indicate steps taken to avoid them (check all that apply)
   ( ) Training of study staff prior to start of enrollment of the proscription, reasons for it, and consequences of protocol violations
   ( ) Study investigator buy-in on policy prior to start of enrollment
   ( ) PPM indicating zero-tolerance for overrides and reporting procedures if they occur

10. Even if the policy is to proscribe overrides there will be pressure to override if recruitment lags. What are the work-arounds to avoid an override? (check one)
    ( ) Barring enrollment of the person pending submission of a protocol amendment for IRB reviews and approvals
    ( ) Authorization of the override and submission of a protocol amendment to remove the condition as an exclusion; no further overrides for that condition without approval of the protocol amendment
    ( ) Other (specify)

    _____

11. Methods of coordinating center on detecting enrollment overrides (check all that apply)
    ( ) Interview of clinic directors as to approach in dealing with ineligibles
    ( ) Questioning study personnel at site visit
    ( ) Data edits for discrepancies between what is keyed and what is recorded on study forms
    ( ) Cross form inconsistency, e.g., indication a person is not taking a proscribed drug on the enrollment form but the medical form completed when the person was enrolled indicates use of the drug
    ( ) Other (specify)

    _____

12. Steps taken by the coordinating center on learning of an enrollment override (check all that apply)
    ( ) Notice of override to coordinating center IRB
    ( ) Request to enrolling clinic that they report the override to its IRB; with evidence of having made the report to the coordinating center
    ( ) Cease and desist order
    ( ) Other (specify)

    _____

13. Is eligibility checked before issue of a treatment assignment?
    ( ) No (explain why not; note that without checking there is no way to know if people enrolled meet specified eligibility criteria)

    _____

    _____

    ( ) Yes (answer items 14 and 15)

14. How is the check performed?
    ( ) By computer from eligibility information keyed from the enrollment form
    ( ) By query of the person requesting a treatment assignment to check for ineligibility
    ( ) Other (specify)

    _____

15. What happens if an enrollment stop condition is encountered?
    ( ) Assignment not issued
    ( ) Investigator requests an override and reasons for the request; request forwarded to study chair or sponsor; if approved, assignment issued and reported to relevant IRBs
    ( ) Coordinating center decides on its own whether to proceed with assignment

( ) Other (specify)

_____

E. Communication structure on issues of enrollment

16. Seat of primary communications node on eligibility
    ( ) Coordinating center
    ( ) Office of study chair
    ( ) Office of study sponsor
    ( ) Other (specify)

    _____

17. If the primary node is not in the coordinating center is the coordinating center consulted in relation to an override?
    ( ) No (fix the communication gap)
    ( ) Yes

18. Who has sign-off authority on overrides?
    ( ) Study chair
    ( ) Director of the coordinating center
    ( ) Unclear (clarify)

    _____

F. Investigator buy-in

> **Note**
> Even though overrides are anathema to coordinating centers, they are not likely to be seen in the same light by clinical investigators because their view of the protocol is more as a guideline than as a blueprint. As a result, the coordinating center will be swimming up stream if there is not investigator buy-in on proscription of overrides. Hence, policy has to be established before the start of enrollment and signed onto by study leaders and then reinforced over the course of the trial when slip-ups occur.

19. Approving body (check all that apply)
    ( ) Steering committee
    ( ) Study chair
    ( ) Study sponsor
    ( ) Treatment effects monitoring committee
    ( ) Other (specify)

    _____

20. Date of approval (day-month-year) . . . . . __—___—____

21. Mode of approval (check one)
    ( ) By closed ballot
    ( ) By show of hand
    ( ) By e-mail vote
    ( ) Other (specify)

4 Data collection tables, worksheets, and checklists

Table 4.1 Contact and data collection schematic for ADAPT (ADAPTDC.Tab)[1]

	El* visit	En* visit	Followup contacts (mos from En visit)								
	-1	0	1	3	6	9	12	15	18	21	24 . . .
Type of visit/contact											
Eligibility	✓										
Enrollment		✓									
Cognitive assessment							✓				✓
Followup visits			✓		✓				✓		
Telephone				✓		✓		✓		✓	
Procedures											
Consent	✓	✓									
Physical exam	✓						✓				✓
Med history	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
Neurological exam	✓						✓				✓
Laboratory tests	✓		✓		✓		✓		✓		✓
DNA sample		✓									
Review of compliance			✓	✓	✓	✓	✓	✓	✓	✓	✓
Review of med use		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Review of adverse events			✓	✓	✓	✓	✓	✓	✓	✓	✓
Dispensing study drug		✓			✓		✓		✓		✓
Neuropsychological tests											
Modified Mini-Mental	✓	✓					✓				✓
Digit span		✓					✓				✓
Generative Verbal Fluency		✓					✓				✓
Rivermead Memory Test		✓					✓				✓
Hopkins Verbal Learning	✓	✓					✓				✓
Visuospatial Memory Test		✓					✓				✓
Self-rating Memory Functions		✓					✓				✓
Geriatric Depression Scale		✓					✓				✓
Dementia Severity Rating	✓	✓					✓				✓

18 April 2011 \CTForms\ADAPTDC.Tab

* El = eligibility; En = enrollment

Table 4.2 Followup specification table (FU.Tab)

When: Before start of data collection

Who: Study leaders

Purpose: To establish the followup data collection schedule

Definitions

dropout - 1. Broadly, one who terminates involvement in an activity by declaration or action; especially one who so terminates because of waning interest or for physical, practical, or philosophical reasons. 2. A person who withdraws from a trial. 3. A person who fails to appear for an unbroken sequence of scheduled followup visits, e.g., a person so classified after having failed to appear for three consecutive followup visits as defined by specified visit time windows.

followup visit schedule - The schedule of followup visits for treatment administration and data collection, as specified in the study protocol.

lost to followup - 1. A person who cannot be found for followup. 2. A person who cannot be followed for some outcome of interest. 3. A person considered unsuitable for followup because of some intervening condition or state, e.g., in a trial, because the person is not receiving or taking the assigned treatment.

missed visit - 1. A scheduled visit that is missed. 2. A visit not made within the specified time window.

time window - The time interval for performing a specified activity or procedure. In trials and other followup studies, usually the window for performing a specified examination or type of data collection, such as for a baseline or followup visit. Types: contiguous time window, disjoint time window, ideal time window, overlapping time window, permissible time window

contiguous time window - A time window constructed to adjoin but not overlap the preceding or following time window.

disjoint time window - A time window neither adjoining or overlapping a preceding or following time window.

overlapping time window - A time window overlapping the preceding or following time window.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

Table 4.2 Followup specification table

B. Followup schedule

4. Modes of followup for data collection (check all that apply, write P in check space to indicate the principal mode of followup)
   ( ) Clinic visits (CV)
   ( ) Home visits (HV)
   ( ) Telephone (TV)
   ( ) Letter (LV)

5. Time unit reflected in contact schedule in item 9 (check one):
   ( ) Hours
   ( ) Days
   ( ) Weeks
   ( ) Months
   ( ) Other (specify)

   _____

6. Is the data collection schedule governed by time windows?
   ( ) No (explain)

   _____

   ( ) Yes (answer item 7)

7. Time window construction for primary mode of data collection (check one)
   ( ) Contiguous
   ( ) Disjoint
   ( ) Overlapping

8. For data not collected within the designated time window for a visit (check all that apply)
   ( ) Data not used and contact counted as missed
   ( ) Contact counted as missed for the time window; data used to satisfy data collection requirements for the open time window
   ( ) Other (specify)

   _____

9. Followup contact schedule for data collection; use letter designations indicated in item 4 to indicate type of contact in Col 1; record idealized time of contact in Col 2 in units indicated in item 5; give time window limits in Cols 3 and 4.

Table 4.2 Followup specification table

Col 1	Col 2	Col 3	Col 4
		Time window	
Contact #	Time fr trt assignment	Lower time limit	Upper time limit

C. Special followup procedures

10. Sweeps to determine vital status of dropouts and persons lost to followup
    ( ) No
    ( ) Not applicable
    ( ) Applicable but sweeps not done
    ( ) Yes (answer items 11 and 12)

11. Frequency of sweeps (check all)
    ( ) Annually
    ( ) At end of trial
    ( ) Other (specify)

    _____

12. Methods used to determine vital status (check all that apply)
    ( ) Social Security Administration death index
    ( ) National Death Index
    ( ) Newspaper obituary listings
    ( ) Next of kin
    ( ) Other (specify)

    _____

13. Steps taken to minimize dropping out (check all that apply)
    ( ) Special clinic hours
    ( ) Home visits
    ( ) Pickup and transport services for people needing such services
    ( ) Payment of cab fares and parking fees

Table 4.2 Followup specification table

( ) Payment of transportation and accommodation charges for out-of-town people
( ) Baby sitting services
( ) Transfer to sister clinics when person moves to another city with a study site (multicenter trials)
( ) Periodic contact of dropouts to determine if they are willing to return to active followup
( ) Other (specify)

_____

14. Efforts at minimizing losses to followup (check all that apply)
    ( ) Periodic vital status sweeps
    ( ) Maintenance of locator information such as person's family members and employer
    ( ) Tracing agency to locate people lost to followup
    ( ) Other (specify)

_____

D. Close of followup

15. Closeout design (check one)
    ( ) Closeout on per person basis after completion of a specified period of followup (anniversary closing date design)
    ( ) Closeout en masse at a common date regardless of period of followup (common closing date design)
    ( ) Other (specify)

_____

16. Activities on closeout (check all that apply)
    ( ) Unmasking of treatment assignment
    ( ) Deconsent
    ( ) Transfer of care responsibilities
    ( ) Update of locator information in the event of future contact
    ( ) Other (specify)

_____

WS 4.1 Data form worksheet (DataForm.WS)

When: Prior to development of data collection forms

Who: Persons responsible for development of data collection forms

Purpose: To establish general policy and guidelines to be followed in production of data collection forms

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Basic design strategies and layout

4. Forms designed (check all that apply):
   ( ) To be opened and closed on the day of use
   ( ) To display codes for keying
   ( ) To be keyed where completed
   ( ) To be self-contained without reference to other documents for completion
   ( ) To be printed on demand at the site of completion
   ( ) To have explicit logic (e.g., to be devoid of constructions where the absence of information is taken to mean something, e.g., as in an instruction to answer only if person is female without information on the form to indicate that the person is female)

5. Paper size
   ( ) 8.5"x11"
   ( ) 8.5"x14"
   ( ) Other (specify) . . . . . _____

6. Page orientation
   ( ) Portrait
   ( ) Landscape
   ( ) Mixed, depending on form

7. Print surfaces
   ( ) Single side
   ( ) Both sides

8. Page layout
   ( ) Single column full page layout
   ( ) Two column layout

( ) Other (specify)

_____

9. Margins
   Top
   ( ) 3/4"
   ( ) Other . . . . . ____ inches
   Bottom
   ( ) 3/4"
   ( ) Other . . . . . ____ inches
   Left
   ( ) 1"
   ( ) Other . . . . . ____ inches
   Right
   ( ) 3/4"
   ( ) Other . . . . . ____ inches

10. Page number location (single side print)
    ( ) Top right
    ( ) Top center
    ( ) Bottom right
    ( ) Bottom center

11. Page numbering format
    ( ) Standard arabic numbering
    ( ) Page x of y (e.g., Page 5 of 7)
    ( ) Other (specify) . . . . . _____

12. Font (specify) . . . . . _____

13. Pitch (specify) . . . . . ___

C. Patient identifiers

14. Id number format (specify structure and number and nature of characters)

    _____

15. Clinic identifier for multicenter trials (specify number of characters and whether to be part of patient Id number)

    _____

16. Second identifier (recommended as a means of checking for proper identification)

    Number of characters . . . . . ____

Method of construction

_____

17. Location of patient identifiers on forms
    ( ) First items on all forms in standard location
    ( ) Other (specify)

    _____

18. Id number on continuation pages of forms?
    ( ) No
    ( ) Yes (specify location)

    _____

D. Form name and number

19. Location of form name on forms
    1st page
    ( ) Top, flushed left
    ( ) Top, centered
    ( ) Top, flushed right
    ( ) Other (specify)

    _____

    Continuation pages
    ( ) Bottom, flushed left
    ( ) Bottom, centered
    ( ) Bottom, flushed right
    ( ) Other (specify)

    _____

20. Forms also identified by Id number?
    ( ) No
    ( ) Yes (answer items 21 thru 24)

21. Form number location
    1st page
    ( ) Top, flushed left
    ( ) Top, centered
    ( ) Top, flushed right
    ( ) Other (specify)

    _____

Continuation pages
- ( ) Bottom, flushed left
- ( ) Bottom, centered
- ( ) Bottom, flushed right
- ( ) Other (specify)

_____

22. Form version number format (specify)

_____

23. Version number location

1st page
- ( ) Top, flushed left
- ( ) Top, centered
- ( ) Top, flushed right
- ( ) Other (specify)

_____

Continuation pages
- ( ) Bottom, flushed left
- ( ) Bottom, centered
- ( ) Bottom, flushed right
- ( ) Other (specify)

_____

24. Form number and version number keyed as data?
    - ( ) No
    - ( ) Yes (recommended)

E. Date and time format on data collection forms

25. Date format
    - ( ) Day Mon Year (e.g., 14 Feb 2011)
    - ( ) Mon/Day/Year (e.g., 2/14/2011)
    - ( ) Day/Mon/Year (e.g., 14/2/2011)
    - ( ) Other (specify)

_____

26. Time format
    - ( ) 12 hour clock, am, pm
    - ( ) 24 hour clock

F. Section and item numbering

27. Section numbering
    ( ) Alphabetic letter (e.g., A, B, C)
    ( ) Roman numeral (e.g., I, II, III)

28. Item numbering
    ( ) Arabic, continuous across sections
    ( ) Arabic, by section
    ( ) Other (specify) _____

G. Check space layout

29. Position of "Yes-No" check spaces
    ( ) Uniform within and across forms
    ( ) Uniform within a form but not across forms
    ( ) Varied within forms

30. Layout of check list
    ( ) Vertical
        ( ) Check space at immediate left of item
        ( ) Check space at immediate right of item
        ( ) Check space flushed right of item without eye leader
        ( ) Check space flushed right of item with eye leader
    ( ) Horizontal
        ( ) Check space to right of item
        ( ) Check space to left of item

31. Instruction items (check any to be used)
    ( ) Stop items (items with stop signs in check spaces indicating the person completing the form should stop (e.g., such items on a baseline enrollment form indicating the person being screened is not eligible for enrollment because of item checked)
    ( ) Goto items (items instructing persons completing forms as to where to skip to continue)
    ( ) Instruction notice; an instruction in the form informing the person completing the form of conditions or requirements for completion
    ( ) Calculation items (items in which the person completing the form is required to use data collected to calculate a score or measure)

H. Measurement units and decimal precision

32. Measurement units
    Height
        ( ) Feet and inches
        ( ) Meters and centimeters
        ( ) Either

Weight
( ) Pounds
( ) Kilograms
( ) Either

Other (specify)
Measure: _____ Unit _____

Measure: _____ Unit _____

Measure: _____ Unit _____

Measure: _____ Unit _____

33. Decimal precision
( ) Free form
( ) Specified
( ) By instruction
( ) By spaces for recording measurement, e.g., by __.__ for a measurement with two decimals of precision

I. Form sign-off information

34. Location
( ) At end of each form
( ) Other (specify) _____

35. Information to be recorded (check all that apply)
( ) Name of responsible study investigator
( ) Date of completion
( ) Name of clinic coordinator responsible for review of form for completeness
( ) Date of review
( ) Id number of reviewer
( ) Other (specify) _____

WS 4.2 Identifier data worksheet (DataId.WS)

When: When the data system is designed

Who: People responsible for the data system

Purpose: To determine the location of data that may be used to identify study subjects

Instructions

For each entry below check Col 1 or Col 2. For any check in Col 2 ("Clinic records") indicate if the information is also recorded in the study dataset by checks in Col 3, and for checks in Col 3 indicate if the information is also to be in datasets intended for sharing outside the investigator group by checks in Col 4.

Definition

identifier data - 1. Data that are capable of identifying a person by name. 2. Any data regarded as having the potential of identifying a person, such as the list of variables in HIPAA regulations regarded as personal identifiers

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Patient identifying data

4. Patient identifiers	Col 1 Not collected	Col 2 Clinic records	Col 3 Study dataset	Col 4 Shared dataset
Study Id number	( )	( )	( )	( )
Name code	( )	( )	( )	( )
Name	( )	( )	( )	( )
Address	( )	( )	( )	( )
E-mail address	( )	( )	( )	( )
Social security number	( )	( )	( )	( )
Home telephone number	( )	( )	( )	( )
Cell phone number	( )	( )	( )	( )
Place of employment	( )	( )	( )	( )
Work phone number	( )	( )	( )	( )
Medical record numbers	( )	( )	( )	( )
Health plan identifiers	( )	( )	( )	( )

WS 4.2 Identifier data worksheet

	Col 1 Not collected	Col 2 Clinic records	Col 3 Study dataset	Col 4 Shared dataset
Other (specify)				
_____		( )	( )	( )
_____		( )	( )	( )
_____		( )	( )	( )
5. Dates				
Patient's birthdate	( )	( )	( )	( )
Visit dates	( )	( )	( )	( )
Dates of telephone contacts	( )	( )	( )	( )
Other dates (specify)				
_____		( )	( )	( )
_____		( )	( )	( )
_____		( )	( )	( )
6. Other patient identifiers				
Fax number	( )	( )	( )	( )
Certificate/license numbers	( )	( )	( )	( )
Medical device serial numbers	( )	( )	( )	( )
Voice recordings	( )	( )	( )	( )
Finger prints	( )	( )	( )	( )
Face pictures	( )	( )	( )	( )
DNA	( )	( )	( )	( )
Other (specify)				
_____		( )	( )	( )
_____		( )	( )	( )
_____		( )	( )	( )
C. Other identifying data				
7. Names of family relatives	( )	( )	( )	( )
8. Addresses of family relatives	( )	( )	( )	( )
9. Telephone nos of family relatives	( )	( )	( )	( )

WS 4.2 Identifier data worksheet

	Col 1 Not collected	**Col 2** Clinic records	**Col 3** Study dataset	**Col 4** Shared dataset
10. Other (specify)				
_____		( )	( )	( )
_____		( )	( )	( )
_____		( )	( )	( )

CL 4.1 Data collection checklist (DataMap.CL) (completed for ADAPT[1])

Randomization unit
( ) Part of a person
(x) Person
( ) Aggregate of persons

Treatment unit
(x) Person
( ) Household
( ) Geographic unit

Primary observation unit
(x) Person
( ) Household
( ) Geographic unit

Modes of data collection from primary observation unit (check all that apply)
Direct
Face-to-face
(x) @ clinic
( ) @ home
Remote
(x) via telephone
(x) via mail
Indirect
(x) Medical records
( ) Other (specify)

Direct data sources
(x) Enrollee
( ) Family member
(x) Surrogate respondent
( ) Other (specify)

Modes of data generation
(x) Examination
(x) Interview of study subject
(x) Self-administered questionnaire
(x) Medical records
(x) Laboratory tests
( ) Readings
(x) Specimen banks
( ) Other (specify)

5 Data processing tables, worksheets, and checklists

WS 5.1 Data system worksheet (DataSys.WS)

When: Prior to start of data collection

Who: Personnel in the coordinating center

Purpose: To establish the data system for the trial

Definitions

centralized data system - A data system established and maintained at a central site (e.g., the data coordinating center) in a multicenter study used for data entry and data capture.

distributed data system - A data system consisting of component parts that are established and maintained at individual data collection or generation sites for data capture.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Data system

4. Type of data system
   - ( ) Distributed
     - ( ) PC-based
     - ( ) Web-based
   - ( ) Centralized
   - ( ) Other (specify) _____

5. Systems custodian
   - ( ) Coordinating center
   - ( ) Contract research organization
   - ( ) Other (specify) _____

6. System server vendor and location

   Vendor: _____

   Location: _____

7. Backup frequency and location of backup files

   Frequency: _____

Location of backup files: _____

8. Data security protections (check all that apply)
   - ( ) Central authority (typically the coordinating center) for authorizing access to the data system via issue of access password
   - ( ) User password for access to data system
   - ( ) Transmission encryption
   - ( ) Training and certification of persons authorized to access the data system
   - ( ) Other (specify)

     _____

9. System applications (check all that apply)
   - ( ) Treatment assignment
   - ( ) Treatment unmasking
   - ( ) Appointment schedules
   - ( ) Data collection reports
   - ( ) Other (specify)

     _____

WS 5.2 Data access worksheet (DataGet.WS)

When: Early in the course of data collection

Who: Coordinating center personnel in conjunction with other study leaders

Purpose: To specify who has access to study data during and after the trial

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—___—____

B. Data access policy during the trial

4. Access to interim treatment results
   ( ) Restricted to people in the data center and to members of the treatment effects monitoring committee
   ( ) Other (explain)

   _____

   _____

5. Access to interim baseline results by treatment group
   ( ) Restricted to study investigators
   ( ) Access allowed external to investigator group on request (explain)

   _____

6. Access to interim results for control-assigned group (check one)
   ( ) Limited to people in the data center and to members of the treatment effects monitoring committee
   ( ) Summary results periodically presented to study investigators
   ( ) Data available to stydy investigators to produce "natural history" papers on control-assigned group
   ( ) Access allowed external to investigator group on request (explain)

   _____

C. Data access policy internal to the study investigatorship after completion of data collection

7. Access to finished dataset?
   ( ) No (justify)

   _____

   ( ) Yes
   If yes, indicate conditions for access (check all that apply)
   ( ) Signed statement accepting dataset
   ( ) Statement indicating assurance to respect patient privacy
   ( ) Statement indicating willingness to maintain chain of custody of dataset
   ( ) IRB approval
   ( ) Other (specify)

   _____

8. Access to finished dataset for paper writing (check one)
   ( ) Access proscribed
   ( ) Unrestricted access
   ( ) Access subject to approval of study leaders; use for paper writing subject to approval of study leaders and review prior to submission for publication
   ( ) Other (specify)

   _____

D. Access by parties external to the study investigatorship

9. Access to treatment results during the trial (check one)
   ( ) Proscribed
   ( ) Other (specify)

   _____

10. Access to baseline results during the trial (check one)
    ( ) Proscribed
    ( ) Other (specify)

    _____

11. Access to results for control-assigned group during the trial (check one)
    ( ) Proscribed
    ( ) Other (specify)

    _____

12. Data access policy after completion of the trial (check any that apply)
    ( ) No access provided

( ) Access provided on a case-by-case basis after review and approval of request by study leaders
( ) Requests for special analyses considered; if approved by study leaders analyses done by study coordinating center and results provided to requesting party
( ) Deidentified dataset on deposit for unrestricted use
( ) Other (specify)

_____

E. Sign-off approval

13. Name of review and approving authority: _____

14. Date of sign-off (day-month-year) . . . . . __—__—____

WS 5.3 Data editing and auditing worksheet (DataEdit.WS)

When: Early in the course of data collection

Who: Coordinating center personnel

Purpose: To outline plans for data editing and auditing

Definitions

data audit - 1. The comparison of data in a source document with those in a secondary document as a means of checking for discrepancies. 2. A comparison of data in a study form with those recorded in a medical chart for discrepancies. 3. A comparison of specified data elements on a study form with the corresponding elements in an electronic file produced from the study form for discrepancies. *Usage note*: Not to be confused with data edit. See usage note for data edit.

data edit - An instance of a change to data as a result of an edit check. ***Usage note***: Not to be confused with data audit. Typically, data audits in studies involving keyed data forms consist of comparison of what is on the study form with what is keyed; done to find discrepancies between the two sources and to resolve the discrepancies. Data edits involve checks of the information recorded for inconsistencies and correction based on the checks performed.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Data editing

4. Edit checks for data to be admitted to the study database (check all that apply)
   - ( ) Check for permuted numbers in Id number via use of check digits
   - ( ) Check of one-to-one correspondence between Id number and name code
   - ( ) Check of visit number and time window for indicated visit
   - ( ) Other (specify)

     _____

5. Data entry and edit change rules (check all that apply)
   - ( ) Key what is recorded on study forms even if known to be wrong when keyed
   - ( ) Document changes to recorded data on study forms to maintain a one-to-one correspondence between what is recorded on study forms and what is keyed (e.g., by requiring study personnel to date and initial strike outs and to write in data replacing those struck)
   - ( ) No white out on study forms
   - ( ) No changes to data on study forms without bases for changes

( ) Indelible audit trail of edit changes
( ) Other (specify)

_____

6. Types of edit checks performed (check all that apply)
   ( ) Data entry with messages to indicate entry of inadmissible codes and to aid entry for skip patterns
   ( ) Edits within forms
   ( ) Edits across forms
   ( ) Edits triggered by data analysis
   ( ) Other (specify)

_____

7. Edit change freezes (check all that apply)
   ( ) Once a dataset is frozen for data analysis
   ( ) Once a dataset has been distributed to study investigators
   ( ) Once a dataset has been deposited in a public archive
   ( ) Other (specify)

_____

8. Describe process for dealing with data errors discovered in datasets supporting publications, including conditions under which editors are notified of errors

_____

_____

9. Describe process for dealing with data errors discovered in distributed datasets; include details as to how users are informed of errors and conditions under which revised datasets issued

_____

_____

C. Data auditing

10. Percentage of data forms routinely audited (if 0% explain) . . . . . ____%

_____

11. Frequency of routine data audits
    ( ) Daily
    ( ) Weekly
    ( ) Monthly

( ) Once every 6 months
( ) Yearly
( ) Other (specify)

_____

12. Method of selection of records for routine audits
    ( ) Random
    ( ) Other (specify)

_____

13. Person or group responsible for auditing
    ( ) Circuit rider
    ( ) Data coordinating center personnel
    ( ) Other (specify)

_____

14. Site of routine data audits
    ( ) On-site
    ( ) Off-site
        ( ) Data coordinating center
        ( ) Office of study chair
        ( ) Office of the study sponsor
        ( ) Contract research organization
        ( ) Other (specify)

_____

15. Trigger points for cause audits (check all that apply)
    ( ) High discrepancy rate in routine audits
    ( ) Data discrepancies suggestive of data falsification
    ( ) Large number of mismatches between what is keyed versus what is recorded on study forms
    ( ) Other (specify)

_____

16. Authorizing authority for cause audits (check any that apply)
    ( ) Coordinating center
    ( ) Study chair
    ( ) Study sponsor
    ( ) Study steering committee

( ) Other (specify)

_____

17. Summary audit reports prepared and distributed to study investigator?
    ( ) Yes
    ( ) No (explain)

_____

18. In multicenter trials, summary report distributed to all participating centers showing audit results by clinic?
    ( ) Yes
    ( ) No (explain)

_____

WS 5.4 Data processing worksheet (DataKey.WS)

When: Prior to the start of data collection

Who: Data coordinating center personnel

Purpose: To outline data capture and processing procedures

Definitions

data harvest - The act of receiving and assembling data from data collection and generation sites, e.g., as accomplished by a data center in a multicenter trial by downloading data residing at study clinics or by receipt of electronic files from study clinics.

dependent double data entry - Double data entry with both entries performed by the same person.

independent double data entry - Data entry in which data are keyed by different people working independently of each other; as distinct from dependent double data entry.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Data capture and harvest

4. Principal mode of data capture (check one)
   - ( ) Keying directly from study forms at site of completion
   - ( ) Keying directly from study forms at central processing center
   - ( ) Keying from code sheets produced from study forms at site of data collection
   - ( ) Keying from code sheets produced from study forms at central processing site
   - ( ) Direct from screens presented on laptops or personal digital assistants during data collection
   - ( ) Electronic data capture (EDC)
   - ( ) Other (specify)

     _____

5. If the primary mode of data capture involves keying from completed data collection forms, indicate steps taken to minimize time lag from data collection to capture for harvest (check all that apply)
   - ( ) Dedicated data entry personnel
   - ( ) Monitoring performance to show differences in lag time from completion to data entry
   - ( ) Site visits to clinics with poor data entry performance

( ) Other (specify)

_____

_____

6. Frequency of data harvests
   ( ) Daily
   ( ) Weekly
   ( ) Monthly
   ( ) Other (specify)

   _____

7. Data entry principles; check all that apply (skip if the principal mode of data capture is not from data collection forms)
   ( ) Key directly from completed data forms with coding indicated on the data collection forms
   ( ) Instructions to data entry personnel to key what is recorded on forms even if known to be incorrect
   ( ) Maintenance of an electronic audit trail reflecting changes to data as results of data edits
   ( ) Double-dependent data entry
   ( ) Double-independent data entry
   ( ) Training and certification of data entry personnel
   ( ) Monitoring of data entry performance (by clinic in multicenter trials); including calculation of the median time to data entry and interquartile time range from completion of a data form to keying
   ( ) Other (specify)

   _____

   _____

6 Organization tables, worksheets, and checklists

Table 6.1 Organizational elements table (Org.Tab)

When: Early in the design phase of the trial during organization

Who: The study chair or director of the coordinating center

Purpose: To define and list the key organizational units in the trial; review and update over the course of the trial

Related forms: Table 6.3, Table 6.4, Table 6.5

Definitions

executive committee (EC) - A committee within some multicenter leadership structures responsible for direction of the day-to-day affairs of the study and accountable to the steering committee; usually consists of the officers of the study and others selected from the steering committee; typically headed by the chair or vice-chair of the steering committee. rt: **study officers**, **steering committee**

key committee - A committee essential to the operation of a trial; generally any of the following: steering committee, executive committee, study officers, treatment effects monitoring committee, advisory-review and treatment effects monitoring committee, and advisory-review committee in multicenter trials.

research group - The entire set of personnel involved in the conduct of a research project; in multicenter trials includes center directors and related study personnel, representatives from the sponsoring agency, and study committee members; aka: collaborative group, investigative group.

resource center - Any center providing expertise and support in a differentiated study structure apart from clinical centers.

steering committee - A committee of an organization responsible for directing or guiding the activities of that organization. In multicenter trials, the committee responsible for conduct of the trial and to which other study committees report. Usually headed by the study chair and consisting of persons designated or elected to represent study centers, disciplines, or activities. One of the key committees in multicenter structures.

study center - An operational unit in the structure of a study separate and distinct from other such units in the structure, responsible for performing specified functions in one or more stages of the study; e.g., a clinical center or resource center.

study officers - The officers of a study; typically in multicenter trials, the study chair, study vice-chair, coordinating center director, coordinating center deputy director, and project officer; one of the key committees in multicenter structures.

support center - Any center providing service or supply in a differentiated study structure apart from clinics and resource centers.

Table 6.1 Organizational elements table

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __-___-____

4. Funding sources (check all that apply)
   ( ) Drug company
   ( ) NIH
   ( ) Foundation
   ( ) Private donor
   ( ) Other (specify)

   _____

B. Centers

5. Sites where persons are enrolled and followed
   Official name to be used in study documents (check one)
   ( ) Study clinic
   ( ) Study field site
   ( ) Other (specify)

   _____

   Number of sites . . . . . ____

6. Resource centers (centers providing support or services in the study structure, apart from study clinics; check all that apply)
   ( ) Coordinating center
   ( ) Data coordinating center
   ( ) Biostatistics support center
   ( ) Data center
   ( ) Treatment coordinating center
   ( ) Central laboratory
   ( ) Reading center
   ( ) Quality control center
   ( ) Office of sponsor
   ( ) Office of the study chair

Table 6.1 Organizational elements table

( ) Other (specify)

_____

_____

Number of resource centers . . . . . _____

7. Support centers (any center providing service or supply in an organization structure apart from study clinics and resource centers; check all that apply)
   ( ) Central study pharmacy
   ( ) Distribution center
   ( ) Procurement center
   ( ) Procurement and distribution center
   ( ) Other (specify)

   _____

   _____

   Number of support centers . . . . . _____

8. Total number of centers (sum of totals in items 5, 6, and 7) . . . . . _____

C. Study officers and research body (see definitions above)

9. Study head/PI _____

10. Study officers

	Name	Title
1		
2		
3		
4		
5		
6		
7		

Table 6.1 Organizational elements table

	Name	Title
8		
9		
10		

11. Size of research body . . . . . _____

D. Study committees

12. Key committees (check all that apply)
    - ( ) Committee of study officers
    - ( ) Executive committee
    - ( ) Steering committee
    - ( ) Treatment effects monitoring committee
    - ( ) Advisory review committee
    - ( ) Other (specify)

13. Other standing committees (check all that apply)
    - ( ) Protocol committee
    - ( ) Laboratory committee
    - ( ) Publication committee
    - ( ) Analysis committee
    - ( ) Ancillary study committee
    - ( ) Natural history committee
    - ( ) Outcomes/endpoints committee
    - ( ) Other (specify)

14. Total number of committees (sum of entries in items 12 and 13) . . . . . _____

Table 6.2 Study officers committee organization table (Officer.Tab)

When: Early in the course of the trial before the start of enrollment

Who: Study chair or director of the coordinating center

Purpose: To set forth rules for designating study officers in a study structure

Definition

study officers - The officers of a study; typically in multicenter trials, the study chair, study vice-chair, coordinating center director, coordinating center deputy director, and project officer; one of the key committees in multicenter structures.

Reminders

- Study officers are necessary in any formalized study structure. They exist whether or not in the presence of other study committees
- They report to the steering committees in structures having steering committees
- Typically they serve in ex-officio capacities
- Not to be confused with executive committee
- Assume the need for officers committee or executive committee if any of the following apply:
  - Single center trial with multiple investigators
  - Multicenter trial
  - Constituted steering committee
- Create before or in conjunction with creation of the steering committee

A. Identifying information

1. Study name: _____

2. Name of group
   ( ) Study officers
   ( ) Study officers committee
   ( ) Other (specify)

   _____

3. Form completed by: _____

4. Date completed (day-month-year) . . . . . __—___—____

B. Composition

5. Persons designated as study officers (check all that apply)
   ( ) Study chair
   ( ) Study vice-chair
   ( ) Director of coordinating center
   ( ) Deputy director of coordinating center

Table 6.2 Study officers committee organization table

( ) Project officer
( ) Deputy project officer
( ) Other (specify)

_____

6. Officers

	Name	Office
1		
2		
3		
4		
5		
6		
7		
8		

C. Meeting modes and frequency

7. Primary meeting mode
   ( ) Face-to-face
   ( ) Conference phone
   ( ) Other (specify)

   _____

8. Number of meetings per year
   ( ) Weekly
   ( ) Monthly
   ( ) Other (specify)

   _____

Table 6.3 Steering committee organization table (SC.Tab)

When: Early in the course of the trial before the start of enrollment

Who: Study chair or director of the coordinating center

Purpose: To set forth rules for staffing and operating the study steering committee

Definitions

steering committee (SC) - A committee of an organization responsible for directing or guiding the activities of that organization. In multicenter trials, the committee responsible for conduct of the trial and to which other study committees report. Usually headed by the study chair and consisting of persons designated or elected to represent study centers, disciplines, or activities. One of the key committees in multicenter structures.

representation construct - Any of various constructs used for representation on the key governing bodies of multicenter studies or study networks; includes advocacy representation, aristocracy representation, center representation, discipline representation, and PI representation.

advocacy representation construct - A representation construct based on advocacy, e.g., one where membership on the steering committee includes persons external to the study chosen to advocate a position or to represent an interest.

aristocracy representation construct - [multicenter studies] A representation construct limited to founding members, e.g., one where membership on the steering committee is limited to persons responsible for getting the study funded.

center representation construct - A representation construct for the governing body of a multicenter trial based on center, e.g., one where membership is by center or one where voting in the governing body is by center.

discipline representation construct - A representation construct for steering committees in multicenter study structures based on disciplines, e.g., one where membership on the steering committee is apportioned by disciplines in the structure.

PI representation construct - [multicenter studies] A leadership representation construct based on PI-ship, especially one where voting membership on the steering committee is limited to PIs.

A. Identifying information

1. Study name: _____

2. Official name of committee
   ( ) Steering committee
   ( ) Other (specify)

   _____

3. Form completed by: _____

Table 6.3 Steering committee organization table

4. Date completed (day-month-year) . . . . . __—__—____

B. Mode of representation

5. Primary representation mode (check one)
   ( ) Advocacy representation
   ( ) Aristocracy representation
   ( ) Center representation
   ( ) Discipline representation
   ( ) PI representation
   ( ) Other (specify)

   _____

6. Secondary representation mode (check all that apply)
   ( ) No secondary representation
   ( ) Advocacy representation
   ( ) Aristocracy representation
   ( ) Center representation
   ( ) Discipline representation
   ( ) PI representation
   ( ) Other (specify)

   _____

C. Representation definitions

7. Advocacy representation (skip if not checked in items 5 or 6)
   ( ) Person with the disease or condition being treated
   ( ) Representative of advocacy lobbying group
   ( ) Other (specify)

   _____

8. Aristocracy representation (skip if not checked in items 5 or 6)
   ( ) Study officers
   ( ) Heads of original set of clinics
   ( ) Other (specify)

   _____

9. Center representation (skip if not checked in items 5 or 6)
   ( ) Clinical centers only
   ( ) Clinical centers and resource centers
   ( ) Other (specify)

   _____

Table 6.3 Steering committee organization table

10. Disciplines representation (skip if not checked in items 5 or 6)
    ( ) Person(s) responsible for treating the condition of interest
    ( ) Clinic coordinator
    ( ) Other (specify)

    _____

11. PI representation (skip if not checked in items 5 or 6)
    ( ) Heads of clinical centers only
    ( ) Heads of clinical or resource centers
    ( ) Other (specify)

    _____

D. Chair

12. Mode of designation
    ( ) Administrative fiat
    ( ) Appointment (specify appointing authority)

    _____

    ( ) Election (specify electing body)

    _____

    ( ) Other (specify)

    _____

13. Term of office
    ( ) Without term
    ( ) With term (specify length of term) _____
        ( ) Single nonrenewable term
        ( ) Renewable term

14. Chair name and title

    Name: _____

    Title: _____

E. Vice chair

15. Vice chair
    ( ) Designated
    ( ) Not designated (skip to next section)

Table 6.3 Steering committee organization table

16. Vice chair name and title

    Name: _____

    Title: _____

17. Mode of designation
    ( ) Administrative fiat
    ( ) Appointment (specify appointing authority)

    _____

    ( ) Election (specify electing body)

    _____

    ( ) Other (specify)

    _____

18. Term of office
    ( ) Without term
    ( ) With term (specify length of term) _____
        ( ) Single nonrenewable term
        ( ) Renewable term

F. SC membership and composition

19. Voting members

	Name	Study title
1		
2		
3		
4		
5		
6		
7		
8		

Table 6.3 Steering committee organization table

	Name	Study title
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		

20. Nonvoting members

	Name	Position
1		
2		
3		
4		
5		

21. Total number of members

Number voting . . . . . ____

Number nonvoting . . . . . ____

Total number . . . . . ____

Table 6.3 Steering committee organization table

22. Composition by study affiliation

Number of members from study research group . . . . . ____

Number of members not affiliated with study research group . . . . . ____

Total number . . . . . ____

23. Composition by position

Clinical center heads . . . . . ____

Resource center heads . . . . . ____

Study officers . . . . . ____

Project officers . . . . . ____

Clinic coordinators . . . . . ____

24. Composition by degree

MD . . . . . ____

PhD . . . . . ____

Other medical degrees . . . . . ____

Other research degrees . . . . . ____

25. Composition by term

Number members elected . . . . . ____

With term . . . . . ____

Without term . . . . . ____

G. Committee rules and operating procedures

26. Quorum requirement (check one)

( ) Majority of voting members and chair or vice chair
( ) Majority of voting members
( ) Two-thirds of voting members and chair or vice chair
( ) Two-thirds of voting members
( ) Other (specify)

27. Primary voting mode for protocol changes
    ( ) Secret ballot
    ( ) Roll call
    ( ) Show of hands
    ( ) Other (specify)

28. Absentee votes
    ( ) Allowed
    ( ) Not allowed

29. Proxy votes
    ( ) Allowed
    ( ) Not allowed

H. Meeting modes and frequency

30. Primary meeting mode
    ( ) Face-to-face
    ( ) Conference phone
    ( ) Other (specify)

31. Number of meetings per year (excluding "as necessary" meetings)
    ( ) One
    ( ) Two
    ( ) Three
    ( ) Four
    ( ) More than four; specify number . . . . . ___

I. Sign-off approval

32. Name of review and approving authority _____

33. Date of sign-off (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

Table 6.4 Executive committee organization table (EC.Tab)

When: Early in the course of the trial before the start of enrollment

Who: Study chair or director of the coordinating center

Purpose: To set forth rules for staffing the study steering committee

Definition

executive committee (EC) - A committee within some multicenter leadership structures responsible for direction of the day-to-day affairs of the study and accountable to the steering committee; usually consists of the officers of the study and others selected from the steering committee; typically headed by the chair or vice-chair of the steering committee.

Reminders

- Executive committee, as used herein, is not to be confused with steering committee. In this document steering committee is regarded as the premiere leadership body. The executive committee under this nomenclature is subservient to the steering committee
- Assume the need for an executive committee if any of the following apply:
  - Multicenter trial
  - Steering committee consists of 10 or more members
  - Steering committee not constituted to deal with the executive functions of the trial
- Create before or in conjunction with creation of the steering committee

A. Identifying information

1. Study name: _____

2. Official name of committee being created
   ( ) Steering committee
   ( ) Other (specify)

   _____

3. Form completed by: _____

4. Date completed (day-month-year) . . . . . __—___—_____

B. Composition

5. Members

	Name	Title
1		
2		

Table 6.4 Executive committee organization table

	Name	Title
3		
4		
5		
6		
7		
8		
9		
10		

6. Membership

   Number voting . . . . . ____

   Number nonvoting . . . . . ____

   Total number . . . . . ____

7. Composition by study affiliation

   Number members from study research group . . . . . ____

   Number members not affiliated with study research group . . . . . ____

   Total number . . . . . ____

8. Composition by position

   Clinical center heads . . . . . ____

   Resource center heads . . . . . ____

   Study officers . . . . . ____

   Sponsor project officers . . . . . ____

   Clinic coordinators . . . . . ____

Table 6.4 Executive committee organization table

9. Composition by term

   With term . . . . . ____

   Without term . . . . . ____

10. Study officers seated as ex-officio members of the EC (check all that apply)
    ( ) Study chair
    ( ) Study vice-chair
    ( ) Director of coordinating center
    ( ) Deputy director of coordinating center
    ( ) Project officer
    ( ) Deputy project officer
    ( ) Other (specify)

    _____

C. Meeting modes and frequency

11. Primary meeting mode
    ( ) Face-to-face
    ( ) Conference phone
    ( ) Other (specify)

    _____

12. Frequency of meetings
    ( ) Weekly
    ( ) Twice monthly
    ( ) Monthly
    ( ) Other (specify)

    _____

Table 6.5 Treatment effects monitoring committee organization table (TEMC.Tab)

When: Before the start of enrollment

Who: Study leaders in conjunction with the study sponsors

Purpose: To establish the organizational structure for treatment effects monitoring

Definition

treatment effects monitoring committee (TEMC) - A standing committee in the structure of single or multicenter trials responsible for the periodic review of accumulating data for evidence of adverse or beneficial treatment effects and for making recommendations for modification of a study treatment, including termination, when appropriate. One of the key committees in the organizational structure of a multicenter trial; usually constituted such that voting privileges are restricted to members not directly involved in the execution of the trial and not associated with participating centers or sponsors of the trial. Others, such as officers of the study or other key study investigators, if included as members, usually serve without vote. Voting members are appointed by the sponsor or research group, often with the advice and consent of the other party. The committee reports to the appointing authority and usually to the other party via the appointing authority or directly. syn: data monitoring committee, data and safety monitoring committee, safety monitoring committee

A. Identifying information

1. Study name: _____

2. Official name of committee
   ( ) Data monitoring committee (DMC)
   ( ) Data and safety monitoring committee (DSMC)
   ( ) Data and safety monitoring board (DSMB)
   ( ) Treatment effects monitoring committee (TEMC)
   ( ) Other (specify)

   _____

3. Form completed by: _____

4. Date completed (day-month-year) . . . . . __—___—____

B. Vetting and appointing authority

5. Who vets voting members of the committee?
   ( ) Study investigators
   ( ) Study sponsor
   ( ) Jointly by study investigators and sponsor

Table 6.5 Treatment effects monitoring committee organization table

( ) Other (specify)

_____

6. Who writes the letter of appointment to vetted members?
   ( ) Study investigators
   ( ) Study sponsor
   ( ) Jointly by study investigators and sponsor
   ( ) Other (specify)

_____

C. Composition

7. Number of members?
   Number voting members . . . . . _____
   Number nonvoting members . . . . . _____
   Total number. . . . . _____

8. Credentials represented in voting members? (check all that apply)
   ( ) Experience treating the condition of interest
   ( ) Medical ethics
   ( ) Experience doing randomized trials
   ( ) Biostatistics
   ( ) Epidemiology
   ( ) Other (specify)

_____

9. TEMC chair qualifications (check all that apply)
   ( ) Experience treating the condition of interest
   ( ) Medical ethics
   ( ) Experience doing randomized trials
   ( ) Biostatistics
   ( ) Epidemiology
   ( ) Other (specify)

_____

10. Nonvoting members of the committee (check all that apply)
    ( ) Study chair/PI
    ( ) Director of coordinating center
    ( ) Study sponsor

Table 6.5 Treatment effects monitoring committee organization table

( ) Other (specify)

_____

11. Standing of nonvoting members relative to voting members (check all that apply)
    ( ) At parity except for voting
    ( ) Excused when results presented
    ( ) Present when results presented, but excused when votes are taken
    ( ) Other (specify)

_____

12. Quorum requirement (check one)
    ( ) Chair or vice chair of TEMC and majority of voting members
    ( ) Chair or vice chair of TEMC and majority of voting and non-voting members
    ( ) Other (specify)

_____

D. Operations

13. Written charge?
    ( ) No
    ( ) Yes
    If yes, written by whom?
    ( ) Study investigators
    ( ) Study sponsor
    ( ) TEMC
    ( ) Other (specify)

_____

14. Meeting frequency?
    ( ) Calendar driven
    ( ) Once yearly
    ( ) Twice yearly
    ( ) Other (specify)

_____

    ( ) Event/landmark driven
    ( ) After specified numbers of events (specify)

_____

Table 6.5 Treatment effects monitoring committee organization table

( ) After enrollment of specified numbers of people (specify)

_____

( ) Other (specify)

_____

15. Compensation for voting members?
    ( ) No
    ( ) Yes
    If yes
    Mode of compensation
    ( ) Retainer (amount) . . . . . _____
    ( ) Per face-to-face meeting (amount) . . . . . _____
    ( ) Per conference phone meeting (amount) . . . . . _____

16. Objectivity constructs imposed
    ( ) No objectivity constructs
    ( ) Stopping rule
    ( ) Stopping guideline
    ( ) Masking
    ( ) Restrictions on number of looks to be performed
    ( ) Other (specify)

_____

17. TEMC reporting structure
    ( ) From TEMC chair to study chair/study PI
    ( ) From TEMC chair to study sponsor and from study sponsor to study chair/study PI
    ( ) From TEMC chair simultaneous to study chair/study PI and study sponsor
    ( ) Other (specify)

_____

18. Treatment effects monitoring reports prepared by (check one):
    ( ) Coordinating center/data center
    ( ) Study sponsor
    ( ) Contract research organization
    ( ) Other (specify)

_____

E. Sign-off approval

Table 6.5 Treatment effects monitoring committee organization table

19. Name of review and approving authority: _____

20. Date of sign-off (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

Table 6.6 Considerations leading to a separate ARC and TEMC or combined ARTEMC (TEM&ARC.Tab)

When: Early in planning, prior to decisions on approach to treatment effects monitoring

Who: Study officers

Purpose: To decide whether to create an advisory review committee independent of the treatment effects monitoring committee

Definitions

advisory-review - Of or relating to providing advice and review; in relation to trials primarily in relation to the design and operation of the trial for the benefit of study investigators and sponsors and offered by persons or a committee independent of the investigators and sponsor.

advisory-review committee (ARC) - [trials] A committee in the organizational structure of a trial responsible for reviewing the design and operations of the trial for the purpose of advising investigators related to the trial; voting members usually not involved in the execution of the trial or associated with any of the participating centers or sponsor of the trial. Selected investigators from the trial may serve as nonvoting members. A committee in the organizational structure of some multicenter treatment trials with method of appointment and route of reporting similar to that described for treatment effects monitoring committee. aka: advisory board, advisory committee, policy-advisory board, policy-advisory committee, policy board, policy committee.

advisory-review and treatment effects monitoring committee (ARTEMC) - A committee that performs the functions of both an advisory-review committee and treatment effects monitoring committee.

treatment effects monitoring committee (TEMC) - [trials] A standing committee in the structure of single or multicenter trials responsible for the periodic review of accumulating data for evidence of adverse or beneficial treatment effects and for making recommendations for modification of a study treatment, including termination, when appropriate. One of the key committees in the organizational structure of a multicenter trial; usually constituted such that voting privileges are restricted to members not directly involved in the execution of the trial and not associated with participating centers or sponsors of the trial.

Considerations for separate ARC and TEMC

- When treatment monitoring activities require frequent meetings and where each meeting requires a half day or more to carry out the necessary data reviews
- When the TEMC meets other general analysis needs of the study (e.g., is responsible for developing analytic approaches for dealing with special analytic problems)
- When the meeting schedule for review is different than that for treatment effects monitoring
- When the trial is investigator-initiated and grant-supported
- When the sponsor and/or investigators desire separate committees

Table 6.6 Separate ARC and TEMC vs combined ARTEMC

Considerations for combined ARTEMC

- When the time required for treatment monitoring is not great relative to the time required to perform more general advisory and review functions
- When there is little or no need for advice or guidance concerning the analysis procedures used for assessing treatment effects
- When the trial is sponsor-initiated
- When the sponsor and/or investigators desire a single combined committee

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Advisory review functions

4. Desired investigator advisory-review functions (check all that apply)
   - ( ) None
   - ( ) Review of the study protocol
   - ( ) Approval of the study protocol
   - ( ) Review to provide go ahead for initiation of enrollment
   - ( ) Review of major protocol changes before implementation
   - ( ) Review of changes in sample size requirements
   - ( ) Review of proposal to change the primary outcome measure
   - ( ) Review of revision of the timetable for the trial
   - ( ) Review of ancillary study proposals
   - ( ) Review of uses of banked specimens
   - ( ) Review of study publications
   - ( ) Other (specify)

     _____

5. Desired sponsor advisory and review functions (check all that apply)
   - ( ) None
   - ( ) Review and approval of the study protocol before implementation of enrollment
   - ( ) Review of major protocol changes before implementation
   - ( ) Review of change in sample size requirements
   - ( ) Review of proposal to change the primary outcome measure
   - ( ) Review of revision of the timetable for the trial
   - ( ) Review of recommendations to add clinical centers
   - ( ) Review of performance of clinical and resource centers
   - ( ) Review of recommendations to terminate funding for centers not performing adequately

Table 6.6 Separate ARC and TEMC vs combined ARTEMC

( ) Review of study publications
( ) Other (specify)

WS 6.1 Research group organization worksheet (RG.WS)

When: The trial is being organized

Who: A study officer

Purpose: To set forth principles of composition of the research group

Definition

research group - The entire set of personnel involved in the conduct of a research project; in multicenter trials, includes center directors and related study personnel, representatives from the sponsoring agency, and study committee members; aka collaborative group, investigative group, study group.

A. Identifying information

1. Study name: _____

2. Official name of research group
   ( ) Research Group
   ( ) Collaborative Group
   ( ) Study Group
   ( ) Other (specify)

   _____

3. Form completed by: _____

4. Date completed (day-month-year) . . . . . __—___—____

B. Composition

5. Basis for membership (check all that apply)
   ( ) Certified by the coordinating center to perform specified study functions
   ( ) Receives salary support from the study
   ( ) Listed as members by center directors
   ( ) Involved as an author on a study publication
   ( ) Other (specify)

   _____

6. Are members listed in a directory?
   ( ) Yes
   ( ) No (explain)

   _____

7. Who maintains the directory?
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

8. Does the directory listing include past members of the research group
   ( ) Yes
   ( ) No

9. Who has access to the directory? (check one)
   ( ) Anyone receiving a printed copy of the directory
   ( ) Anyone with access to the password-protected study website
   ( ) Open; posted to a public website
   ( ) Other (specify)

   _____

C. Modes of communications and meetings

10. Principal modes of communications with the research group: (check one)
    ( ) E-mail
    ( ) Letter
    ( ) Telephone
    ( ) Conference telephone (specify frequency)
        ( ) As needed
        ( ) Weekly
        ( ) Monthly
        ( ) Other (specify) _____
    ( ) Face-to-face meetings (specify frequency)
        ( ) As needed
        ( ) Twice yearly
        ( ) Once yearly
        ( ) Other (specify) _____

WS 6.2 Committee organization and meeting rules worksheet (MeetRule.WS)

When: In conjunction with creation of a key committee

Who: The chair or vice chair of the committee

Purpose: To put forth basic organization and operating rules for the committee

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Committee to which form pertains (check one)
   ( ) Steering committee
   ( ) Executive committee
   ( ) Study officers committee
   ( ) Treatments effects monitoring committee
   ( ) Other (specify)

   _____

4. Date (day-month-year) . . . . . __–__–____

B. Chair and vice-chair

5. Chair

   Name: _____

   Method of selection
   ( ) Appointment
   ( ) Election
   ( ) Fiat
   ( ) Other (specify)

   _____

   Term
   ( ) Without term
   ( ) With term (specify term)

   _____

   ( ) Renewable
   ( ) Not renewable

6. Vice chair

   Name: _____

   Method of selection
   - ( ) Appointment
   - ( ) Election
   - ( ) Fiat
   - ( ) Other (specify)

     _____

   Term
   - ( ) Without term
   - ( ) With term (specify term)

     _____

     - ( ) Renewable
     - ( ) Not renewable

C. Membership

7. Mode of designation
   - ( ) By appointment (specify appointing authority)

     _____

   - ( ) By election (specify electing body)

     _____

   - ( ) By virtue of positions in study (specify positions)

     _____

   - ( ) Other (specify)

     _____

8. Members

   _____ Voting members

   _____ Nonvoting members

   _____ Total number

9. Terms
   ( ) Without term
   ( ) With term (specify)

_____

D. Rules and meeting procedures

10. Quorum requirement (specify)

_____

11. Primary mode of voting
    ( ) Ballot
    ( ) Show of hands
    ( ) E-mail
    ( ) Other (specify)

_____

12. Voting rules
    Absentee votes
    ( ) Allowed
    ( ) Not allowed
    Proxy votes
    ( ) Allowed
    ( ) Not allowed

13. Primary meeting mode
    ( ) Face-to-face
    ( ) Conference phone
    ( ) Other (specify)

_____

14. Rules of order
    ( ) Robert's
    ( ) Other (specify)

_____

E. Housekeeping

15. Rapporteur _____

16. Location of repository of minutes

WS 6.3 Credits and acknowledgments worksheet (Credit.WS)

When: Early in the course of the trial

Who: A person designated by the study chair; typically a person located in the office of the study chair/PI or in the study coordinating center

Purpose: To establish and maintain a list of credits and acknowledgments for use in study documents and publications

Definitions

acknowledgment - A written expression of such appreciation or thanks, e.g., as appearing in a published manuscript.

study credit roster - A list or roll of names of persons, institutions, businesses, agencies, or organizations having some role, function, or association with a study; such a list as appearing at the end of a study manuscript.

full study credit roster - A roster of all study centers and all members of the research group, past and present; such a list of current centers and current members of the research group.

partial study credit roster - A credit roster of selected study centers or of selected members of the research group.

study directory - A directory of centers and personnel involved in a study; such a directory maintained over the life of a study.

Reminders

- The credit and acknowledgment list in a publication will be incomplete without efforts to maintain the list as the study proceeds
- A full study credit roster can always be abridged but the reverse is not possible
- Ninety percent of the effort in credit rosters is in maintaining them

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . ___—___—_____

B. Study directory

4. Content of basic study directory (check all that apply)
   - ( ) Present and past participating clinics
   - ( ) Present and past participating resource centers
   - ( ) Present and past study personnel by center
   - ( ) Subdirectories of personnel by study function
   - ( ) Study committees and composition

( ) Other (specify)

_____

5. Form of study directory (check one)
   ( ) Electronic
   ( ) Paper
   ( ) Both

C. Credit formats and rosters

6. Centers listing
   ( ) Differentiated, e.g., list of clinical centers and locations followed by list of resource centers and their respective locations
   ( ) Undifferentiated, e.g., alphabetic listing of centers without indication as to whether a clinic or resource center
   ( ) Other (specify)

   _____

7. Personnel listing
   ( ) Differentiated, e.g., list of clinical centers and locations followed by list of resource centers and their respective locations
   ( ) Undifferentiated, e.g., alphabetic listing of centers without indication as to whether a clinic or resource center
   ( ) Other (specify)

   _____

8. Committee listing
   ( ) Current membership
   ( ) Present and past members
   ( ) Other (specify)

   _____

9. Does the study maintain a cumulative credit roster of all members of the research group from beginning to present? (recommended)
   ( ) No
   ( ) Yes

   If yes
   Who is responsible for maintaining the roster?

   _____

10. Does the study maintain an abbreviated study credit roster? (recommended)
    ( ) No
    ( ) Yes

    If yes
    Who is responsible for maintaining it?

    _____

D. Acknowledgments list

11. Does the study maintain an acknowledgment list? (recommended)
    ( ) No
    ( ) Yes

    If yes
    Who is responsible for maintaining the list?

    _____

12. Contents of the acknowledgment list (check all that apply)
    ( ) Sponsoring agency
    ( ) Funding sources; including grant and contract numbers in the case of NIH funding
    ( ) Drug suppliers
    ( ) Suppliers of study equipment
    ( ) Other (specify)

    _____

    _____

7 Operations tables, worksheets, and checklists

Table 7.1 Coordinating center activities by stage of multicenter trial (CCStage.Tab)

Initial design stage

- Calculate required sample size
- Outline data collection schedule, quality control procedures, data analysis plans, and data intake and editing procedures
- Develop organizational structure of the trial
- Prepare funding proposal for coordinating center
- Coordinate preparation of the funding applications

Protocol development stage

- Develop treatment assignment procedures
- Develop data system and related computer programs for receiving, processing and editing data
- Design and test data collection forms
- Develop interface for data transmission from clinics and other resource centers to coordinating center
- Train clinic personnel in required data collection procedures
- For trials with distributed data systems, train clinic personnel for data entry
- Implement clinic and personnel certification procedures
- Distribute study data forms
- Develop manuals and handbooks needed in the trial, including the treatment protocol, clinic manual of operations/handbook, coordinating center manual of operations/handbook, etc.
- Establish repository for official records of the study, including minutes of meetings, manuals/handbooks, etc.
- Serve as funding center for trial operated under a consortium mode of funding unless function fulfilled by some other center
- Serve as the procurement and payment center for general study needs, such as drug purchase and packaging, study insurance if desired, laboratory services, etc., when not performed elsewhere in the study structure

Patient recruitment stage

- Administer treatment assignment process, including monitoring for breakdowns in the assignment process
- Assume leadership role in outlining study needs for quality assurance
- Implement editing procedures to detect data deficiencies
- Develop procedures for monitoring performance of clinics in regard to enrollment, followup, adherence to the protocol, and data collection
- Develop treatment effects monitoring procedures
- Site visit to participating clinics
- Prepare study progress reports for submission to sponsor
- Prepare, in conjunction with the study leadership, renewal or supplemental funding requests as needed
- Update study manuals and handbooks

Treatment and followup stage

- Prepare data reports for treatment effects monitoring committee
- Prepare reports on performance of clinical and resource centers
- Carry out training sessions to maintain proficiency at clinics in treatment and data collection procedures
- Evaluate data processing procedures and modify as necessary
- Develop and test data collection forms for close-out stage
- Prepare summary of study results for presentation to participating investigators for use in close-out stage
- Locate study participants lost to followup
- Review study priorities and propose changes in the organizational and operating structure of the trial as needed
- Assume major role in writing paper on design, methods, and baseline results

Table 7.1 Coordinating center activities by stage of multicenter trial

Patient close-out stage

- Monitor for adherence to established patient close-out procedures
- Develop plans for final data editing
- Design and test computer programs needed for final data analysis
- Develop plans for final disposition of study data
- Coordinate logistics of patient disengagement from treatment
- Assume key role in primary results papers
- Develop plans for disengagement of clinical centers from the trial

Termination stage

- Perform final data edit and undertake final analysis of data according to plans outlined by study leadership
- Implement study plans for disposition of study records
- Assume leadership role in paper writing activities
- Undertake extra measures to locate patients lost to followup
- Supervise collection and disposal of unused study medications
- Distribute draft manuscripts and published papers to participating centers
- Serve as funding center for activities in the trial after termination of support for clinics

Post-trial followup stage (optional)

- Compile a list of patients eligible for post-trial followup
- Implement procedures to locate patients whose current whereabouts are unknown
- Coordinate mailings, telephone calls, or clinic visits required for post-trial followup
- Update existing data files with data collected during post-trial followup
- Assume leadership role in drafting and distributing manuscripts using post-trial followup results
- Ensure storage, under adequate security, of names of study patients and other identifying information for possible future contact or followup

Table 7.2 Treatment effects monitoring issues and recommendations (TEMCRec.Tab)

Philosophical issues	
Whether to monitor	Assume need unless one can argue that absence of monitoring does not pose risk for persons studied
Monitoring policy	Should be set by investigators with advice and consent role for sponsor
Monitoring body	Preferred approach is one involving a dedicated body commissioned specifically for monitoring
Responsibility	Conducting periodic reviews of interim data from the trial for the purpose of recommending whether the trial should proceed unaltered; authority should be as a recommending body as distinct from decision making body
Reporting	Recommendations should be reported directly to study investigators (via Study Chair) or simultaneous to study investigators and sponsor
Written rules	Ideally yes; should be written by study investigators; if written by the monitoring body then with the advice and consent of investigators
Masked monitoring	Not recommended because of impact on competency
Firewalls	Not recommended because of impact on competency
Look restrictions	Not recommended because of impact on competency
Stopping rules	Not recommended because of impact on competency
Stopping guidelines	Optional provided they are not seen as rules
Commissioning	
Vetting authority	Investigators with the advice and consent of the sponsor, or sponsor with the advice and consent of the investigators
Appointing authority	Investigators with the advice and consent of the sponsor, or sponsor with the advice and consent of the investigators
Chair	Person with credentials in the medical field of interest or experienced in trials; independent of the study and sponsor
Term limit	Not recommended
Attendance requirement	Preferred; requirement should be part of the vetting process and should be stated in the letter of appointment
Pay for members	Yes for voting members; no for nonvoting members
Payor	The study or sponsor; preferably the study
Amount	Modest; not so large so as to make members reluctant to recommend stopping because doing so will end their pay
Membership	
Composition	People with the collective disciplines, skills, and areas of expertise needed to ensure competent monitoring
Size (voting and nonvoting)	No larger than necessary consistent with competency requirements
Voting members	Independent of the study and sponsor
Ethicist	Optional
Lay representative	Optional

Table 7.2 Treatment effects monitoring issues and recommendations

Patient advocate	Optional
Activists	Optional
Nonvoting members	Study officers
Study representatives	Yes, as nonvoting members; typically, the study officers
Treater from the trial	All things considered, preferred
Membership parity	The same for all members except for act of voting
Membership listing	Listing should include all members; voting and non-voting
Meetings	
Frequency	At least twice a year; more often if necessary
Mode	Preferably face-to-face at least once per year
Time and location	Weekday; convenient site
Quorum	Specified in rules for the committee when formed; should include quorum requirement for voting and for nonvoting members
Absentee and proxy votes	No
Executive sessions	No
Operations	
Conflict of interest disclosure	Yes; disclosure should be part of the initial vetting process; disclosures should be updated on an annual basis
Report production	Coordinating Center
Distribution of reports	Coordinating Center
Report repository	Coordinating Center
Rapporteur	Typically, study staff from the Coordinating Center or Office of the Chair
Reporting to IRBs	Typically, via the Coordinating Center

Table 7.3 Guidelines for committee operations (CommOp.Tab)

A. General

- Create no more committees than necessary
- Provide a written charge for each committee outlining charge and function
- Indicate the individual or group that has authority to appoint or dissolve committees
- Avoid overlap of responsibilities with other committees
- Outline the relationship of one committee to another and the communication structure for committee-to-committee interactions
- Specify whether or not a committee has decision-making authority; if so, indicate areas of authority

B. Chair

- Specify the method of selection (e.g., election or appointment) and the term of office
- Designate a chair for each committee created; a vice-chair should also be designated for any committee that is to perform essential ongoing functions in the trial

C. Membership

- Specify the membership criteria for each committee
- Specify the methods to be used for rotation of members (if any), for filling vacancies, and for replacing non-functioning members
- Indicate ex-officio committee positions (e.g., chair of the study, director of the coordinating center and whether seated with or without vote)
- Specify conditions that disqualify individuals from filling a committee position, including conflicts of interest

D. Voting

- Specify quorum requirement for conduct of business
- Identify voting and nonvoting committee members and ex-officio voting and nonvoting positions
- Specify committee voting rules

E. Documentation and maintenance

- Maintain up-to-date list of committee members, their respective terms of office, and voting rights
- Designate an individual to serve as committee secretary
- Carry out periodic reviews in which committee charges are updated and committee-to-committee communication structures revised, where appropriate
- Dissolve committees that have completed their work or that are no longer functional

Table 7.4 Dos and don’ts for production of format robust documents (DoTemp.Tab)

Do

Establish and promulgate rules and procedures for document production, including rules on use of headers and footers
Tab paragraphs
Use white space to separate paragraphs in text documents
Use special marks to denote the end of documents, tables, and figures
Use italics or boldface (not underline) for emphasis
Use headers to indicate chapters and sections in manuscripts, manuals, handbooks, and monitoring reports
Use footers to indicate date of creation or of last update, producer, and file location
Use right or decimal align tabs to array arithmetic numbers in tables
Strip document of unnecessary electronic codes and settings (just trouble waiting to happen)
Turn widow and orphan protection on when producing text documents
Page number
Practice good housekeeping procedures; get rid of extra codes; turn off features turned on in the document at end of document; discontinue headers and footers

Don’t

Use the space bar to arrange or position text; the extra spaces will cause text to be in disarray when imported into a document with font or printer definitions different from those in place when the document was created
Use the tab key to position text; extra tabs will be problematic if font or pitch is changed
Intermingle use of the tab and indent key even if the two codes appear to create the same effect; the difference in function is not noticed until or unless text breaks to a second line
Use underlining or all capital for emphasis (underlined text and all cap text is harder to read)
Start new paragraphs without indenting, i.e., no "block paragraphing"
Left align arithmetic numerals in data tables
Use the enter key to manage line breaks; let the word processor do the managing
Use hard returns to manage page breaks; use "block protect", "conditional end of page" code, or other word processor features to do the managing
Turn on features not used
Leave features turned on; the codes are active and will influence text down stream when retrieved into a master document
Create documents using the default setting provided by the vendor

Table 7.5 Template and master document format specification worksheet (Format.Tab)

Template specifications

Page orientation
( ) Portrait (recommended)
( ) Landscape
( ) Mixed (best avoided, especially if documents are to be assembled into a master document)

Page margins

_____ Top (0.75" recommended)

_____ Bottom (0.75" recommended)

_____ Left (1" recommended)

_____ Right (1" recommended)

Font

Face _____

Point size ____

Page numbering
( ) No
( ) Yes (recommended)
Style
( ) Roman
( ) Arabic
Position
One-sided print
( ) Top right (recommended)
( ) Top center
( ) Bottom right
( ) Bottom center
Two-sided print
( ) Top outer (recommended)
( ) Top center
( ) Bottom outer
( ) Bottom center
Property
( ) Continuous (recommended)
( ) By section/chapter

Document settings
( ) Center page (recommended for "table" templates)
( ) Force odd page start (recommended for "chapter" templates)
( ) Orphan protection (recommended)

Table 7.5 Template and master document format specification worksheet

( ) Widow protection (recommended)
( ) Left justification
( ) Right justification (not recommended)

1st page suppressions
( ) Headers and footers
( ) Headers, footers, and page number
( ) Headers and footers; page number at bottom center
( ) Main header only
( ) Other (specify)

_____

Markings
( ) Mark title for list generation
( ) Mark title for table of contents generation
( ) Mark section headings for list generation
( ) Mark section headings for table of contents generation

End codes
( ) Discontinue headers/footers
( ) Hard page code
( ) Other (specify)

_____

Master document specifications

Document type
( ) Study protocol
( ) Study manual of operations/study handbook
( ) Treatment effects monitoring report
( ) Performance monitoring report
( ) Steering committee meeting book
( ) Research group meeting book
( ) Results manuscript
( ) Other (specify)

_____

Front matter
( ) Title and date
( ) Place of production
( ) Table of contents

Paper stock
Size
( ) 8.5x11"
( ) 8.5x14"

Table 7.5 Template and master document format specification worksheet

Color
( ) White
( ) Other _____

Weight
( ) 20 lb
( ) Other _____

Three hole paper
( ) Yes
( ) No

Print side
( ) One side (recommended for working documents)
( ) Both sides (not recommended absent page numbering, headers, and footers designed for two-sided printing)

Dividers
( ) No
( ) Yes

Number . . . . . ____

Labeling _____

Binding
( ) Paper clip (not acceptable)
( ) Bull clip (generally not advisable)
( ) Stapled, top left corner
( ) Stapled, top, center, and bottom left
( ) 3-ring loose leaf notebook (preferred for meetings involving review of tables, e.g., as in treatment effects monitoring reports)
( ) Single O ring (not recommended)
( ) O ring, top and bottom (acceptable)
( ) Other

_____

Covers
( ) Front
( ) Back
( ) Spine

Table 7.5 Template and master document format specification worksheet

Production

_____ Number of distribution copies

_____ Number of file copies

_____ Number of extra copies

_____ Total number

Mode of distribution
( ) Electronic (acceptable but rarely as sole means for important documents)
( ) Mailed
  ( ) Regular mail
  ( ) Commercial courier
( ) Hand delivered at meeting

Place of production: _____

Due date (day-month-year) . . . . . __—___—_____

WS 7.1 Document production and archiving worksheet (DocMake.WS)

When: Early in the design phase of the trial

Who: Coordinating center personnel in conjunction with the study chair

Purpose: To establish production and archiving locations for key study documents

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—___—____

B. Base documents

4. Study protocol
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____
5. Prototype consent form
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____
6. Investigator's brochure
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____
7. Data collection forms
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____

8. Manual of operations
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____

9. Study handbook
   - Production loci . . . . . _____
   - Distribution loci . . . . . _____
   - Archive loci . . . . . _____

C. Monitoring reports

10. Performance monitoring reports
    - Production loci . . . . . _____
    - Distribution loci . . . . . _____
    - Archive loci . . . . . _____

11. Treatment effects monitoring reports
    - Production loci . . . . . _____
    - Distribution loci . . . . . _____
    - Archive loci . . . . . _____

12. Site visit reports
    - Production loci . . . . . _____
    - Distribution loci . . . . . _____
    - Archive loci . . . . . _____

13. Minutes of study meetings
    - Production loci . . . . . _____
    - Distribution loci . . . . . _____
    - Archive loci . . . . . _____

14. Study progress reports
    - Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

D. Datasets

15. Analysis datasets

Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

16. Manuscript datasets

Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

17. Public use datasets

Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

E. Other documents

18. Study design synopsis

Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

19. Study CV

Production loci . . . . . _____

Distribution loci . . . . . _____

Archive loci . . . . . _____

WS 7.2 Investigator assurances worksheet (Assure.WS)

When: Before the start of enrollment

Who: Any person involved in the trial in clinics or study resource centers

Purpose: As an aid to reminding people of their responsibilities in the trial

A. Identifying information

1. Study name: _____

2. Study investigator: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Attestations

4. Study protocol
( ) Familiar with the study protocol
( ) Willing to follow the study protocol
( ) Read consent form used for enrollment of persons into trial

5. Tenets of the trial
( ) Objective of trial reasonable
( ) Question worth answering
( ) Sample size goal reasonable and feasible
( ) Treatments safe
( ) Willing to enroll and follow patients in the trial

6. Responsibilities
( ) Respect privacy of study subjects
( ) Protect confidentiality of study data
( ) Not to engage in practices that bring discredit to the study
( ) Comply with IRB policies and procedures underlying research on human beings
( ) Report practices that are wrong or fraudulent

C. Disclosures

7. Conflict of interest disclosure?
( ) No
( ) Yes
If yes, are the conflicts likely to seen by the public as sufficient to disqualify one from certain aspects or functions in the trial?

( ) Yes (specify)

_____

_____

( ) No

8. Conflict of interest disclosures on file for other investigators to see?
( ) Yes
( ) No (explain)

_____

9. Publications or public positions inconsistent with tenets of trial?
( ) No
( ) Yes (explain)

_____

WS 7.3 Study website (Website.WS)

When: Early in the trial, before the start of data collection

Who: A person designated by the director of the data center

Purpose: To provide a central, readily accessible archive of materials needed for conduct of the trial

Reminders and recommendations

- Consider establishing a password-protected website for any study involving geographically disbursed personnel whether single-center or multicenter
- Consider placing important study documents that do not have to be password-protected on open portion of the website
- Do not set up a study website without plans for maintenance and updating over the course of the study

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

4. Website address: . . . . . _____

B. Study centers

5. Website access (check one)
   ( ) Limited to study personnel via password protection (L)
   ( ) Open to public (O)
   ( ) Both a public and password-protected portion (B)

6. Content (check all that apply)

L	O	B	
( )	( )	( )	Current version of study forms
( )	( )	( )	Previous versions of study forms
( )	( )	( )	Current version of study protocol
( )	( )	( )	Previous versions of study protocols
( )	( )	( )	Current version of study handbooks/manuals of operations
( )	( )	( )	Prototype consent and assent forms
( )	( )	( )	Study directory
( )	( )	( )	Study CV
( )	( )	( )	Study synopsis
( )	( )	( )	Study centers
( )	( )	( )	Study registration site

L	O	B	
( )	( )	( )	Study committees and membership
( )	( )	( )	Study credit roster
( )	( )	( )	Policy and procedures memoranda
( )	( )	( )	Minutes of study meetings
( )	( )	( )	Site visit reports
( )	( )	( )	Meeting materials
( )	( )	( )	Performance reports
( )	( )	( )	Available datasets
( )	( )	( )	Publications
( )	( )	( )	Presentations
( )	( )	( )	Slide sets
( )	( )	( )	Other (specify) _____
( )	( )	( )	Other (specify) _____
( )	( )	( )	Other (specify) _____

C. Website custodian and maintenance

7. Custodian (check one)
   - ( ) Data center/coordinating center
   - ( ) Office of study chair/PI
   - ( ) Sponsor
   - ( ) Other (specify)

   _____

8. Frequency of updates (check one)
   - ( ) As needed
   - ( ) Weekly
   - ( ) Monthly
   - ( ) Other (specify)

   _____

9. Authority for issue and de-issue of passwords for website access (check one)?
   - ( ) Data center/coordinating center
   - ( ) Office of study chair/PI
   - ( ) Sponsor
   - ( ) Other (specify)

   _____

D. Sign-off

10. Content checklist (item 6) reviewed and approved by study leadership
    ( ) Yes (essential for content of public portion of website)
    ( ) No (Stop if website has a public portion)

11. Reviewing and approving body: _____

12. Date of sign-off (day-month-year) . . . . . __—___—_____

WS 7.4 Conflicts of interest worksheet (CoI.WS)

When: Before the start of data collection

Who: Study officers

Purpose: To set-forth policy on disclosure of conflicts of interest

Definition

conflict of interest - 1. An interest deriving from financial holdings, proprietorship in some business, relationship to some product, post or position held, or stand taken by a person, group, agency, firm, or institution that is acknowledged by that person or party as constituting a conflict in relation to some activity, function, judgment, or action performed or to be performed. 2. A conflict due to competing needs, e.g., the conflict of a physician engaged in caring for patients under a treatment protocol when deciding whether to choose in favor of one's patient or protocol when in conflict; such a conflict arising from pursuit of conflicting values, e.g., the value of unmasked treatment effects monitoring in regard to competency requirements versus the value of masked treatment effects monitoring in regard to objectivity requirements. 3. A moral dilemma arising from the need to engage in some act or process that is at odds with one's belief or conviction, e.g., the dilemma of a physician engaged in recruiting patients for enrollment into a randomized trial in the absence of a state of equipoise, or the dilemma of one in a coordinating center in performing treatment effects monitoring considered to violate competency requirements. ***Usage note***: Most often used in relation to financial, business, or proprietary interests, but can be used in relation to one's post or employment, or more broadly in relation to a philosophical position or point of view considered to be in conflict with one's duty or to have the potential of influencing one's judgment or action in relation to some activity or function. Avoid as an implied charge or in a speculative sense. Generally, unless supported with factual information detailing the nature of the interest or circumstance considered to constitute a conflict, the term should not be used in an accusatory sense. Avoid, as well, suppositions as to effect. The direction or nature of the effect of a conflict of interest may be opposite to the one suggested in cases in which the individual is aware of the conflict and "overcompensates" for it.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Disclosure process

4. Persons required to disclose conflicts (check all that apply)
   - ( ) Center directors
   - ( ) Deputy center directors
   - ( ) Study officers
   - ( ) Steering committee members

( ) Executive committee members
( ) Treatment effects monitoring committee members
( ) Study physicians
( ) Data collectors
( ) Other (specify)

_____

_____

_____

5. Mode of disclosure (check all that apply)
   ( ) Discussion of what constitutes conflicts of interest at investigator meetings followed by round table oral disclosure of possible conflicts
   ( ) Written, via signed and dated disclosure statement

6. Frequency of disclosures?
   ( ) Once, at the beginning of the trial
   ( ) Annually over the course of the trial

   ( ) Other (specify) _____

C. Review

7. Body responsible for reviewing disclosures and for deciding whether conflicts disclosed are sufficient to disqualify
   ( ) Study chair
   ( ) Study officers
   ( ) Steering committee
   ( ) Sponsor
   ( ) Advisory committee independent of study investigators
   ( ) Other (specify)

   _____

8. Is there a process for dealing with conflicts considered to be sufficient to disqualify a person from some position or activity in the trial?
   ( ) No
   ( ) Yes (describe)

   _____

   _____

D. Disclosure repository

9. Location of where disclosure statements are filed
   - ( ) Not stored
   - ( ) Sponsor
   - ( ) Office of the study chair
   - ( ) Coordinating center
   - ( ) Other (specify)

     _____

10. Disclosure statements available to study investigators for inspection?
    - ( ) No
    - ( ) Yes

11. Disclosure statements available to the public?
    - ( ) No
    - ( ) Yes
      - ( ) Posted to public section of study website
      - ( ) On request
      - ( ) Other (specify)

        _____

WS 7.5 Study training and certification worksheet (Train.WS)

When: Prior to the start of data collection

Who: Leaders of the data center

Purpose: To specify training and certification procedures to be followed in the trial

Definition

certification - In the case of trials, a process for clearing a center or study personnel for participation. In regard to a center, a process intended to ensure that it has the requisite facilities, equipment, staffing, approvals, and that it meets specified standards; may involve onsite inspections. In regard to personnel, typically a process involving study specific training and evidence of proficiency in regard to performing key procedures and activities related to data collection.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Training

4. Personnel training prior to start of enrollment (check all that apply)
   - ( ) IRB training
   - ( ) Meeting of the research group prior to start of enrollment devoted to:
     - ( ) Review of the study protocol
     - ( ) Review of data collection procedures
     - ( ) Review of consent procedures
     - ( ) Review of responsibilities for integrity
     - ( ) Review of consequences of scientific misconduct
   - ( ) Completion of a knowledge assessment test based on the study protocol
   - ( ) Start-up site visits to study centers
   - ( ) Other (specify)

     _____

5. Study personnel subject to start-up training (check all that apply)
   - ( ) Center directors
   - ( ) Study physicians
   - ( ) Study nurses
   - ( ) Center coordinators
   - ( ) Data collectors
   - ( ) Data keyers

Table 7.5 Training and certification worksheet

( ) Other (specify)

_____

6. Methods of ongoing training of study personnel (check all that apply)
   ( ) Periodic meetings of the research group
   ( ) Periodic meetings of clinic coordinators
   ( ) Staff newsletters
   ( ) Site visits
   ( ) Policy and procedures memoranda from the coordinating center regarding changes to study procedures or protocol
   ( ) Other (specify)

_____

7. Personnel subject to periodic retraining (check all that apply)
   ( ) Center directors
   ( ) Study physicians
   ( ) Study nurses
   ( ) Center coordinators
   ( ) Data collectors
   ( ) Data keyers
   ( ) Other (specify)

_____

8. Method of training new personnel during the trial (check all that apply)
   ( ) None
   ( ) Job apprenticeship
   ( ) Formal testing
   ( ) Site visit
   ( ) Other (specify)

_____

C. Certification

9. Clinic certification?
   ( ) No
   ( ) Yes (check all that apply)
      ( ) IRB approvals
      ( ) Adequate examination area
      ( ) Standard examination room equipment
      ( ) Secure area for filing study forms and records
      ( ) Secure area for storage of study drugs
      ( ) Properly equipped blood draw area
      ( ) Refrigeration for blood specimens

Table 7.5 Training and certification worksheet

( ) Computer equipment and internet connection
( ) Other

_____

_____

10. Personnel certification?
    ( ) No
    ( ) Yes (check all that apply)
        ( ) Physicians
        ( ) Nurses
        ( ) Coordinators
        ( ) Data collectors
        ( ) Data keyers
        ( ) Readers
        ( ) Other (specify)

_____

_____

11. Certifying authority (check one)
    ( ) Coordinating center
    ( ) Office of study chair
    ( ) Sponsor
    ( ) Other (specify)

_____

12. Certification numbers issued by:
    ( ) Coordinating center
    ( ) Office of study chair
    ( ) Sponsor
    ( ) Other (specify)

_____

13. Are certification numbers of persons responsible for data collection recorded on study forms?
    ( ) No (explain)

_____

    ( ) Yes

Table 7.5 Training and certification worksheet

14. If numbers are issued describe process for de-certification if a person leaves the study or is barred from data collection

WS 7.6 Site visiting worksheet (SiteLook.WS)

When: Prior to the start of data collection

Who: Leaders of the coordinating center with input from study officers

Purpose: To layout plans for site visiting during the trial

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Visiting plans and site visit reports

4. Clinic visits (check all that apply)
   ( ) Before start of enrollment
   ( ) Regularly over the course of the trial (specify frequency)

   _____

   ( ) For cause for performance or irregularities
   ( ) Other (specify)

   _____

5. Coordinating center visits (check all that apply)
   ( ) Before start of enrollment
   ( ) Regularly over the course of the trial (specify frequency)

   _____

   ( ) For cause for performance or irregularities

6. Other resource center visits (check all that apply)
   ( ) Office of study chair
   ( ) Reading centers
   ( ) Other (specify)

   _____

7. Site visit reports (check all that apply)
   ( ) Written report produced following visit by site visitors
   ( ) Report indicates date and place of visit, persons visited, and visiting team

( ) Report lists problems and deficiencies noted and recommended corrective actions
( ) Draft report sent to group visited for comment prior to finalizing
( ) Finished report distributed to group visited
( ) Finished report distributed to study leadership body for review and comment
( ) Repository for finished reports at study coordinating center
( ) Finished report posted to password-protected study website
( ) Other (specify)

_____

C. Clinic site visits

8. Startup visits?
   ( ) No
   ( ) Yes, answer questions below.

9. Composition of visiting team
   ( ) Persons from the coordinating center . . . . . Number ___

   ( ) Persons from other study clinics . . . . . Number ___
   ( ) Study chair
   ( ) Study sponsor
   ( ) Person not associated with the trial
   ( ) Other (specify)

   _____

10. Usual size of visiting team . . . . . Number _____

11. Visit activities (check all that apply)
    ( ) Kickoff meeting with all study staff
    ( ) Tour of facilities
    ( ) Wrap-up meeting
    ( ) Other (specify)

    _____

12. Things reviewed and checked
    ( ) IRB documents and approvals
    ( ) Date stamped IRB approved consent form
    ( ) Clinic space
    ( ) Examining facilities
    ( ) Inventory of equipment needed for the trial
    ( ) Location of study documents such as protocols, handbooks, and study forms
    ( ) Location of study files and security of files
    ( ) Storage area for study drugs
    ( ) Blood drawing facilities

( ) Staffing and qualification
( ) Infrastructure
( ) Other (specify)

_____

13. Routine clinic site visits?
( ) No
( ) Yes, answer questions below

14. Frequency of visits
( ) Once a year
( ) Once every two years
( ) Other (specify)

_____

15. Composition of visiting team
( ) Persons from the coordinating center . . . . . Number ___

( ) Persons from another clinic . . . . . Number ___
( ) Study chair
( ) Study sponsor
( ) Person not associated with the trial
( ) Other (specify)

_____

16. Usual size of visiting team . . . . . Number _____

17. Visit activities (check all that apply)
( ) Kickoff meeting with all study staff
( ) Tour of facilities
( ) Walk through of a "typical" data collection visit
( ) Interview of a study patient
( ) Review of study records and filing and storage
( ) Audit of selected forms
( ) Wrap-up meeting
( ) Other (specify)

_____

18. Things reviewed and checked
( ) Check of study documents including the study protocol and handbooks
( ) Check of study forms to verify clinic using most recent version
( ) Staff qualification, training, and certification

( ) Patient flow for treatment and data collection visits
( ) Procedures for keeping track of study patients and for scheduling appointments
( ) Count of persons lost to followup
( ) Clinic performance statistics
( ) Data deficiencies
( ) On-site keying procedures
( ) Staffing and qualification
( ) Clinic infrastructure and communication structure
( ) Other (specify)

_____

D. Coordinating center site visits

19. Site visits?
    ( ) No
    ( ) Yes, answer items below

20. Frequency of visits
    ( ) Once over life of trial
    ( ) Once every three years
    ( ) Other (specify)

    _____

21. Composition of visiting team
    ( ) Persons from other study centers . . . . . Number ___
    ( ) Study chair
    ( ) Study sponsor
    ( ) Persons from other coordinating centers . . . . . Number ___
    ( ) Other (specify)

    _____

22. Size of visiting team . . . . . Number _____

23. Visit activities and reviews (check all that apply)
    ( ) Presentations of organization of coordinating center and overview of its functions and activities and discussion
    ( ) Tour of facilities
    ( ) Review of treatment assignment procedure
    ( ) Staffing qualifications and training
    ( ) Overview of data system and of methods of harvesting, processing, and analyzing data
    ( ) Review of data backup procedures
    ( ) Review of data security procedures
    ( ) Review of performance monitoring procedures

( ) Review of treatment effects monitoring procedures
( ) Review of data editing and auditing procedures
( ) Review of methods for dealing with data irregularities
( ) Clinic site visiting procedures
( ) Quality control of analysis procedures
( ) Role in writing study papers
( ) Method of assigning analysis tasks to center personnel and of monitoring activities
( ) IRB approvals
( ) Management of protocol changes and changes to data collection forms
( ) Data entry and harvest procedures
( ) Center infrastructure and internal communication structure
( ) Other (specify)

CL 7.1 Maintenance activity checklist worksheet (KeepUp.CL)

To be completed in conjunction with study leadership as part of planning for start-up and to be reviewed and updated periodically over the course of the trial. Use spaces at left to indicate required activities during the trial. For items checked, indicate details as to when the activity is to be performed and who is to perform it.

A. Funding/letters of agreements/IND/IDE

( ) Progress reports to funding agency

Who: _____

When: _____

( ) Funding renewals

Who: _____

When: _____

( ) IND/IDE application

Who: _____

When: _____

( ) IND/IDE reporting

Who: _____

When: _____

B. Monitoring

( ) IRB renewals
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) Monitoring for near lapsed IRB approvals
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor

( ) Other (specify)

_____

( ) Monitoring for use of signed/dated consents at clinics
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Compliance to AE reporting procedures
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Drug supply
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

C. Updating

( ) Protocol
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Handbook/manual of operations
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Study forms
  ( ) Coordinating center
  ( ) Other (specify)

_____

( ) Data system
  ( ) Coordinating center
  ( ) Other (specify)

_____

( ) Study governance system
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Authorship policy
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Conflict of interest disclosures
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Study roster
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Registration of trial
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Study website
  ( ) Coordinating center
  ( ) Other (specify)

_____

( ) Study design synopsis
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Study CV
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

D. Tracking

( ) IRB renewal submissions
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor
  ( ) Other (specify)

_____

( ) Protocol amendments
  ( ) Coordinating center
  ( ) Office of study chair
  ( ) Sponsor

( ) Other (specify)

_____

E. Reporting

( ) TEMC recommendation to investigators
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) TEMC recommendation to IRBs
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) AEs to the FDA
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

F. Drugs

( ) Drug ordering
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) Distribution of drugs to clinics
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Central pharmacy
- ( ) Sponsor

( ) Other (specify)

_____

( ) Accountability of drugs used
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

G. Other

( ) Training
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) Draft manuscripts to investigators
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Writing committee chairs
- ( ) Sponsor
- ( ) Other (specify)

_____

( ) Published manuscripts to investigators
- ( ) Coordinating center
- ( ) Office of study chair
- ( ) Sponsor
- ( ) Other (specify)

_____

CL 7.2 Start-up requirements checklist worksheet (StartCk.CL)

To be completed in conjunction with the study leadership body as part of planning for start-up. Use check spaces at the left to indicate requirements for start-up and check spaces at the right to indicate things accomplished.

A. Executed funding agreements

( ) Clinics . . . . . ( )
( ) Coordinating center . . . . . ( )
( ) Other centers (specify) . . . . . ( )

_____

( ) Support centers (specify) . . . . . ( )

_____

B. Letters of agreement

( ) Drug company for supply of drug . . . . . ( )
( ) Other (specify) . . . . . ( )

_____

C. IND/IDE

( ) IND (specify) . . . . . ( )

_____

( ) IDE (specify) . . . . . ( )

_____

( ) Other (specify) . . . . . ( )

_____

D. Basics

( ) Approved study name . . . . . ( )
( ) Approved study nickname . . . . . ( )
( ) Approved study logo . . . . . ( )
( ) Approved statement of objective . . . . . ( )
( ) Approved primary outcome measure . . . . . ( )
( ) Approved treatment protocol . . . . . ( )
( ) Approved data collection schedule . . . . . ( )
( ) Approved design synopsis . . . . . ( )

( ) Sample size goal . . . . . ( )
( ) Approved study timetable . . . . . ( )
( ) Approved randomization design . . . . . ( )
( ) Approved treatment effects monitoring plan . . . . . ( )
( ) Other (specify) . . . . . ( )

E. Essential documents

( ) Study protocol . . . . . ( )
( ) Study handbook/manual of operations . . . . . ( )
( ) IRB approved consent form . . . . . ( )
( ) Approved data collection forms . . . . . ( )
( ) Investigator's brochure . . . . . ( )
( ) Study roster/directory . . . . . ( )
( ) Other (specify) . . . . . ( )

F. Governance and study policy

( ) Investigator-ratified study governance structure . . . . . ( )
( ) Approved authorship policy . . . . . ( )
( ) Approved conflict of interest disclosure procedures . . . . . ( )
( ) Approved policy on presentations . . . . . ( )
( ) Approved policy on publications . . . . . ( )
( ) Other (specify) . . . . . ( )

G. Data collection

( ) Approved screening procedures . . . . . ( )
( ) Approved consent process . . . . . ( )
( ) Approved baseline data collection forms . . . . . ( )
( ) Approved followup data collection forms . . . . . ( )
( ) IRB approved data collection forms . . . . . ( )
( ) Tested data collection forms . . . . . ( )
( ) Kickoff training meeting . . . . . ( )
( ) Personnel certification . . . . . ( )
( ) Other (specify) . . . . . ( )

H. Data system

( ) Data entry tutorial . . . . . ( )
( ) Tested randomization system . . . . . ( )
( ) Tested data system . . . . . ( )

( ) Operational data system . . . . . ( )
( ) Training meeting . . . . . ( )
( ) Other (specify) . . . . . ( )

I. IRB approvals

( ) Study protocol . . . . . ( )
( ) Consent process and consent/assent forms . . . . . ( )
( ) Data collection forms . . . . . ( )
( ) Approval for at least one clinic . . . . . ( )
( ) Approval for the data center/coordinating center . . . . . ( )
( ) Other IRB approvals (specify) . . . . . ( )

J. Other approvals

( ) Funding agency approval of study protocol . . . . . ( )
( ) Funding agency approval of data collection forms . . . . . ( )
( ) TEMC approval of study protocol . . . . . ( )
( ) Other (specify) . . . . . ( )

K. Other

( ) Study website . . . . . ( )
( ) Registration . . . . . ( )
( ) Drugs/devices packaged and ready for use . . . . . ( )
( ) TEMC appointed . . . . . ( )
( ) OMB clearance of study forms . . . . . ( )
( ) Other (specify) . . . . . ( )

L. Clinic clearance for enrollment

( ) IRB approval . . . . . ( )
( ) Evidence of IRB approval supplied to coordinating center . . . . . ( )
( ) Date-stamped consent form . . . . . ( )
( ) Evidence of IRB training for study personnel . . . . . ( )
( ) Other (specify) . . . . . ( )

CL 7.3 Training and certification checklist (Train.CL)

When: Prior to the start of data collection

Who: Coordinating center personnel in conjunction with study officers

Purpose: To outline training and certification procedures for the trial

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Personnel training (check all that apply)

4. Personnel to be trained
   - ( ) Center and deputy center directors
   - ( ) Study coordinators
   - ( ) Study physicians
   - ( ) Data collectors
   - ( ) Data keyers
   - ( ) Data processors
   - ( ) Data analysts
   - ( ) Study officers
   - ( ) Steering committee members
   - ( ) Treatment effects monitoring committee members
   - ( ) Other (specify)

     _____

5. Method of training (check all that apply)
   - ( ) Didactic at kick-off research group meeting
   - ( ) On-line training
   - ( ) Testing
   - ( ) Site visiting
   - ( ) Other (specify)

     _____

6. Method of ongoing training during the trial (check all that apply)
   - ( ) Didactic at research group meeting
   - ( ) On-line training
   - ( ) Testing
   - ( ) Site visiting

( ) Newsletter
( ) Other (specify)

_____

7. Method of training new personnel during the trial (check all that apply)
   ( ) On-site training by existing personnel
   ( ) On-line training
   ( ) Testing
   ( ) Other (specify)

_____

C. Personnel certification and decertification

8. Does the trial require certification of study personnel for clearance to collect or process study data?
   ( ) No
   ( ) Yes

9. If yes, list personnel to be certified for data collection (check all that apply)
   ( ) Center and deputy center directors
   ( ) Study coordinators
   ( ) Study physicians
   ( ) Data collectors
   ( ) Data keyers
   ( ) Data processors
   ( ) Data analysts
   ( ) Study officers
   ( ) Steering committee members
   ( ) Treatment effects monitoring committee members
   ( ) Other (specify)

_____

10. If yes, who issues certifications?
    ( ) Coordinating center
    ( ) Other (specify)

_____

11. If yes, what is done if data are collected by a person not certified for data collection? (check all that apply)
    ( ) Data rejected
    ( ) Data accepted but flagged
    ( ) Clinic notified of protocol deviation

( ) Other (specify)

_____

12. If yes, who deactivates certifications?
    ( ) Coordinating center
    ( ) Other (specify)

_____

13. If yes, what are conditions for deactivation of certifications? (check all that apply)
    ( ) Departure from the study
    ( ) Data irregularities
    ( ) Other (specify)

_____

CL 7.4 Clinic site visit checklist (SiteCl.CL)

When: In relation to a study site visit

Who: The organizer of the site visit

Purpose: To outline the activities of a site visit and to document activities of a site visit

A. Identifying information

1. Study name: _____
2. Clinic being visited: _____
3. Date of visit (day-month-year) . . . . . __—__—____

B. Visit particulars

4. Visit history
   ( ) 1st visit
   ( ) Previous visits (list dates from 1st to most recent visit)

   Visit 1: _____

   Visit 2: _____

   Visit 3: _____

5. Purpose of this visit
   ( ) Routine
   ( ) For cause (check one)
      ( ) Poor performance
      ( ) Data irregularities
      ( ) Other (specify)

      _____

6. Roster of visitors and visitees

Name	Title
Visitors	
1:	
2:	
3:	

Name	Title
4:	
5:	
6:	

Visitees

1:	
2:	
3:	
4:	
5:	
6:	

7. Name and address of place of visit

   Name: _____

   Address: _____

8. Time of visit

   Start: _____ . . . . . End: _____

C. Document and activity checklist (use the list to indicate what is to be checked during the visit and to indicate what has been checked after the visit is finished)

	Check	Checked
9. Site visit checklist		
IRB approvals	( )	( )
IRB file of amendments and AE reports	( )	( )
IRB training of study personnel	( )	( )
Current protocol	( )	( )
Current Investigator's Brochure	( )	( )
Current handbook/manual of operations	( )	( )
Current version of study forms	( )	( )
Policy and procedures memoranda	( )	( )
Date stamped IRB approved consent form	( )	( )

CL 7.4 Clinic site visit checklist

	Check	Checked
Clinic space	( )	( )
Examining facilities	( )	( )
Inventory of equipment needed for the trial	( )	( )
Location of study documents, handbooks, and study forms	( )	( )
Location of study files and file security	( )	( )
Storage area for study drugs	( )	( )
Blood drawing facilities	( )	( )
Staffing and qualification	( )	( )
Personnel training and certifications	( )	( )
Personnel directory	( )	( )
Clinic infrastructure	( )	( )
Protocol deviations	( )	( )
Random forms audit	( )	( )
Audit trail of treatment assignments	( )	( )
Eligibility check of persons enrolled	( )	( )
Drug dispensing and drug accountability	( )	( )
Other		
_____	( )	( )
_____	( )	( )
_____	( )	( )

CL 7.5 Coordinating center site visit checklist (SiteCC.CL)

When: In relation to a coordinating center site visit

Who: The organizer of the site visit

Purpose: To outline the activities of the site visit and to document activities of the site visit

A. Identifying information

1. Study name: _____

2. Study investigator: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Visit particulars

4. Visit history
   ( ) 1st visit
   ( ) Previous visits (list dates from 1st to most recent visit)

   Visit 1: _____

   Visit 2: _____

   Visit 3: _____

5. Purpose of this visit
   ( ) Routine
   ( ) For cause (check one)
      ( ) Poor performance
      ( ) Data irregularities
      ( ) Other (specify)

   _____

6. Roster of visitors and visitees

Name	Title
Visitors	
1:	
2:	
3:	

Name	Title
4:	
5:	
6:	

Visitees

1:	
2:	
3:	
4:	
5:	
6:	

7. Name and address of place of visit

   Center name: _____

   Address: _____

8. Time of visit

   Start: _____ . . . . . End: _____

C. Document and activity checklist (use the list to indicate what is to be checked during the visit and to indicate what has been checked after the visit is finished)

	Check	Checked
9. Document and activity checklist		
IRB approvals	( )	( )
IRB file of amendments and AE reports	( )	( )
IRB training of study personnel	( )	( )
Current protocol	( )	( )
Current Investigator's Brochure	( )	( )
Current handbook/manual of operations	( )	( )
Forms list and revision history	( )	( )
Procedure for forms revisions	( )	( )
Policy and procedures memoranda procedures	( )	( )

CL 7.5 Coordinating center site visit checklist

	Check	Checked
Date stamped IRB approved consent form	( )	( )
Center space and equipment	( )	( )
Location of study documents, handbooks, and study forms	( )	( )
Location of study files and security of files	( )	( )
Staffing and qualification	( )	( )
Data processing staffing	( )	( )
Analysis staffing	( )	( )
Personnel training and certifications	( )	( )
Personnel directory	( )	( )
Center infrastructure	( )	( )
Security of data storage	( )	( )
Protocol deviations	( )	( )
Forms audits	( )	( )
Audit trail of treatment assignments	( )	( )
Eligibility check of persons enrolled	( )	( )
Drug dispensing and drug accountability	( )	( )
Review of study data systems	( )	( )
Review of center data security procedures	( )	( )
Study paper writing production and procedures	( )	( )
Data access policy	( )	( )
Internal quality control procedures	( )	( )
Performance monitoring procedures	( )	( )
Treatment effects monitoring procedures	( )	( )
Standing of center in the organizational structure of the trial	( )	( )
Other (specify)		
_____	( )	( )
_____	( )	( )
_____	( )	( )

8 IRB tables, worksheets, and checklists

Table 8.1 IRB approvals and reports to IRBs (IRBModel.Tab)

When: Before the start of data collection

Who: Coordinating center personnel in conjunction with study officers

Purpose: To set-forth IRB approval and reporting procedures

Definitions

associate center - A center, established or adopted by a parent center, that is responsible for performing specified functions in association with or as an agent of the parent; may or may not receive financial support from the parent.

central institutional review board - An IRB having review authority over a multicenter study, especially one where approval by such a board is sufficient to allow investigators at study centers to proceed without additional review or approval.

commercial institutional review board - A board performing functions similar to an institutional review board on a fee-for-service for investigators directed to submit to it by the IRB offices of their respective institutions or for investigators not affiliated with institutions having IRBs; increasingly used to review proposals coming from investigators heading centers in multicenter studies at sites not having IRBs.

institutional review board (IRB) - A board, as set forth in guidelines and regulations emanating from the United States Public Health Service, concerned with research involving human beings; appointed by authorities of the institution housing the board and constituted to review and approve studies involving human beings by investigators from the appointing institution.

local institutional review board - The institutional review board of one's own institution.

parent center - 1. A study center that gives rise to or nurtures other centers. 2. A study center that has administrative or operational primacy over other centers. 3. A study center having an affiliate, associate, field, or satellite center.

protocol amendment - A proposed protocol change submitted to an IRB; such a proposed change approved by an IRB. Technically, any change to an approved protocol is an amendment, but usually best reserved for changes submitted to IRBs for review and approval – generally, any change that can be reasonably argued as having the potential of changing the risk-benefit ratio for persons studied, or having potential to influence a person's decision as to whether to enroll or to remain in a study. In trials, including changes to the treatment protocol, study procedures, schedule of study visits, or period of followup; especially any such changes considered to require changes to existing consent forms or to require reconsent.

satellite center - A center, subordinate to a parent center, organized to perform a designated set of functions at the behest of or as an agent of that parent.

Table 8.1 IRB approval and reports to IRBs

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—_____

B. IRB map

4. Centers represented in the trial (check all that apply)

( ) Study clinics . . . . . Number ___

( ) Associate clinics . . . . . Number ___

( ) Satellite clinics . . . . . Number ___

( ) Coordinating centers/data centers . . . . . Number ___

( ) Associate/satellite coordinating centers/data centers . . . . . Number ___

( ) Treatment coordinating centers . . . . . Number ___

( ) Reading centers . . . . . Number ___

( ) Central laboratories . . . . . Number ___

( ) Central specimen repositories . . . . . Number ___

( ) Other (specify) . . . . . Number ___

_____

Sum of values above . . . . . ____

5. Number of centers required to submit to IRBs . . . . . Number ___

If number less than the sum in item 4, list the centers not requiring IRB approvals and reasons why not required

_____

_____

_____

_____

Table 8.1 IRB approval and reports to IRBs

6. Types of IRBs represented by the number represented in item 5 (check all that apply)
   ( ) Central IRBs . . . . . Number ___
   ( ) Local IRBs . . . . . Number ___
   ( ) Commercial IRBs . . . . . Number ___
   Total number of IRBs . . . . . Number ___

C. Management of IRB submissions

7. Who is responsible for preparing the protocol used by clinics in their submissions to IRBs? (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

8. Who is responsible for providing clinics with the official study protocol for submission to IRBs? (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

9. Who is responsible for instructing clinics as to when to submit to IRBs for new protocol versions and revised consent forms? (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

10. Consents submitted by clinics for IRB approval (check all that apply):
    ( ) Produced from prototype consent provided by coordinating center or office of study chair
    ( ) Clinics instructed as to when to submit to respective IRBs by the coordinating center or office of study chair
    ( ) Approved forms reviewed by coordinating center or office of the study chair to ensure they are factually correct and that they contain the basic information contained in the prototype

( ) Other (specify)

_____

11. Minimal IRB approvals required to start enrollment and treatment in the trial (check one)
    ( ) IRB approval of the study protocol and consent procedures at one clinic
    ( ) IRB approval of the study protocol and consent procedures at one clinic and IRB approval of the coordinating center
    ( ) IRB approval of the study protocol and consent procedures at all clinics
    ( ) IRB approval of the study protocol and consent procedures at all clinics and IRB approval of the coordinating center
    ( ) Other (specify)

_____

D. Protocol changes

12. Who decides when a change requires IRB approval prior to implementation?
    ( ) Coordinating center
    ( ) Office of the study chair
    ( ) Study sponsor
    ( ) Study officers
    ( ) Steering committee
    ( ) Other (specify)

_____

13. Who is responsible for providing clinics with documents needed for submission of the proposed change to IRBs? (check one)
    ( ) Coordinating center
    ( ) Office of the study chair
    ( ) Study sponsor
    ( ) Study officers
    ( ) Steering committee
    ( ) Other (specify)

_____

14. Who is responsible for deciding how and when the change is implemented? (check one)
    ( ) Coordinating center
    ( ) Office of the study chair
    ( ) Study sponsor
    ( ) Study officers
    ( ) Steering committee
    ( ) Other (specify)

_____

Table 8.1 IRB approval and reports to IRBs

15. Changes implemented without IRB review (check all that apply)
    ( ) Minor word changes to data collection forms
    ( ) Changes in general care procedures
    ( ) Changes reducing the risk or nuisances of being studied
    ( ) Termination of harmful study treatment
    ( ) Other (specify)

    _____

16. Changes requiring IRB review prior to implementation (check all that apply)
    ( ) Addition of procedures considered to involve more than minimal risk or added inconvenience to study subjects
    ( ) Addition of sensitive questions to data collection forms
    ( ) Changes to consent procedures
    ( ) Increase in contact schedule for data collection
    ( ) Addition of specimen collection for future use
    ( ) Other (specify)

    _____

E. Reports and notices to IRBs

17. Reports and notices originating at study clinics (check all that apply)
    ( ) Adverse events
    ( ) Overdoses; treatment mistakes
    ( ) Breach of confidentiality
    ( ) Deaths
    ( ) Other (specify)

    _____

18. Are reports and notices arising at the clinic level of operations as listed in item 17 sent to other study centers for submission to their respective IRBs?
    ( ) Yes
    ( ) No (explain)

    _____

    _____

19. If item 18 answered yes, indicate conduit for transmission to other IRBs
    ( ) Coordinating center
    ( ) Office of the study chair
    ( ) Study sponsor
    ( ) Other (specify)

    _____

Table 8.1 IRB approval and reports to IRBs

20. For trials with treatment effects monitoring committees, who is responsible for notifying IRBs of meetings of the committee? (check one)
    ( ) Coordinating center
    ( ) Office of the study chair
    ( ) Study sponsor
    ( ) Other (specify)

_____

Table 8.2 IRB log (IRBHis.Tab)

When: At the outset and continuously over time

Who: Persons at the coordinating center

Purpose: To provide a log of protocol versions and changes to the protocol over the course of the trial

A. Identifying information

1. Study name: _____

2. Form maintained by (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

B. Protocol versions

3. How are versions of the protocol identified (check one)
   ( ) By version number
   ( ) By date
   ( ) By version number and date
   ( ) Other (specify)

   _____

4. Who decides when versions are issued (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

5. Who is responsible for preparing and distributing protocol versions
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

Table 8.2 IRB log

6. Who is responsible for orchestrating submission of versions to IRBs?
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

Note: The IRB serving the place named in item 6 is, herein, referred to as the parent IRB

7. Check the item below that best describes the IRB submission process
   ( ) Ordered: Submitted to the parent IRB and not sent to other centers until approved by the parent
   ( ) Simultaneous: Distributed to clinics for submission to their respective IRBs when submitted to the parent IRB

8. Implementation model for new versions of the protocol (check one)
   ( ) Model 1: By clinic whether or not approved by the parent IRB
   ( ) Model 2: By clinic once approved by the parent IRB
   ( ) Model 3: No implementation until version approved by all IRBs of record
   ( ) Model 1, 2, or 3 depending on the nature of the change

9. Protocol versions

   Version number ____ . . . . . Date: _ _-_ _ _-_ _ _ _

   Version number ____ . . . . . Date: _ _-_ _ _-_ _ _ _

   Version number ____ . . . . . Date: _ _-_ _ _-_ _ _ _

   Version number ____ . . . . . Date: _ _-_ _ _-_ _ _ _

C. Log of IRB submissions for approval: Parent IRB perspective

10. IRB submission and approval log of protocol versions

Version number	Version date	Submission date to parent	Approval date of parent

Table 8.2 IRB log

11. IRB submission and approval log of protocol amendments separate and apart from those included in different versions of the protocol

    1: Describe _____

    Date submitted: _ _-_ _ _-_ _ _ _ . . . . . Date approved by parent: _ _-_ _ _-_ _ _ _

    2: Describe _____

    Date submitted: _ _-_ _ _-_ _ _ _ . . . . . Date approved by parent: _ _-_ _ _-_ _ _ _

    3: Describe _____

    Date submitted: _ _-_ _ _-_ _ _ _ . . . . . Date approved by parent: _ _-_ _ _-_ _ _ _

    4: Describe _____

    Date submitted: _ _-_ _ _-_ _ _ _ . . . . . Date approved by parent: _ _-_ _ _-_ _ _ _

    5: Describe _____

    Date submitted: _ _-_ _ _-_ _ _ _ . . . . . Date approved by parent: _ _-_ _ _-_ _ _ _

D. Log of adverse events reported to parent IRB

12. Adverse events reported from participating clinics

    1 Event: _____ . . . . . Clinic _____

    Date received at CC: _ _-_ _ _-_ _ _ _ . . . . . Date of event: _ _-_ _ _-_ _ _ _

    2 Event: _____ . . . . . Clinic _____

    Date received at CC: _ _-_ _ _-_ _ _ _ . . . . . Date of event: _ _-_ _ _-_ _ _ _

    3 Event: _____ . . . . . Clinic _____

    Date received: _ _-_ _ _-_ _ _ _ . . . . . Date of event: _ _-_ _ _-_ _ _ _

    4 Event: _____ . . . . . Clinic _____

    Date received: _ _-_ _ _-_ _ _ _ . . . . . Date of event: _ _-_ _ _-_ _ _ _

    5 Event: _____ . . . . . Clinic _____

    Date received: _ _-_ _ _-_ _ _ _ . . . . . Date of event: _ _-_ _ _-_ _ _ _

13. Reportable events originating in the center named in item 6

1 Event: _____

Date occurred: _ _-_ _ _-_ _ _ _ . . . . . Date submitted: _ _-_ _ _-_ _ _ _

2 Event: _____

Date occurred: _ _-_ _ _-_ _ _ _ . . . . . Date submitted: _ _-_ _ _-_ _ _ _

E. Log of other communications with parent IRB

14. Notice of meetings of the treatment effects monitoring committee

Mtg	Mtg date	Mtg mode	Date sent to parent	IRB response
1				
2				
3				
4				

Table 8.3 IRB approval monitoring (IRBMon.Tab)

When: Periodically over the course of the trial

Who: Persons in the data center

Purpose: To monitor IRB approval status of participating centers to prevent lapses of approvals

A. Identifying information

1. Study name: _____

2. Monitoring done by: (check one)
   ( ) Coordinating center
   ( ) Office of the study chair
   ( ) Study sponsor
   ( ) Other (specify)

   _____

3. Information below as of (day-month-year): . . . . . _ _-_ _ _-_ _ _ _

B. Clinical centers

Clinic Id	Cl location	Last renewal	Expiration date	Status*
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				

Table 8.3 IRB approval monitoring

9.				
10.				

* **OK**: Expiration at least 6 wks away; **L**: lapsed; **NL**: 4 wks from lapse

C. Resource centers

Center Id	Location	Last renewal	Expiration date	Status*
1.				
2.				
3.				
4.				

* **OK**: Expiration at 6 wks away; **L**: lapsed; **NL**: 4 wks from lapse

Table 8.4 Consent, reconsent, and deconsent design (ConPlan.Tab)

When: The trial is being designed and before submission of the protocol and consent forms to IRBs

Who: Persons in the coordinating center or office of the study chair

Purpose: To set forth design and operating procedures on consenting and deconsenting

Definitions

assent - Expression of acquiescence to something proposed. Usage note: Not to be confused with consent. Generally in research settings, assent by the person to be studied is required whenever consent is given by someone else on behalf of that person, and when that person has sufficient mental capacity to understand the nature and extent of what is being proposed. The starting age at which assent is required may vary, but is usually 5, or thereabouts, for most institutional review boards. For persons unable to read, the assent may be oral after the person has been presented with an explanation of what is involved. For persons able to read (e.g., children aged 7 or 8 to the age of majority), the process may require the use of a written assent form and a signed assent before proceeding. The process, while used primarily in relation to children, extends as well to adults with limited but sufficient mental capacities to allow them to assent.

consent - Voluntary agreement or acquiescence by a person, or by that person's guardian or representative on their behalf, to undertake, submit to, or comply with an act or procedure that is to be done by another person, party, or agency.

consent renewal - [trials] A formal or informal process in which persons enrolled in a trial are reminded of what the trial involves to provide persons with opportunity to ask questions and to formally or informally affirm willingness to continue in the trial

deconsent - 1. An active communication process taking place on completion or cessation of a person's role in a research project that is intended to impart information deemed necessary and appropriate for an informed separation. In the case of treatment trials, the information imparted relates to treatment received (including identity of assigned treatment in the case of a trial involving masked treatment), findings from the trial and relevance for the person departing, and observations and recommendations regarding the person's subsequent care and treatment. 2. A process taking place on separation of a person from a study aimed at assessing the adequacy of consent by the amount of information recalled during the consent process. 3. A process taking place on completion of a single- or double-masked trial, usually in relation to a close-out followup visit, in which the departing person is asked to state a guess as to treatment assigned or received.

reconsent - 1. Documented consent to continue in a study following disclosure and discussion of information considered to change the risk-benefit ratio for participation; especially in relation to a treatment protocol change or other protocol amendments. 2. updated consent

Table 8.4 Consent, reconsent, and deconsent design

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. Study population

4. People to be enrolled (check all that apply)
   ( ) Adults
   ( ) Children
   ( ) Children and adults
   ( ) Infants
   ( ) Pregnant women
   ( ) Mentally limited
   ( ) Other (specify)

   _____

5. If children are to be enrolled are they at or above the age of assent (age varies depending on IRBs but usually around ages 5 or 6)
   ( ) No
   ( ) Yes (Child's parent or guardian has to consent and child has to assent to being studied)

C. Consent/assent forms

6. Use the checklist below to indicate consents/assents required in the trial (check all that apply)
   Study subject consent
   ( ) Screening
   ( ) Enrollment
   ( ) Specimen collection
   ( ) Specimen banking
   ( ) DNA analysis
   ( ) DNA banking
   ( ) Other (specify)

   _____

   Other consents
   ( ) Surrogate respondent
   ( ) Guardian of patient
   ( ) Patient's care giver
   ( ) Other (specify)

   _____

Table 8.4 Consent, reconsent, and deconsent design

Assent of minor study subject

( ) Screening
( ) Enrollment
( ) Specimen collection
( ) Specimen banking
( ) DNA analysis
( ) DNA banking
( ) Other (specify)

_____

7. Number of separate consent/assent forms represented by checks in item 6 . . . . Number _____

8. Disclosures included in enrollment consent (check all that apply)
   ( ) Where study data are received, processed, and stored
   ( ) Who, outside the investigator group, are eligible to review data collected on study subjects
   ( ) Intent to deposit deidentified datasets under NIH data sharing requirements and risk of identification
   ( ) Use of banked specimens and whether study subjects will be informed of uses and results of relevance to them
   ( ) Whether investigators stand to profit from use of banked specimens
   ( ) Funding sources of the trial
   ( ) Investigator conflicts of interest
   ( ) Investigators standing to gain financially from results of the trial
   ( ) Right to withdraw at any time without prejudice
   ( ) Data collected may not be withdrawn even if person withdraws
   ( ) Other (specify)

_____

9. Check-offs included in enrollment consent to indicate acceptance or rejection of (check all that apply):
   ( ) DNA analysis
   ( ) Banking of specimens for future use
   ( ) Other (specify)

_____

D. Consent/assent process

10. Usual setting (check one)
    ( ) Clinic
    ( ) Home
    ( ) Telephone

Table 8.4 Consent, reconsent, and deconsent design

( ) Other (specify)

_____

11. Person usually obtaining consent/assent (check one)
    ( ) Study physician
    ( ) Study nurse
    ( ) Other (specify)

_____

12. Documentation of consent/assent (check all that apply)
    ( ) Signed and dated
    ( ) Witnessed signing
    ( ) Other (specify)

_____

13. Consent assurance safeguards (check all that apply)
    ( ) Two stage process with > 24 hours between being asked to enroll and consenting to enrollment
    ( ) Would be study subject given copy of consent to take home to review with family members before being asked to consent
    ( ) Would be study subject given opportunity to question person soliciting consent before consenting
    ( ) Would be study subject required to answer basic questions correctly about the trial as a condition for enrollment
    ( ) Other (specify)

_____

E. Reconsent/consent renewal

14. Circumstances under which reconsent deemed necessary (check all that apply)
    ( ) Results from another trial indicating that a study treatment is harmful or beneficial
    ( ) Decision to stop a study treatment because of harm or benefit but where treatment with a lesser dose of the same treatment continues
    ( ) Change in the formulation of a study treatment
    ( ) Dosage change of a study treatment
    ( ) Change in the treatment schedule
    ( ) Other (specify)

_____

15. Circumstances under which consent renewal deemed necessary or appropriate (check all that apply)
    ( ) Suggested or ordered by IRBs

( ) Evidence of confusion in the study population as to purpose of trial
( ) Flagging interest in the study population
( ) Increasing rate of dropout or of noncompliance
( ) Other (specify)

_____

F. Deconsent plan

16. Information to be imparted to participant on close of followup (check all that apply)
    ( ) Summary of findings from the trial
    ( ) Treatment person assigned to if masked to treatment assignment
    ( ) Availability of study treatment if found to be effective
    ( ) Treatment and care recommendations based on findings from the trial
    ( ) Possibility of future contact by study investigators for followup
    ( ) Other (specify)

    _____

17. Method of close out
    ( ) Common closing date regardless of when enrolled
    ( ) Close out on a per person basis after a specified period of followup (anniversary form of close out)
    ( ) Other (specify)

    _____

Note: Method of close out relevant to type of information that can be imparted to persons on close out. Unmasking on a per person basis in the anniversary form of close out may not be possible if unmasking serves to unmask others not yet closing out (e.g., as with the bin Id system of drug supply). Likewise, there will be no results to summarize for the first persons departing under the anniversary form of close out.

WS 8.1 Adverse event reporting worksheet (AE.WS)

When: Prior to the start of data collection

Who: Study chair or director of study coordinating center

Purpose: To outline procedures for reporting adverse events to IRBs

Definitions

adverse event - 1. Any unfavorable sign, symptom, state, condition, or laboratory finding in a study subject. 2. reportable event

reportable event - 1. adverse drug experience, serious adverse drug experience, unexpected adverse drug experience 2. adverse event 3. Any event or experience relating to a study subject and relevant to an oversight body, such as an IRB, in determining whether an approval should be maintained; any such event or occurrence listed as needing to be reported to an oversight body, such as an IRB as a condition for approval or maintaining approval. 4. Any event, circumstance, or occurrence threatening the integrity of a study. 5. Any event or occurrence listed as reportable by an extant governing, funding, oversight, or regulatory authority, such as the NIH, FDA, and ORI. *Usage note*: Problematic when used in the absence of defining detail regarding what, when, how, and where to report. The domain of reportable events is subject to change depending on perspective. Events considered not reportable during conduct of a study may be seen as reportable when a study is audited or reviewed. It is up to study investigators to develop and maintain essential reporting procedures in regard to the domain of reportable events. The duty to report extends to the broad class of events, including events of fraud, though the guidelines for deciding when the suspicion of fraud is sufficient to trigger a report to one's institutional committee dealing with such matters, or to the ORI, are largely lacking. All research involving human beings is under the purview of IRBs or like named bodies. Approvals from those bodies carry reporting obligations. In all cases, investigators are obliged to report mistakes or misadventures occurring in relation to the processes of enrolling, studying, treating, or following study subjects, and to do so regardless of whether such occurrences were of consequence to persons studied. Generally, approvals are predicated on the presumption that investigators will report deaths and morbidities occurring in the study population, that they will do so in a timely fashion, and that they will do so regardless of whether they are considered to be study-related. The presumption, in the case of multicenter studies, should be that study population is as represented by the population enrolled from all participating clinics and, therefore, that all investigators and associated IRBs are to receive reported events regardless of where first reported. IRBs may limit reporting to study-related deaths and morbid events in long-term treatment trials where the population being treated has high underlying mortality and morbidity rates. The reporting procedures imposed by the FDA relate to adverse events arising in relation to drugs, biologics, and devices being tested in relation to possible licensure. There are no corresponding procedures for trials of surgical procedures, trials of established medical treatments, or trials of other treatments not under the purview of the FDA. Hence, in those cases, investigators are largely left to establish definitions and procedures for reporting and informing investigators and associated IRBs. The likely minimum reporting requirements (in addition to those concerning mistakes or misadventures as mentioned above) are morbid events or deaths induced or likely

caused by a study procedure (including those where it is reasonable to so assume because of temporal relationship), any event occurring in conjunction with a study procedure, administration of a study treatment, or in relation to a change in treatment, deaths or major morbidities occurring in association with initiation or change of treatment, and events or occurrences leading to contact of an IRB by a study subject or representative of the study subject, and judged by that IRB to have legitimacy.

safety report - A report to the Food and Drug Administration of an adverse drug experience that is both serious and unexpected; written or telephoned; investigational new drug safety report; also IND safety report.

serious adverse drug experience - In FDA parlance, as contained in the Code of Federal Regulations for drugs for that agency: (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.80; CFR, title 21, vol 5, revised 1 April 2011) *Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.*

unexpected adverse drug experience - In FDA parlance: (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.80; CFR, title 21, vol 5, revised 1 April 2011) *Any adverse drug experience that is not listed in the current labeling for the drug product. This includes events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labeling only listed cerebral vascular accidents. "Unexpected," as used in this definition, refers to an adverse drug experience that has not been previously observed (i.e., included in the labeling) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.*

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—__—____

B. Background information

4. Does the trial involve drugs, biologics, or devices?
   ( ) No
   ( ) Yes

If yes, is the trial subject to reporting requirements for investigational drugs, biologics, or devices?
( ) No
( ) Yes

5. Are treatments double-masked?
   ( ) No
   ( ) Yes
   If yes, are events reported without knowledge of treatment assignment?
   ( ) No
   ( ) Yes

6. Does the study handbook or manual of operations contain definitions and instructions on reporting adverse events to local IRBs and to the coordinating center in multicenter trials?
   ( ) No (revise to include)
   ( ) Yes

7. Does the study handbook or manual of operations contain instructions as to whether the assigned treatment is to be continued in the face of adverse events?
   ( ) No (revise to include)
   ( ) Yes

C. Reporting procedure

8. Number of IRBs with authority over the trial?
   ( ) One
   ( ) More than one
   If more than one are all IRBs of record to be informed of events?
   ( ) No (explain why not)
   ( ) Yes
   Note: The usual reporting procedure in multicenter trials for events occurring at a study clinic is as follows:
   - Clinic reports event to its IRB
   - Clinic sends report to the coordinating center
   - CC sends report to all other centers with instructions to send to their respective IRBs if required by their IRB

9. In unmasked trials, are events reported to the coordinating center in multicenter trials distributed to clinics without treatment revealed?
   ( ) No (explain; the usual approach is to distribute without treatment revealed even if treatments are not masked)

   _____

   _____

   ( ) Yes

10. If treatments are administered double-masked, what events require unmasking? Note: The usual approach is simply to stop treatment absent unmasking. The only exceptions are emergencies where knowing treatment is of immediate importance to the person or to a member of the person's family for treatment

    _____

    _____

D. Aggregate review of adverse events

11. Is there a review and analysis of aggregate events by treatment group?
    ( ) No (explain; the expectation is that such reviews take place over the course of the trial)

    _____

    _____

    ( ) Yes

12. Does the trial have a treatment effects monitoring committee, aka data and safety monitoring committee?
    ( ) No (explain why not)

    _____

    _____

    ( ) Yes

13. If item 11 answered yes, who does the analysis?
    ( ) Coordinating center
    ( ) Sponsor
    ( ) Other (specify) _____

14. If item 11 answered yes, who reviews the analysis?
    ( ) Treatment effects monitoring committee/Data and safety monitoring committee
    ( ) Study officers
    ( ) Study steering committee
    ( ) Other (specify) _____

15. If item 12 answered yes, are IRBs informed of the review and recommendations of the monitoring committee?
    ( ) No (explain why not)

    _____

    _____

    ( ) Yes

16. If item 15 answered yes, who is responsible for sending the reports to centers for distribution to their respective IRBs?
    ( ) Coordinating center
    ( ) Study chair
    ( ) Sponsor
    ( ) Other (specify) _____

CL 8.1 Consent content checklist (Consent.CL)

When: The prototype consents are drafted prior to submission to IRBs and as checks of approved consent forms

Who: Persons in the coordinating center or office of the study chair

Purpose: For use in drafting prototype consents and for checking approved consent forms to make certain they contain necessary basic information

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Consent content checklist

4. General descriptive and design information
   - ( ) Description of the disease or condition being studied and how the person qualifies for the study
   - ( ) Type of persons being studied and the number to be enrolled
   - ( ) Anticipated length of treatment and followup
   - ( ) Description of data collection schedule procedures
   - ( ) Registration number on clinicaltrials.gov or other like websites

5. Treatment information
   - ( ) List of treatments to be studied and rationale for choice
   - ( ) Treatment alternatives available outside the study
   - ( ) Nature of the control or comparison treatment
   - ( ) Method of assigning persons to treatment
   - ( ) Method of treatment administration
   - ( ) Level of treatment masking and rationale
   - ( ) Nature of information regarding treatment results that will be made available to persons during and at the conclusion of the trial

6. Risk-benefit information
   - ( ) Description of the risks and benefits that may accrue to persons from participation in the trial
   - ( ) Enumeration of the potential risks and benefits associated with the study treatments and of likely side effects of treatment
   - ( ) Description of procedures that will be performed, including enumeration of the risks and benefits associated with those procedures, and the time points at which they are to be performed

7. Responsibilities of persons studied and their safeguards
   - ( ) Outline of responsibilities of persons enrolled in the trial, including discussion of the importance of adherence to treatment and followup
   - ( ) Outline of what is expected of persons in following the examination schedule and in carrying out special procedures between visits
   - ( ) Outline of safeguards to prevent continued exposure of persons to harmful study treatments or denial of beneficial treatments
   - ( ) Outline of safeguards for protecting a person's right to privacy and confidentiality
   - ( ) Enumeration of right of persons to withdraw from the trial without penalty or loss of benefits to which otherwise entitled
   - ( ) Statement of the policy of the investigator's institution on compensation for, or treatment of, study-related injuries
   - ( ) Statement of the person's right to have questions concerning the trial answered and enumeration of items of information that will not be disclosed (e.g., treatment assignment in double-masked trials)
   - ( ) Statement of the length of time personal identifiers will be retained after the close of the trial, where such information will be retained, and the reasons for keeping such information (e.g., for use in contacting or recalling persons after the close of the trial, if necessary); statement should also indicate ways in which the information may be used (e.g., to access the National Death Index or other information sources for determining mortality status after the close of the trial, if applicable)

8. Other information
   - ( ) Name and address of local study investigator
   - ( ) Name and address of IRB contact person
   - ( ) Registration number and web address of registration site
   - ( ) Enumeration of costs, if any, to study participants for tests or procedures performed
   - ( ) Approximate number of persons to be enrolled in trial

9 Masking tables, worksheets, and checklists

Table 9.1 Masking and separation specifications table (Mask.Tab)

When: In the design phase of the trial; update as necessary over the course of the trial

Who: Coordinating center

Purpose: To lay out masking and separation procedures to be practiced in the trial

Related form: WS 9.2

Definitions

bin number drug system - A system in double-masked randomized trials in which treatment assignment is indicated by bin number; typically a system in which more than one person receives medication from the same bin; system easier to implement and manage than unique medication number system and typically more medication conserving; downside relates to potential for collateral unmasking if a bin number is unmasked.

mask - A condition imposed on an individual (or group of individuals) for the purpose of keeping that individual (or group of individuals) from knowing or learning of some condition, fact, or observation, such as treatment assignment, as in single-masked or double-masked trials.

masking level - The degree to which treatment assignment and treatment administration is masked in a trial:

full masking - Masking in which neither study subjects nor study personnel know the treatments being administered and such that all treatments are similarly masked to each other, e.g., as in the Coronary Drug Project with all five test treatments masked against a single placebo.[4]

partial masking - Masking that is not full; single masking; masking imposed only on designated groups of persons: e.g., patients, treaters, data collectors, readers, monitors, or analysts; double dummy masking; masking in which only some of the treatments are masked, e.g., as in the University Group Diabetes Program[14] with the insulin treatments not masked and the two oral antidiabetic agents masked using a double dummy design.

none - No masking of treatment administration.

med Id number drug system - A drug dispensing system in which assigned treatment is indicated by a med number, e.g., a system in which patient Id number corresponds to med Id; dispensing system more difficult and expensive to implement and manage and less medication conserving than the bin number dispensing system, but immune to collateral unmasking because of unique numbering scheme.

separation - In the jargon of trials, the state of separating people responsible for treatment administration from people responsible for data collection in order to minimize the risk of treatment-related bias in unmasked trials.

A. Identifying information

1. Study name: _____

Table 9.1 Masking and separation specification table

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Study treatments

4. Treatment groups

   Test treatments . . . . . Number ___

   Control treatments . . . . . Number ___

5. Modes of treatment administration (check all that apply for the combination of test and control treatments)
   ( ) Oral
   ( ) Injected
   ( ) Implanted
   ( ) Suppository
   ( ) Other (specify)

   _____

C. Masking possibilities

6. Is the mode of administration the same for all study treatments (including the control treatment)?
   ( ) Yes
   ( ) No

7. Are the administration schedules the same for all study treatments?
   ( ) Yes
   ( ) No

8. Is the data collection schedule the same for all study treatments?
   ( ) Yes
   ( ) No

9. Is it safe to mask treatments?
   ( ) Yes
   ( ) No

10. Is it practical to mask treatments?
    ( ) Yes
    ( ) No

Note: Full double masking is possible only if all items in this section are answered yes. Partial double masking is possible if the study treatments include at least one test treatment and a control treatment where it is possible to answer yes to all of the questions above. Single masking is practical only if information on treatment can be kept from patients or treaters and only if it is safe to do so.

Table 9.1 Masking and separation specification table

Masking is not practical if there are obvious differences in how treatments are administered, differences in data collection schedules by treatment group, or if patients and treaters need to know treatment for proper care.

D. Full masking

11. Packaging of study treatments dispensed to patients
    - ( ) Bottles
    - ( ) Blister packs
    - ( ) Electronic pill dispenser
    - ( ) Syringe
    - ( ) Other (specify)

    _____

12. Distribution of study treatments to study clinics
    - ( ) Central pharmacy
    - ( ) Local pharmacies
    - ( ) Other (specify)

    _____

13. Method of denoting treatment assignments
    - ( ) Bin Id number
    - ( ) Med Id number
    - ( ) Other (specify)

    _____

E. Partial double masking

14. List the test treatments to be double masked among the set of test treatments

    1: . . . . . _____

    2: . . . . . _____

    3: . . . . . _____

15. Matching control treatment?
    - ( ) Yes
    - ( ) No

F. Single masking

16. Type of single masking
    - ( ) Patient masked, treaters not masked
    - ( ) Treater not masked, patients masked

Table 9.1 Masking and separation specification table

17. List the treatment to be single masked

    1: . . . . . _____

    2: . . . . . _____

    3: . . . . . _____

18. Method of masking treatment assignments to patients or treaters

    _____

    _____

    _____

G. Separations (not necessary with full double masking)

19. Does the study involve a design in which there is an attempt to keep data collectors from knowing treatment assignment?
    ( ) Yes
    ( ) No
    If yes, describe methods of keeping them from knowing assignments

    _____

    _____

    _____

H. Review and sign-off

20. Reviewing and approving body: _____

21. Date of sign-off (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

WS 9.1 Treatment masking worksheet (DrugMask.WS)

When: In the design phase of the trial

Who: Coordinating center personnel in conjunction with study officers

Purpose: To set-forth the masking procedures to be followed in the trial

Definitions

bin number drug system - A system in double-masked randomized trials in which treatment assignment is indicated by bin number; typically a system in which more than one person receives medication from the same bin; system easier to implement and manage than unique medication number system and typically more medication conserving; downside relates to potential for collateral unmasking if a bin number is unmasked.

double placebo - A placebo having two different shapes or forms, e.g., a tablet and a capsule, as needed in a double placebo treatment design; also double dummy placebo.

mask - A condition imposed on an individual (or group of individuals) for the purpose of keeping that individual (or group of individuals) from knowing or learning of some condition, fact, or observation, such as treatment assignment, as in single-masked or double-masked trials.

masking level - The degree to which treatment assignment and treatment administration is masked in a trial:

full masking - Masking in which neither study subjects nor study personnel know the treatments being administered and such that all treatments are similarly masked to each other, e.g., as in the Coronary Drug Project with all five test treatments masked against a single placebo.[4]

partial masking - Masking that is not full; single masking; masking imposed only on designated groups of persons: e.g., patients, treaters, data collectors, readers, monitors, or analysts; double dummy masking; masking in which only some of the treatments are masked, e.g., as in the University Group Diabetes Program[14] with the insulin treatments not masked and the two oral antidiabetic agents masked using a double dummy design.

none: No masking of treatment administration.

med Id number drug system - A drug dispensing system in which assigned treatment is indicated by a med number, e.g., a system in which patient Id number corresponds to med Id; dispensing system more difficult and expensive to implement and manage and less medication conserving than the bin number dispensing system, but immune to collateral unmasking because of unique numbering scheme.

separation - In the jargon of trials, the state of separating people responsible for treatment administration from people responsible for data collection in order to minimize the risk of treatment-related bias in unmasked trials. rt: **masking**, **shielding**

WS 9.1 Treatment masking worksheet

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . ___—___—____

B. Study treatments characteristics

4. Is the mode/route of administration the same for study treatments (test and control treatments)?
   ( ) Yes
   ( ) No

5. If item 4 answered no, is the mode/route of administration the same for some of the study treatments?
   ( ) Yes
   ( ) No

6. Is the administration schedule the same for the study treatments?
   ( ) Yes
   ( ) No

7. If item 6 answered no, is the administration schedule the same for some test treatments and a control treatment?
   ( ) Yes
   ( ) No

8. Is the data collection and followup schedule the same for all study treatment groups?
   ( ) Yes
   ( ) No

9. If item 8 answered no, is the data collection and followup schedule the same for some of the test treatments and a control treatment?
   ( ) Yes
   ( ) No

10. Are there circumstances in which treatment dosages have to be individualized?
    ( ) Yes
    ( ) No

11. Are there circumstances in which treatment dosage is titrated to achieve a desired blood level?
    ( ) Yes
    ( ) No

12. Is it possible to package and administer study treatments in identical fashion?
    ( ) Yes
    ( ) No

13. Is it safe to administer study treatments in double-masked fashion?
    ( ) Yes
    ( ) No

14. If item 13 is answered no, is it safe to administer treatments in single-masked fashion?
    ( ) Yes
    ( ) No

15. Is the risk of administering placebos minimal?
    ( ) Yes
    ( ) No

16. Is it feasible to mask the study treatments?
    ( ) Yes
    ( ) No

17. Level of masking possible
    ( ) Full double masking (items 4, 6, 12, 13, 15, and 16 answered yes; items 10, and 11 answered no)
    ( ) Partial masking (items 5, 7, 9, or 14 and 16 answered yes)
    ( ) None (items 14 or 16 answered no)

C. Study treatments and masking plan

18. List study treatment and level of masking relative to other treatments. If a treatment is single masked indicate nature of masking by checking "Pat" or "Phy" if the masking applies to persons receiving the treatment or to persons administering the treatment.

Test treatments	Full double masking	Partial double masking	Single masking		No masking
			Pat	Phy	
1 _____	( )	( )	( )	( )	( )
2 _____	( )	( )	( )	( )	( )
3 _____	( )	( )	( )	( )	( )
4 _____	( )	( )	( )	( )	( )
5 _____	( )	( )	( )	( )	( )

Control/comparison treatments

6 _____ ( ) ( ) ( ) ( ) ( )

7 _____ ( ) ( ) ( ) ( ) ( )

19. Level of masking to be practiced?
    ( ) Full double masking (answer questions in Section D)
    ( ) Partial masking (answer questions in Section E)
    ( ) None (answer questions in Section F)

20. Forms of placebos to be used (check all that apply)
    ( ) Pills/capsules
    ( ) Injections
    ( ) Implants
    ( ) Suppositories
    ( ) Ointments
    ( ) Other (specify)

_____

D. Full double masking

21. Mode of masking (check one)
    ( ) Single matching placebo
    ( ) Double placebo
    ( ) Other (specify)

_____

22. System for dispensing masked treatments (check one)
    ( ) Med Id number
    ( ) Bin number
    ( ) Other (specify)

_____

E. Partial masking

23. Extent of partial masking
    ( ) Single masking (answer items 24 - 26)
    ( ) Partial double masking (answer item 27)

24. Form of single masking
    ( ) Patients masked to treatment (specify treatment numbers from item 18; answer item 25) . . . . . _____
    ( ) Treaters masked to treatment (specify treatment numbers from item 18; answer item 26) . . . . . _____

25. Mode of patient masking
    - ( ) Nondisclosure (i.e., not telling patients of treatment being administered)
    - ( ) Sham
    - ( ) Subterfuge
    - ( ) Other (specify)

    _____

26. Mode of treater masking
    - ( ) Separation
    - ( ) Masking
    - ( ) Other (specify)

    _____

27. Partial double masking
    Give numbers of treatments from item 18 to be double masked . . . . . _____

    Mode of masking
    - ( ) Single placebo
    - ( ) Double placebo
    - ( ) Other (specify)

    _____

    System for dispensing masked drug (check one)
    - ( ) Med Id number
    - ( ) Bin number
    - ( ) Other (specify)

    _____

F. Treatments not masked

28. Treatments not masked (specify treatment numbers from item 18) . . . . . _____

29. In regard to unmasked treatments, will there be efforts to block flow of information on treatment to study patients or clinic personnel?
    - ( ) Yes
    - ( ) No

    If yes, indicate blocks (check all that apply)
    - ( ) Study patients not told treatment assignment
    - ( ) Clinic personnel not told of treatment assignment
    - ( ) Study patients asked not to reveal treatment assignment to personnel responsible for data collection

( ) Other (specify)

_____

G. Review and sign-off

30. Reviewing and approving body: _____

31. Date of sign-off (day-month-year) . . . . . __—__—____

WS 9.2 Shielding and blackout worksheet (Shield.WS)

When: Prior to the start of data collection

Who: Study leaders

Purpose: To establish policy regarding access to interim treatment results

Related form: Table 9.1

Definitions

blackout - In the jargon of trials, a proscription on the flow of information outside the trial until finished or some other condition is satisfied, e.g., a blackout of treatment results until published.

shielding - The act or process of keeping designated types or classes of information (e.g., interim results) from specified groups or classes of persons (e.g., clinic personnel) during conduct of a trial.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __-___-____

B. Shielding and blackouts

4. Are results shielding and blackouts practiced?
   ( ) No
   ( ) Yes

5. Persons and groups to be shielded or blacked out from interim treatment results (check all that apply)
   ( ) Study patients
   ( ) All study personnel responsible for treatment administration or for data collection
   ( ) Study sponsors
   ( ) IRBs
   ( ) Other (specify)

   _____

   _____

6. Persons and groups seeing interim treatment results (check all that apply)
   ( ) Study PI/Study chair
   ( ) Director of data center/coordinating center

( ) Study officers (if not all officers specify officers who are shielded)

_____

( ) Project officer
( ) Voting members of the treatment effects monitoring committee
( ) Nonvoting members of the treatment effects monitoring committee
( ) Persons in the data center/coordinating center preparing treatment effects monitoring reports
( ) Others (specify)

_____

_____

7. Mode of shielding (check all that apply)
   ( ) By proscription on analyses that can be performed by individual investigators
   ( ) By restriction of access to data by treatment
   ( ) By proscription of presentation or publication of interim results
   ( ) Other (specify)

   _____

8. Points at which the shield is lifted (check all that apply)
   ( ) When the trial is finished
   ( ) When a treatment is stopped because of evidence of harm or benefit
   ( ) Other (specify)

   _____

9. Results provided investigators operating under results shield (check all that apply)
   ( ) Performance monitoring reports
   ( ) Adverse event reports
   ( ) Recommendations of treatment effects monitoring committee regarding continuation of the trial
   ( ) Results of the control-assigned group
   ( ) Other (specify)

   _____

C. Review and sign-off

10. Reviewing and approving body: _____

11. Date of sign-off (day-month-year) . . . . . __—__—____

CL 9.1 Treatment unmasking and unshielding procedures worksheet (UnMask.CL)

When: Early in the trial before there is need to unmask

Who: Persons in the coordinating center

Purpose: To set forth policy and procedures to be followed in unmasking in relation to trials involving masking or shielding

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—___—_____

B. Basics

4. Type of treatment structure (check one)
   ( ) Crossover
   ( ) Parallel

5. Followup design (check one)
   ( ) Common closing date
   ( ) Anniversary closing date

6. Treatment masking (check one)
   ( ) Single (check one)
      ( ) Patient masked; treater not masked
      ( ) Patient unmasked; treater masked
   ( ) Double

7. Reason for unmasking (check reason)
   ( ) End of trial
   ( ) Early stop
   ( ) End of followup for a person (anniversary close out)
   ( ) Emergency (e.g., overdose or child of patient swallowing several pills of patient's medication)
   ( ) Patient demand
   ( ) Other (specify)

   _____

C. Unmasking

8. Extent of unmasking allowed (check all that apply)
   ( ) Single assignment in relation to emergency or patient demand

( ) Patients and study personnel as patients exit the study on completion of followup
( ) En masse, some patients (e.g., in relation to a trial involving multiple treatment groups in which one of the treatments is stopped because of harmful effects)
( ) En masse, all patients (e.g., when the trial is stopped or finished)
( ) Other (specify)

_____

9. If single assignment unmasking in relation to emergency or patient demand, how is assignment unmasked?
   ( ) By study personnel opening a sealed envelope or label revealing assignment
   ( ) By study personnel calling a 1-800 number
   ( ) By study personnel calling the coordinating center
   ( ) Other (specify)

   _____

10. If unmasking in relation to anniversary close out, is it possible to unmask without collateral unmasking?
    ( ) Yes (med Id system of identification)
    ( ) No (bin Id system of identification)

11. If en masse for some patients in relation to a stop of one or more treatments while continuation of others, are those not receiving the treatments being stopped informed of the action and reasons for it?
    ( ) Yes
    ( ) No (explain why not)

    _____

12. If en masse for some or all patients, how are people informed of the treatment they received?
    ( ) By letter
    ( ) By telephone
    ( ) At the next study visit
    ( ) Other (specify)

    _____

13. For routine unmasking, are study patients and/or clinic personnel asked to guess the treatment assigned before unmasking?
    ( ) Yes
    ( ) No

14. For en masse unmasking of some patients in relation to a trial involving multiple treatment groups in which one of the treatments is stopped because of harmful effects, are patients remaining on study treatments reconsented with updated consents?

( ) Yes
( ) No (explain)

_____

D. Unshielding

15. Do investigators see interim treatment results?
    ( ) No
    ( ) Yes

16. If no, when do investigators see interim results?
    ( ) At a meeting where results are presented
    ( ) By circulation of a draft manuscript
    ( ) When results are published
    ( ) Other (specify)

_____

10 Monitoring tables, worksheets, and checklists

WS 10.1 Treatment effects monitoring specification worksheet (Tem.WS)

When: Before the treatment effects monitoring committee is appointed

Who: Director of the coordinating center or chair of the study

Purpose: To elucidate treatment effects monitoring policy and procedures

Definitions

firewall *n* - 1. A construct or device designed to prevent entry of or access to specified types or classes of information. 2. A construct within an organizational structure designed to keep specified people from having access to certain types or classes of information, e.g., such a construct in a coordinating center of a multicenter trial designed to keep the director of the center from seeing interim treatment results.

masked treatment effects monitoring *n* - Treatment effects monitoring in which results are masked to treatment assignment.

masked treatment effects monitoring committee *n* - A treatment effects monitoring committee masked to treatment assignment, e.g., as achieved by presenting the committee with a treatment effects monitoring report with treatment groups denoted by codes.

masked treatment effects monitoring report *n* - A report in which treatment group is coded to obscure its identity, e.g., a report in a trial involving a single test and a single control treatment in which results are identified to "Trt A" or "Trt B". The effect of the coding is to leave reviewers uncertain as to whether "Trt A" identifies the test or control treatment.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date (day-month-year) . . . . . __—___—____

B. Trial particulars

4. Name of trial _____

5. Type of trial (check one)
   ( ) Single center
   ( ) Multicenter
   ( ) Other (specify)

   _____

6. Class of trial (check one)
   ( ) Treatment

( ) Primary prevention
( ) Secondary prevention
( ) Other (specify)

_____

7. Treatment design (check one)
   ( ) Parallel
   ( ) Crossover
   ( ) Other (specify)

_____

8. Phase (check one)
   ( ) 1 or 2
   ( ) 3
   ( ) 4
   ( ) Other (specify)

_____

9. Test treatment(s) (check all that apply)
   ( ) Drug
   ( ) Surgery
   ( ) Radiation
   ( ) Biologic
   ( ) Device
   ( ) Exercise
   ( ) Life style change
   ( ) Other (specify)

_____

10. Control (comparison) treatment(s) (check all that apply)
    ( ) Placebo
    ( ) Sham
    ( ) Medical
    ( ) Observation
    ( ) Other (specify)

_____

11. Study treatment groups

    Test-treated groups . . . . . Number _____

Control-treated groups . . . . . Number _____

Total . . . . . Number _____

12. Assignment ratio to lowest whole numbers (e.g., 2:2:2:2:2:5 for trial with 2.5 times as many people in the control-assigned group than in any one of the 5 test-assigned treatment groups) . . . . . _____

13. Planned total sample size . . . . . _____

14. Primary outcome variable (check one)
    ( ) Death

    ( ) Cause specific death (specify) . . . . _____

    ( ) Morbid event (specify) . . . . . _____

    ( ) Change variable (specify) . . . . . _____

    ( ) Composite (specify) . . . . . _____

    ( ) Other (specify) . . . . . _____

15. Secondary outcome measures

    1 _____

    2 _____

    3 _____

    4 _____

C. Treatment effects monitoring test (a "yes" answer to any of the questions below implies a need for treatment effects monitoring)

16. Does the trial involve 2 or more study treatments? . . . . . ($_{y}$) ($_{n}$)

17. Are treatments assigned by randomization? . . . . . ($_{y}$) ($_{n}$)

18. Is the ethical basis for randomization subject to change as a result of accumulating data internal or external to the trial during conduct? . . . . . ($_{y}$) ($_{n}$)

19. Is the period of enrollment 6 months or longer? . . . . . ($_{y}$) ($_{n}$)

20. Are investigators shielded from interim results? . . . . . ($_{y}$) ($_{n}$)

21. Do the treatments carry risks for persons receiving them? . . . . . (y) (n)

22. Are treatments administered in masked fashion? . . . . . (y) (n)

23. Does the trial involve avoidable risk? . . . . . (y) (n)

24. Is the risk of avoidable harm likely to be reduced by treatment effects monitoring? . (y) (n)

D. Monitoring prerequisites (a "no" to any of the questions below serves to raise questions concerning adequacy of the data system and organizational structure of the trial to support monitoring)

25. Does the trial have a visit-driven (as opposed to batch-driven) data collection system? . . . . . (y) (n)

26. Do data forms get data entered on or shortly after completion? . . . . . (y) (n)

27. Does the study have a system for timely harvest of data for analysis? . . . . . (y) (n)

28. Does the trial have a data or coordinating center adequately staffed for interim data analyses? . . . . . (y) (n)

29. Is there an organizational structure for addressing issues of safety and for acting upon results-based recommendations from monitoring? . . . . . (y) (n)

E. Monitoring approach and policy

30. Number of monitoring bodies
    - ( ) One
        - ( ) Dedicated (i.e., trial specific)
        - ( ) Shared (i.e., responsible for monitoring several trials)
    - ( ) Two
        - ( ) One for safety and one for efficacy
        - ( ) One appointed by sponsor and one appointed by investigators
        - ( ) Other (specify)

_____

31. Responsible monitoring party (check one)
    - ( ) Sponsor (not recommended)
    - ( ) Single person (not recommended)
    - ( ) Principal investigator/study director
    - ( ) Study investigators
    - ( ) Steering committee
    - ( ) Monitoring committee
    - ( ) Other (specify)

_____

32. Who sets monitoring policy? (check one)
    ( ) Sponsor
    ( ) Investigators
    ( ) Monitoring committee
    ( ) Other (specify)

    _____

33. Who has the final say on monitoring policy? (check one)
    ( ) Sponsor
    ( ) Study investigators
    ( ) Monitoring committee
    ( ) Parent IRB
    ( ) Other (specify)

    _____

F. Monitoring duties and responsibilities

34. Primary duty of monitoring body?
    ( ) Safety monitoring
    ( ) Efficacy monitoring
    ( ) Both safety and efficacy

35. Monitoring functions (check all that apply)
    ( ) Review of safety reports
    ( ) Review of adverse events
    ( ) Review of treatment-related protocol deviations
    ( ) Review of treatment errors
    ( ) Review of treatment differences for primary and secondary outcome measures
    ( ) Results-based recommendations regarding continuation
    ( ) Other (specify)

    _____

36. Other duties and responsibilities (check all that apply)
    ( ) Performance monitoring
    ( ) Advisory to sponsor
    ( ) Advisory to investigators
    ( ) Protocol review
    ( ) Protocol approval
    ( ) Review of protocol changes
    ( ) Approval of protocol changes
    ( ) Review of ancillary studies
    ( ) Approval of ancillary studies
    ( ) Review of study manuscripts
    ( ) Approval of study manuscripts

( ) Proposals for analysis
( ) Analysis
( ) Other (specify)

_____

G. Name of monitoring body

37. Base name
    ( ) Committee (recommended)
    ( ) Board
    ( ) Other (specify)

    _____

38. Descriptor name
    ( ) Treatment effects monitoring
    ( ) Data and safety monitoring
    ( ) Safety monitoring
    ( ) Other (specify)

    _____

39. Full name

    _____

40. Acronym . . . . . _____

H. Charge and appointment

41. Charging authority
    ( ) Investigators (recommended)
        ( ) With advice and consent of sponsor
        ( ) Independent of sponsor
    ( ) Sponsor
        ( ) With advice and consent of investigators
        ( ) Independent of investigators
    ( ) Treatment effect monitoring body itself

42. Appointing authority
    ( ) Investigators
        ( ) With advice and consent of sponsor
        ( ) Independent of sponsor
    ( ) Sponsor
        ( ) With advice and consent of investigators
        ( ) Independent of investigators (not recommended)

43. Vetting authority
    ( ) Investigators
    ( ) Sponsor
    ( ) Investigators and sponsor

44. Letter of appointment to voting members of the committee from:
    ( ) Investigators
    ( ) Sponsor
    ( ) Investigators and sponsor

45. Conditions and expectations of appointee (as outlined in appointment letter; check all that apply)
    ( ) None
    ( ) Meeting attendance
    ( ) Disclosure of financial conflicts of interest
    ( ) Disclosure of scientific conflicts of interest
    ( ) Confidentiality
    ( ) IRB training
    ( ) HIPPA training
    ( ) Study knowledge assessment test
    ( ) Scientific neutrality on question being addressed
    ( ) Other (specify)

    _____

46. Term

    Chair

    ( ) With term (specify)

    _____

    ( ) Without term

    Voting members

    ( ) With term (specify)

    _____

    ( ) Without term

I. Pay and reimbursement for voting members (skip if voting members not paid)

47. Amount paid (check one)
    ( ) Retainer . . . . . Amount _____
    ( ) Per face-to-face meeting . . . . . Amount _____

( ) Per conference phone meetings . . . . . Amount _____

48. Payer
    ( ) Study
    ( ) Sponsor
    ( ) Other (specify)

    _____

J. Composition and qualifications

49. Membership by voting status

    Voting members (recommended: ≥ 3 but ≤ 7) . . . . . Number _____

    Non-voting members (equal to or less than voting members) . . . . . Number _____

    Total members . . . . . Number _____

50. Membership by study relationship

    Not study affiliated . . . . . Number _____

    Study affiliated . . . . . Number _____

    Total . . . . . Number _____

51. Required disciplines/specialities/experience of non-study members (check any that apply)
    ( ) Medicine
    ( ) Surgery
    ( ) Biostatistics
    ( ) Bioethics
    ( ) Clinical trials
    ( ) Other (specify)

    _____

52. Required disciplines/specialities/experience of study members (check all that apply)
    ( ) Medicine
    ( ) Surgery
    ( ) Biostatistics
    ( ) Bioethics
    ( ) Clinical trials
    ( ) Other (specify)

    _____

53. Required expertise of study members
    - ( ) Enrollment and consenting
    - ( ) Treatment under the study protocol
    - ( ) Data collection
    - ( ) Biostatistics
    - ( ) Data processing
    - ( ) Data analysis
    - ( ) Other (specify)

_____

54. Study positions to be represented on monitoring body (check all that apply)
    - ( ) Study chair
    - ( ) Study vice chair
    - ( ) Chair of steering committee
    - ( ) Director of coordinating center
    - ( ) Project officer
    - ( ) Other (specify)

_____

55. Desired discipline of committee chair
    - ( ) Biostatistics
    - ( ) Epidemiology
    - ( ) Clinical trials
    - ( ) Medicine
    - ( ) Bioethics
    - ( ) Other (specify)

_____

56. Desired chair experience (check at least one)
    - ( ) Directing a coordinating center
    - ( ) Clinical investigator in a clinical trial
    - ( ) Experience with treatments being tested
    - ( ) Other (specify)

_____

57. Voting member requirements (check all that apply)
    - ( ) Not affiliated with sponsor
    - ( ) Not affiliated with a study center
    - ( ) Not affiliated with any institution funding or receiving funding for the study
    - ( ) Other (specify)

_____

58. Standing of study members relative to nonstudy members
    ( ) Parity (except for voting)
    ( ) Non-parity (check all that apply)
        ( ) Excused when treatment-related results reviewed
        ( ) Absent during discussion and votes on treatment-related recommendations
        ( ) Excused from executive sessions of voting members

59. Study officers in attendance (check all that apply)
    ( ) Study chair/PI
    ( ) Director of coordinating center
    ( ) Project officer
    ( ) Other (specify)

_____

K. Meeting rules and policy

60. Quorum requirement (check one)

    Voting members
    ( ) Simple majority of voting members
    ( ) 2/3rds majority of voting members
    ( ) Other (specify)

_____

    Nonvoting study members (check one)
    ( ) Majority of nonvoting study members
    ( ) Director of coordinating center
    ( ) Director of coordinating center and chair of the study
    ( ) No requirement

61. Voting of chair of the committee (check one)
    ( ) Only in case of tie
    ( ) Other (specify)

_____

62. Voting method
    ( ) Secret ballot
    ( ) Revealed secret ballot
    ( ) Roll call
    ( ) Show of hands
    ( ) Other (specify)

_____

63. Voting provisions (check all that apply)

( ) Proxy
( ) Absentee
( ) Other (specify)

_____

64. Vote requirement for results-based recommendation
( ) Majority of voting members
( ) Majority of voting members present
( ) 2/3rds majority of voting members
( ) 2/3rds majority of voting members present
( ) Other (specify)

_____

65. Attendance requirement for voting members? . . . . . (y) (n)

If yes

Number of absences leading to warning letter . . . . . Number _____

Number of absences leading to dismissal . . . . . Number _____

L. Production and distribution of monitoring reports

66. Center responsible for production of monitoring reports (check one)
( ) Coordinating center
( ) CRO
( ) Office of study chair
( ) Sponsor
( ) Other (specify)

_____

67. Center/group responsible for distribution of monitoring reports to committee members (check one)
( ) Coordinating center
( ) CRO
( ) Office of study chair
( ) Sponsor
( ) Other (specify)

_____

68. Method of distribution of reports to committee members (check one)
( ) Hard copy at meeting
( ) Hard copy by mail

( ) Hard copy by express courier
( ) Electronic as pdf (not recommended if confidentiality required)
( ) Other (specify)

_____

69. Report features (check all that apply)
( ) Bound via stapling, O rings, or in notebook binder
( ) Sequential page numbering
( ) Table of contents
( ) Common cutoff date for tables and analyses in report
( ) Other (specify)

_____

_____

70. Confidentiality safeguards (check all that apply)
( ) Cover page indicating date of report, producer, distributor, and notice that contents are confidential
( ) Copies collected at end of meeting
( ) Copies numbered identified to individual members
( ) Other (specify)

_____

71. Minutes

Taken by?
( ) Study staff person
( ) Sponsor (not recommended)
( ) Study officer
( ) Other (specify)

_____

Distributed by?
( ) Office of study chair
( ) Coordinating center
( ) Sponsor (not recommended)
( ) Other (specify)

_____

Official repository of minutes?
( ) Office of study chair
( ) Coordinating center

( ) Sponsor (not recommended)
( ) Other (specify)

_____

Official repository of notice of meeting for distribution to local IRBs?
( ) Office of study chair
( ) Coordinating center
( ) Sponsor (not recommended)
( ) Other (specify)

_____

72. Warnings and instructions for committee members (check all that apply)
( ) Risk of insider trading (in trials involving proprietary products)
( ) Conflicts of interest
( ) Requirement for confidentiality
( ) Case studies of how leaks occur
( ) Other (specify)

_____

M. Meeting modes and arrangements

73. Usual meeting mode
( ) Conference phone
( ) Face-to-face
Usual meeting location?
( ) Airport
( ) Coordinating center
( ) Office of study chair
( ) Sponsor
( ) Other (specify)

_____

74. Timing of meetings
( ) Variable
( ) Based on enrollment landmarks
( ) Based on number of events
( ) Other (specify)

_____

( ) Fixed calendar time
( ) Once a year
( ) Twice a year

( ) Other (specify)

_____

75. Usual meeting time
    ( ) Daytime
    ( ) Evening

76. Usual meeting day
    ( ) Tue - Thur
    ( ) Monday
    ( ) Friday
    ( ) Sat
    ( ) Sun
    ( ) Any weekday
    ( ) Any weekend day

77. Meeting scheduler
    ( ) Office of study chair
    ( ) Coordinating center
    ( ) Sponsor
    ( ) Other (specify)

_____

78. Travel arrangements and hotel booking?
    ( ) By traveler
    ( ) By scheduler
    ( ) Other (specify)

_____

N. Proposed objectivity constructs

79. Coordinating center firewall (not recommended)? . . . . . (y) (n)

80. Masked monitoring (i.e., where treatment groups are identified by letter or number code)? (y) (n)
    If yes, what is the nature of masking?
    ( ) Imposed (i.e., where treatment groups are identified by arbitrary letter codes and where the mask remains in place until formal action of the committee to lift the mask)
    ( ) Voluntary (i.e., where treatment groups are identified by arbitrary letter codes, but where individual members are provided with the codes in envelopes to be opened when individual members so elect)
    ( ) Disclosed (i.e., where treatment groups are identified by arbitrary letter codes, but where the coding is revealed to members prior to the start of each review)
    ( ) Other (specify)

81. If imposed masking, what are the provisions for lifting the mask?
    - ( ) Not specified (fix by specifying provisions)
    - ( ) Majority vote; all members
    - ( ) Majority vote; voting members only
    - ( ) 2/3rds majority vote; all members
    - ( ) 2/3rds majority vote; voting members only
    - ( ) Other (specify)

82. Look restrictions (not recommended)? . . . . . (y) (n)
    If yes, specify

    Number of looks . . . . . Number _____

    Based on:
    - ( ) Calendar time
    - ( ) Enrollment landmarks
    - ( ) Number of events

83. Stopping rule (not recommended)? . . . . . (y) (n)

    If yes, specify rule

84. Stopping guideline? . . . . . (y) (n)

    If yes, specify guideline

85. Coordinating center firewall (not recommended)? . . . . . (y) (n)
    If firewalled

    Who is firewalled (check all that apply)?
    - ( ) Center director
    - ( ) Statisticians
    - ( ) Programmers
    - ( ) Other (specify)

    When is the firewall lifted (check any that apply)?
    - ( ) Not specified (fix by specifying)

( ) When the trial is finished
( ) When there is a recommendation for an early stop
( ) When results are being prepared for presentation or publication
( ) Other (specify)

_____

O. Recommendation process and procedures for results-based recommendations

86. Mode of communication of recommendations to study leaders (check one)
( ) Oral
( ) Via chair of monitoring committee
( ) Via sponsor
( ) Via study chair
( ) Via coordinating center director
( ) Other (specify)

_____

( ) Written (recommended)
( ) Via chair of monitoring committee
( ) Via sponsor
( ) Via study chair
( ) Via coordinating center director
( ) Other (specify)

_____

87. Timing of communication (check one):
( ) At conclusion of meeting
( ) Within 24-hours of meeting
( ) Other (specify)

_____

88. Method of informing IRBs of committee meetings
( ) Via prototype letter to center directors for transmission to directors IRBs
( ) Other (specify)

_____

If via prototype letter, who produces and distributes the letter?
( ) Coordinating center
( ) Office of study chair
( ) Sponsor
( ) Other (specify)

89. Usual time lag for notice to study center directors for transmission to local IRBs

    Lag time . . . . . _____ days

90. Nature of report to IRBs (check all that apply)
    ( ) Time and place of meeting
    ( ) Persons in attendance
    ( ) Types of data reviewed
    ( ) Recommendation
    ( ) Other (specify)

91. Steps in implementing results-based recommendations (check all that apply)
    ( ) Notification of investigators via conference call or face-to-face meeting
    ( ) Notification of sponsor (and FDA when necessary)
    ( ) Development of plans for notifying patients of proposed change
    ( ) Developments of forms and documents needed to document communication of change to affected patients
    ( ) Revision of consent documents
    ( ) Notification of IRBs
    ( ) Other (specify)

P. Adequacy analysis (a "no" to any of the questions below suggests that the monitoring approach does not provide adequate protections for persons enrolled or for investigators doing the trial and should be cause for revision of the monitoring approach)

92. Is the monitoring body comprised to include study representatives to ensure competency in regard to the study protocol and data collection procedures? . . . . . ($_{y}$) ($_{n}$)

93. Is the monitoring body free to act and deliberate without constraint? . . . . . ($_{y}$) ($_{n}$)

94. Is the monitoring body inalienably linked to study investigators? . . . . . ($_{y}$) ($_{n}$)

95. Is there assurance that recommendations for result-based changes will pass to study investigators expeditiously? . . . . . ($_{y}$) ($_{n}$)

96. Is there assurance that recommendations for result-based changes will flow to IRBs in a timely fashion? . . . . . ($_{y}$) ($_{n}$)

97. Are investigators free to report recommendations for result-based changes without constraint or restriction of sponsors? . . . . . ($_{y}$) ($_{n}$)

98. Is the monitoring body free to meet and deliberate as it deems necessary without restriction or constraint? . . . . . (y) (n)

99. Has the IRB of the coordinating center and office of the study chair been appraised of monitoring procedures, policies, and practices? . . . . . (y) (n)

100. Will the consent form indicate how monitoring is to be done, detail constrictions placed on the monitoring body, and detail how recommendations for results-based changes will flow to investigators and via them to IRBs? . . . . . (y) (n)

101. Would you enroll your Mother in this trial with the monitoring proposed? . . . . . (y) (n)

WS 10.2 Treatment effects monitoring committee masking worksheet (TEMMask.WS)

When: The treatment effects monitoring committee is appointed and is to be masked to treatment group

Who: Director of the coordinating center

Purpose: To establish procedures for masking and for when the mask is lifted

Definitions

disclosed masked monitoring - Masking of monitoring reports where members are informed of the masking as a prelude to review; done primarily as protection against leaks of interim results in the event monitoring reports are seen by nonmembers.

imposed masked monitoring - Masking of monitoring reports held in place until lifted by action of the monitoring committee; typically in relation to treatment results considered sufficient to require unmasking

voluntary masked monitoring - Masking of monitoring reports where members of the monitoring committee are free to unmask themselves, typically with notice of other members; accomplished by providing members with envelopes revealing masking to be opened at will

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date (day-month-year) . . . . . __—___—_____

B. Background

4. Authority making the decision to mask the monitoring committee
   ( ) Study chair
   ( ) Steering committee
   ( ) Study officers
   ( ) Coordinating center
   ( ) Study sponsor
   ( ) Monitoring committee
   ( ) Other (specify)

   _____

5. Rationale for masking (check all that apply)
   ( ) To comply with sponsor guidelines for monitoring
   ( ) To force monitors to evaluate treatment differences without regard to sign of the treatment effect

( ) To protect results from inadvertent leaks
( ) Other (specify)

_____

6. Consent form includes statement indicating masked monitoring
   ( ) Yes
   ( ) No (explain)

   _____

7. IRBs informed that monitors will be masked
   ( ) Yes
   ( ) No (explain)

   _____

C. Masking method and procedure

8. Method of masking
   ( ) Imposed
   ( ) Voluntary
   ( ) Disclosed
   ( ) Other (specify)

   _____

9. System of masking
   ( ) Constant across reports (i.e., a given treatment code identifies the same treatment group over time across reports)
   ( ) Varied across reports (i.e., codes for identification of treatment groups varied from report to report)
   ( ) Other (specify)

   _____

10. Extent of masking (check "yes" or "no" as to whether or not masked in monitoring reports)
    Note: The effectiveness of the mask depends on the extent to which results unmask. For example, side effects are generally unique to treatments. Masking treatment group for summaries of side effects will likely having the effect of unmasking the coding.
    ($_{y}$) ($_{n}$) Primary outcome data
    ($_{y}$) ($_{n}$) Secondary outcome data
    ($_{y}$) ($_{n}$) Side effects data
    ($_{y}$) ($_{n}$) Compliance data
    ($_{y}$) ($_{n}$) Counts of enrollment by treatment group

Other (specify)

_____

_____

_____

D. Unmasking imposed masking

11. Trigger point for unmasking
    ( ) Stopping rule based
    ( ) Committee discretion
    ( ) Other (specify)

    _____

12. Unmasking deliberations and vote

    Debate regarding unmasking
    ( ) Initiated by request of any member to unmask
    ( ) Motion, moved and seconded, to unmask
    ( ) Other (specify)

    _____

    Vote
    ( ) 2/3rds majority of voting members
    ( ) Majority of voting members
    ( ) Other (specify)

    _____

13. Bodies informed of unmasking (check all that apply)
    ( ) Steering committee
    ( ) Study officers
    ( ) Study sponsor
    ( ) IRBs
    ( ) Other (specify)

    _____

E. Review and sign-off

14. Reviewing and approving body: _____

15. Date of sign-off (day-month-year) . . . . . ___—___—____

CL 10.1 Monitoring and quality control specification checklist (MonSpec.CL)

When: Early in the course of the trial

Who: Director of the data coordinating center

Purpose: To outline monitoring and quality control procedures to be practiced in the trial

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date: . . . . . __—___—____

B. Performance monitoring checklist (check if to be performed and indicate frequency of report to study investigators)

Legend: **W**: Weekly; **M**: Monthly; **Q**: Quarterly; **SA**: Semiannually; **A**: Annually

		W	M	Q	SA	A
4. Enrollment						
( )	Enrollment measured against stated time	( )	( )	( )	( )	( )
( )	Enrollment by clinic	( )	( )	( )	( )	( )
( )	Demographic characteristics of enrollee	( )	( )	( )	( )	( )
5. Randomization and treatment						
( )	Persons randomized overall and by treatment group .	( )	( )	( )	( )	( )
( )	Persons randomized by clinic	( )	( )	( )	( )	( )
( )	Persons refusing the assigned treatment	( )	( )	( )	( )	( )
( )	Persons receiving treatment different from that assigned	( )	( )	( )	( )	( )
( )	Persons randomized not meeting eligibility requirements overall and by clinic	( )	( )	( )	( )	( )
( )	Persons off treatment	( )	( )	( )	( )	( )

		W	M	Q	SA	A
6. Followup and data collection						
( )	Missed visits overall, by clinic, and by treatment group	( )	( )	( )	( )	( )
( )	Dropouts overall, by clinic, and by treatment group	( )	( )	( )	( )	( )
( )	Persons withdrawing consent by treatment group and by clinic	( )	( )	( )	( )	( )
( )	Persons lost to followup overall, by clinic, and by treatment group	( )	( )	( )	( )	( )
( )	Persons with vital status unknown overall, by clinic and by treatment group	( )	( )	( )	( )	( )
( )	Unscheduled visits by treatment group	( )	( )	( )	( )	( )
( )	Person yrs, weeks, or days of followup overall and by treatment group	( )	( )	( )	( )	( )
7. Data entry and editing						
( )	Number of data forms keyed; total number and for current time interval	( )	( )	( )	( )	( )
( )	Number of data forms keyed within 7 days of completion over entire period of data collection and for the current time period; total and by clinic	( )	( )	( )	( )	( )
( )	Median and 90th percentile interval for time to data entry over the entire period of data collection and for the current time period, total and by clinic	( )	( )	( )	( )	( )
( )	Expected number of data forms in backlog awaiting data entry overall and by clinic	( )	( )	( )	( )	( )
( )	Edit discrepancy rate per form overall time and current edit period by clinic and total	( )	( )	( )	( )	( )
( )	Edit discrepancy rate overall time and for the current edit period by clinic and total	( )	( )	( )	( )	( )
8. Site visiting						
( )	Cumulative count of site visits to-date	( )	( )	( )	( )	( )
( )	Cumulative count of site visits for cause	( )	( )	( )	( )	( )

		W	M	Q	SA	A
( )	List of site visits done in the last reporting interval	( )	( )	( )	( )	( )
( )	List of site visits planned in next reporting interval	( )	( )	( )	( )	( )

9. Protocol changes, IRB approvals, and consent
   - ( ) Cumulative list of protocol changes
   - ( ) Cumulative list of policy and protocol memoranda
   - ( ) Protocol versions; numbers and dates of issue
   - ( ) Table giving dates of submissions and approvals of IRBs for protocol changes and amendments
   - ( ) Copy of all versions of prototype consent forms
   - ( ) Checklist of content and promises made in consent forms used at individual clinics
   - ( ) Other (specify)

_____

10. Protocol deviations and overrides
    - ( ) Count of protocol deviations by time and clinic
    - ( ) Classification of protocol deviations by severity
    - ( ) Protocol overrides by time and clinic
    - ( ) Other (specify)

_____

11. Other performance issues (check all that apply)
    - ( ) Maintained list of clinics added and departing the trial
    - ( ) Log of revisions to the sample size requirement and time table of the trial
    - ( ) Maintained list of funding renewals
    - ( ) Other (specify)

_____

C. Treatment effects monitoring checklist (check all that apply)

- ( ) Circulation of adverse events as they occur to clinics and IRBs
- ( ) Treatment effects monitoring committee in place with written operating policy
- ( ) Treatment effects monitoring reports summarizing treatment difference by treatment group as prepared by the data coordinating center
- ( ) Membership list of voting and nonvoting members maintained
- ( ) Notification of IRBs of meetings of the treatment monitoring committee
- ( ) Other (specify)

_____

D. Quality control checklist (check all that apply)

( ) Data editing
( ) Independent double data entry
( ) Dependent double data entry
( ) Routine site visiting
( ) Site visiting for cause
( ) Repeat readings
( ) Independent counts of key events
( ) Independent reprogramming for verification of key results prior to publication
( ) Storage of sample drugs as checks on labeling and for purity analyses
( ) Other (specify)

11 Analysis tables, worksheets, and checklists

Table 11.1 Analysis specification table (AnalSpec.Tab)

When: Early in the course of the trial, ideally before the start of data collection and reviewed and periodically updated over the course of the trial

Who: Leadership persons in the data center

Purpose: To cause study leaders to be proactive in addressing key questions regarding approaches to analysis

Definitions

design variable - The variable used for determining sample size in planning a trial.

final dataset - The dataset compiled on completion of a study for use in final data analysis and for archiving.

interim analysis - Any analysis for treatment effects before data collection is finished.

interim dataset - A dataset prepared during a trial for some purpose, especially one prepared for treatment effects monitoring and involving a snapshot of data collected and processed through a specified cutoff date.

primary outcome - The event or condition a trial is designed to treat, ameliorate, delay, or prevent.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Basics

4. Primary mode of data collection
   ( ) Direct from study subjects via examination and interview
   ( ) Indirect
      ( ) From medical records
      ( ) Other (specify)

      _____

5. Primary method of data entry
   ( ) At collection sites
      ( ) via laptops
      ( ) From completed forms via the internet web

Table 11.1 Analysis specification table

( ) Other (specify)

_____

( ) At the data center from completed data forms
( ) Other (specify)

_____

6. Official repository of study data
   ( ) Data center/coordinating center
   ( ) Sponsor
   ( ) Contract research organization
   ( ) Other (specify)

_____

7. Official study analysis center
   ( ) Data center/coordinating center
   ( ) Sponsor
   ( ) Contract research organization
   ( ) Other (specify)

_____

8. Access to interim treatment results
   ( ) Restricted
      ( ) Limited to data center
      ( ) Limited to data center and treatment effects monitoring committee (TEMC)
      ( ) Limited to data center, TEMC, and sponsor
      ( ) Other (specify)

_____

   ( ) Unrestricted within the investigator group
   ( ) Other (specify)

_____

9. Primary outcome measure
   ( ) Event
      ( ) Death (all cause)
      ( ) Cause specific death (specify)

_____

Table 11.1 Analysis specification table

( ) Morbid event (specify)

_____

( ) Other (specify)

_____

( ) Change measure (specify)

_____

( ) Other (specify)

_____

10. The variable used for sample size calculations (design variable)
    ( ) Same as in item 9
    ( ) Different from item 9 (specify variable used)

_____

11. Publication policy (check all that apply)
    ( ) Publication of treatment results prior to presentation
    ( ) Publication of interim results leading to a decision to halt treatment because of evidence of harm or of benefit
    ( ) Publication of final treatment results regardless of direction or nature and prior to presentation
    ( ) Other (specify)

_____

C. Counting and analysis rules and principles

12. Definition of "primary analysis" (check all that apply)
    ( ) Treatment comparisons involving the primary outcome
    ( ) Treatment comparisons based on analyses by assigned treatment
    ( ) Analysis of greatest relevance to the objective of the trial
    ( ) Treatment comparisons involving all persons randomized by treatment assignment
    ( ) Other (specify)

_____

13. Definition of "secondary analysis" (check all that apply)
    ( ) Treatment comparisons involving a secondary outcome measure
    ( ) Treatment comparisons of relevance to a secondary aim of the trial
    ( ) Treatment comparisons not according to the intention to treat (ITT) principle

Table 11.1 Analysis specification table

( ) Other (specify)

_____

14. Definition of "subgroup analysis" (check all that apply)
    ( ) Treatment comparisons within subgroups of people defined by baseline or entry characteristics
        ( ) Subgroups specified when trial was designed
        ( ) Subgroup analyses performed to check on homogeneity of treatment effects across subgroups
    ( ) Treatment comparisons within subgroups of people defined by variables observed after randomization
    ( ) Other (specify)

    _____

15. Counting principles and rules (check all that apply)
    ( ) Person counted as randomized when treatment assignment revealed to clinic personnel
    ( ) Person counted to assigned treatment group in primary analyses regardless of subsequent nature or course of treatment
    ( ) Outcomes counted to the assigned treatment regardless of nature or course of treatment
    ( ) The starting point for counts of events is the moment of randomization, even if events observed before application of the first treatment

16. Primary treatment comparisons to be done by the intention-to-treat analysis principle?
    ( ) Yes
    ( ) No (explain)

    _____

    _____

    _____

17. If item 16 is answered "yes" and there are three or fewer checks in item 15, explain; counting rules inconsistent with requirements for ITT analyses

    _____

    _____

    _____

Table 11.1 Analysis specification table

D. Interim analyses for treatment effects monitoring

18. Person/group responsible for treatment effects monitoring
    ( ) Study statistician
    ( ) Committee
    ( ) Other (specify)

    _____

19. Frequency of interim looks
    ( ) Calendar-based (e.g., every 6 months)
    ( ) Enrollment-based (e.g., after enrollment of the 50th person, 100th person, etc.)
    ( ) Event-based (e.g., after a specified number of outcomes)
    ( ) Other (specify)

    _____

20. Monitoring constructs (check all that apply)
    ( ) Masking
    ( ) Stopping rule
    ( ) Stopping guideline
    ( ) Adjustment of p-values for multiple looks
    ( ) Adjustment of p-values for multiple comparisons
    ( ) None
    ( ) Other (specify)

    _____

E. Datasets

21. Interim datasets (check all that apply)
    ( ) Prepared by data center
    ( ) Analyses performed by data center
    ( ) Analyses done from frozen dataset
    ( ) Analyses done from live dataset
    ( ) Dataset includes data under edit
    ( ) Dataset excludes data under edit

22. Datasets underlying results publications (check all that apply)
    ( ) Cutoff date and rationale listed in publication
    ( ) Dataset available on request
    ( ) Data center custodian of dataset
    ( ) Other (specify)

    _____

23. Final dataset (check all that apply)
    ( ) Cutoff date beyond which edits and changes no longer accepted

( ) Cutoff date listed in publications based on the final dataset
( ) Notice of availability of deidentified dataset included in primary results publication
( ) Other (specify)

_____

F. Review and sign-off approval

24. Name of review and approving authority: _____

25. Date of sign-off (day-month-year) . . . . . ___—___—____

CL 11.1 Interim analysis checklist (IntAnal.Cl)

When: In relation to interim analyses done for treatment effects monitoring

Who: Senior analysis people in the coordinating center

Purpose: To outline checking procedures for a particular meeting of the treatment effects monitoring committee

Definition

interim data analysis - Any data analysis for treatment effects before data collection is finished.
Usage note: Strictly speaking, the term applies to any analysis in fixed or sequential sample size designs. However, the general convention is to reserve the term for fixed sample size designs and "sequential data analysis" for analyses done in relation to sequential designs.

A. Identifying information

1. Study name: _____

2. Interim analysis for treatment effects monitoring committee meeting of: . . . . . __—___—_____

3. Form completed by: _____

4. Date (day-month-year) . . . . . __—___—_____

B. Dataset and analysis policy

5. Analysis dataset
   ( ) Live
   ( ) Frozen (recommended)
   Freeze date . . . . . __—___—_____

   Data harvest through: . . . . . __—___—_____

6. Dataset prepared by:
   ( ) Coordinating center
   ( ) Contract research organization
   ( ) Sponsor
   ( ) Other (specify)

   _____

7. Features of the dataset (check any that apply)
   ( ) Dirty data (data with outstanding edits) included
   ( ) Imputation of missing values
   ( ) Data not deidentified

( ) Other (specify)

_____

8. Analysis done by:
   ( ) Coordinating center
   ( ) Contract research organization
   ( ) Sponsor
   ( ) Other (specify)

   _____

9. Purpose of analysis
   ( ) Efficacy analysis
   ( ) Safety analysis
   ( ) Efficacy and safety analysis

10. Counting principles and rules (check all that apply)
    ( ) Person counted as randomized when treatment assignment revealed to clinic personnel
    ( ) Person counted to assigned treatment group in primary analyses regardless of subsequent nature or course of treatment
    ( ) Outcomes counted to the assigned treatment regardless of nature or course of treatment
    ( ) The starting point for counts of events is the moment of randomization, even if events observed before application of the first treatment
    ( ) Other (specify)

    _____

11. Treatment comparisons adjusted for baseline difference?
    ( ) No
    ( ) Yes
    If "yes" list variables used for adjustment

    _____

12. P-values for treatment comparisons adjusted for multiple looks?
    ( ) No
    ( ) Yes
    If "yes" describe adjustment

    _____

C. Content of interim analysis report (check all that apply)

( ) Table of contents
( ) Enrollment by treatment group
( ) Baseline data by treatment group
( ) Dropouts by treatment group
( ) Losses to followup by treatment group
( ) Persons with vital status unknown by treatment group
( ) Treatment comparisons for primary outcome measure by treatment group
( ) Treatment comparisons for secondary outcome measures by treatment group
( ) Treatment comparisons for safety outcome measures
( ) Treatment comparisons within baseline subgroups of patients for the primary outcome measures
( ) Treatment comparisons within baseline subgroups of patients for secondary outcome measures
( ) Other (specify)

_____

D. Table layout and treatment labels

13. "As of date" cutoff date the same for all tables?
    ( ) Yes
    ( ) No (explain why dates differ)

    _____

14. Are treatments masked in the report of interim results?
    ( ) No (skip to item 17)
    ( ) Yes

15. Are all tables masked?
    ( ) Yes
    ( ) No
    If "no" what tables are not masked

    _____

16. For results that are masked is the labeling of treatment groups the same across tables (i.e., is the same code used to identify treatments across all tables in a report)?
    ( ) Yes
    ( ) No; give rationale

    _____

17. Is the ordering of results by treatment group the same across tables?

( ) Yes (e.g., in masked reports the control treatment is in the same column position across tables; in unmasked reports in a trial involving two test treatments, Test Trt 1 and Test Trt 2, and a control treatment, Ctrl 1, the ordering of columns is invariant across tables)
( ) No; explain

18. Are denominator data indicated in tables?
( ) Yes
( ) No (explain why not)

CL 11.2 Results paper analysis checklist (Anal.Cl)

When: In relation to manuscripts containing study results

Who: Senior analysis coordinating center personnel

Purpose: To provide checks to be made when preparing analyses for inclusion in finished manuscripts

Definitions

adjudication - In the context of trials and observational studies, a process involving a person or panel of persons to review raw events reported in a study to provide a coding independent of study investigators. Typically, regarded as superior to counts of raw unadjudicated events because of variation in the way they are reported and because of the risk of bias in how events are codified.

per assignment analysis (PAA) - Analysis by assigned treatment. syn: intention to treat analysis ant: per protocol analysis

per protocol analysis (PPA) - Analysis by administered treatment.

A. Identifying information

1. Study name: _____
2. Title of paper being checked: _____
3. Form completed by: _____
4. Date (day-month-year) . . . . . __—___—____

B. Dataset and analysis policy

5. Analysis dataset freeze cutoff date . . . . . __—___—____
6. Data harvest through: . . . . . __—___—____
7. Database custodian
   ( ) Coordinating center
   ( ) Other (specify)

   _____
8. Rationale for cutoff date included in manuscript
   ( ) No
   ( ) Yes (recommended)

9. Features of dataset (check any that apply)
   ( ) Dirty data (data with outstanding edits) not included
   ( ) Imputation of missing values
   ( ) Cumulative from beginning of trial to cutoff date
   ( ) Other (specify)

   _____

10. Counting principles and rules (check all that apply)
   ( ) Person counted as randomized when treatment assignment revealed to clinic personnel
   ( ) Person counted to assigned treatment group in primary analyses regardless of subsequent nature or course of treatment
   ( ) Outcomes counted to the assigned treatment regardless of nature or course of treatment
   ( ) The starting point for counts of events is the moment of randomization, even if events observed before application of the first treatment

11. Primary mode of presentation of treatment comparisons (check all that apply)
   ( ) P-values for treatment comparisons adjusted for multiple looks
   ( ) Confidence intervals for comparisons
   ( ) Treatment comparisons adjusted for baseline differences
   ( ) Per protocol analysis
   ( ) Missing values imputed
   ( ) None of the above

C. Quality control checks

12. Independent verification of counts represented in manuscript?
   ( ) No
   ( ) Yes (recommended)

13. Independent replication of analyses supporting manuscript?
   ( ) No
   ( ) Yes (recommended)

14. Adjudication of raw event data?
   ( ) No
   ( ) Yes

D. Table checks

15. Counts in tables based on the four counting principles listed in item 10?
   ( ) No (explain)

   _____

   ( ) Yes

16. Denominators for treatment groups indicated in tables?
    ( ) No (fix to include)
    ( ) Yes

17. Is the ordering of results by treatment group the same across tables?
    ( ) Yes
    ( ) No; explain; varied ordering makes comparisons across tables difficult

18. Table titles and footnotes to tables sufficient for persons to understand tables without having to read text in manuscript?
    ( ) No (revise as necessary)
    ( ) Yes

19. Arithmetical numbers in tables right aligned; decimal numbers aligned on decimal?
    ( ) No (revise as necessary)
    ( ) Yes

20. Decimal precision uniform within table and no more than the accuracy of the measure?
    ( ) No (fix)
    ( ) Yes

E. Cross checks

21. Numbers and p-values reported in abstract are as found in tables?
    ( ) No (fix)
    ( ) Yes

22. Numbers and p-values in body of manuscript are as found in tables and figures in the paper?
    ( ) No (fix)
    ( ) Yes

23. Differences in counts as contained in tables explained in text?
    ( ) No (fix)
    ( ) Yes
    ( ) Not applicable

24. Differences in totals across tables explained in text?
    ( ) No (fix)
    ( ) Yes
    ( ) Not applicable

F. Discussion and conclusions

25. Rationale for analysis approach described?
    ( ) No (add)
    ( ) Yes

26. If rates in tables not adjusted for baseline differences, does the text contain a statement indicating that adjustment made no material difference?
    ( ) No (explain)

    _____

    ( ) Yes

27. Baseline comparability of treatment groups addressed in manuscript?
    ( ) No (fix)
    ( ) Yes
        ( ) Baseline table included in paper
        ( ) Other (specify)

        _____

28. Original sample size goal and time table stated in manuscript?
    ( ) No (fix)
    ( ) Yes

29. If the dataset contains data irregularities or if data were purged from the dataset, are the irregularities or purges explained?
    ( ) No (fix)
    ( ) Yes

30. If conclusion is no treatment effect, does the text contain a statement indicating the power for detecting a difference?
    ( ) No (fix)
    ( ) Yes

31. If the treatment effect featured in the conclusions is for a subgroup of study subjects, is the difference likely to be reproducible?
    ( ) No (conclusion questionable)
    ( ) Yes

12 Publication tables, worksheets, and checklists

Table 12.1 Content suggestions for results study publication (PubCont.Tab)

1. Title section
- Descriptive title
- List of author-selected key words indicating general content of paper (useful for readers and as aids to NLM indexers)
- Author(s)
- Source(s) of financial support for the study
- Acknowledgements
- Credit roster
- Address of corresponding author

2. Abstract section
- Purpose of study
- Primary outcome measure
- Test treatment(s)
- Control treatment(s)
- Level of treatment masking
- Number of patients enrolled
- Method of treatment assignment
- Conclusion(s)
- Registration number and site

3. Introduction section
- Historical background of trial
- Rationale for the trial
- Objective(s)
- Rationale for choice of test and control treatment(s)
- Literature review

4. Methods section
- Study population
  - Eligibility and exclusion criteria
  - Method of patient recruitment
- Treatments
  - Study treatments
  - Method of treatment administration
  - Level of treatment masking
  - Treatment proscriptions
  - Methods of measuring treatment adherence
- Outcome measures
  - Primary and secondary outcome measures
  - Diagnostic criteria for outcome measurements
  - Methods for coding and classifying outcomes
- Design specifications
  - Method of randomization
  - Description of safeguards used to ensure integrity of the assignment process
  - List of stratification variables
  - Blocking specifications
  - Description of procedures for packaging and dispensing study medications in the case of masked drug trials
  - Primary outcome measure and rationale for choice
  - Planned length of patient followup and rationale for specification
  - Planned recruitment goal
  - Type I and II error protection levels for planned recruitment goal
- Patient safeguards
  - Outline of steps for obtaining patient consent
  - Method of updating consent
  - Measures taken to protect patient confidentiality
  - Description of procedures used to monitor study results for evidence of treatment effects
- Data collection schedule
  - Sequence of baseline and followup visits
  - List of data items collected
  - Definition of missed visits and dropouts
  - Name of person or agency to contact for copies of data forms, study manuals, etc.
- Data processing
  - Cut-off date for data included in manuscript
  - Description of approach and supporting rationale for dealing with missing data and departures from the treatment protocol (statement especially important if analysis

Table 12.1 Content suggestions for results study publication

method departs from preferred approach)
- Literature references for methods used
- Description of any special analysis procedures not already described in existing literature
- Methods for judging statistical importance of differences observed (e.g., nominal and adjusted *p*-values; confidence intervals)

• Quality control procedures
- General data editing
- Quality control of laboratory tests and for special reading and coding procedures
- Checks on data entry, programming, and analysis
- Other quality controls, such as site visits to clinics, training and certification, etc.

• Performance monitoring
- Measures used for assessing performance of participating clinics and resource centers
- Frequency of performance assessments
- Methods used for reviewing performance monitoring reports and for implementing corrective action based on those reviews

• Treatment monitoring
- Frequency of interim analyses for treatment monitoring
- Methods used to carry out interim analyses
- Individual or group responsible for carrying out interim analyses
- Procedures for implementing protocol changes based on results from interim analyses
- Masking

• Organizational structure
- Number and location of participating centers
- Location of data center
- Location of other resource centers
- Standing committees and their membership
- Mode of funding (e.g., grant or contract, individual or consortium award)
- Policy on investigator conflicts of interest and method used to monitor for potential conflicts of interest

• Other items
- Notation and language conventions in manuscript
- Listing of special actions taken during the trial including:
  · Addition or deletion of treatments
  · Addition or separation of study clinics
  · Data purges because of questions concerning data reliability or accuracy
  · Major modifications of data collection forms or coding procedures during the course of the trial

5. Results section

• Number of patients enrolled by treatment group
• Number of deaths by treatment group
• Comparison of treatment groups for primary and secondary outcome measures using various analytic techniques, including simple comparisons of proportions, as well as lifetable methods, etc.
• Indicators of the completeness of followup by treatment group, such as:
- Number of missed examinations
- Number of dropouts
- Number of patients lost to followup

• Indicators of treatment adherence, such as:
- Comparison of treatment groups using an adherence score or some laboratory measure
- Count of number of patients in each treatment group not receiving any of the assigned treatment

Table 12.1 Content suggestions for results study publication

- Count of number of patients in each treatment group receiving alternative treatments
- Assessment of the comparability of the treatment groups with regard to important baseline characteristics
- Treatment group comparisons for differences in:
  - Occurrence of serious side effects
  - Rate of hospitalization
  - Other general health indicators
- Treatment comparisons by selected baseline characteristics
- Multiple regression analyses using baseline characteristics to provide adjusted treatment comparisons
- Treatment comparisons by level of adherence
- Treatment comparisons by clinic in multicenter trials
- Other special analyses relating to followup data for a variable (e.g., cholesterol level) to a primary or secondary outcome measure (e.g., death)

6. Discussion section

- Discussion of how reported findings relate to previous studies, paying particular attention to those considered to be new and those that are not consistent with findings of previous studies
- Discussion of the implications of the findings
- Enumeration of questions or areas needing further analysis or research

7. Conclusion section

- Statement of conclusion
- Limits on generalization of the conclusions, including discussion of observed statistical power if no treatment difference is detected

8. Reference section

- List of literature references in required journal format
- Suitable reference citations for:
  - References to previous work
  - Data analysis methods
  - Laboratory methods
  - Coding or reading procedures for abstracting information from special records or documents
  - Treatment methods
  - Study rationale
  - Discussion of results
- List of study documents that may be obtained on request or via study website, such as study manual of operations, study data forms, data listings, data files, etc.

9. Appendix section*

- Description of special procedures needed to understand results, but too detailed to be included in the body of the publication
- List of definitions, codes, diagnostic criteria, etc.
- Special analyses, tabulations, and data listings
- Sample data forms

*Not required if previous publications contain essential details or if authors have provided some other means of supplying them (e.g., by depositing documents containing details in a public repository or by supplying them upon written request) or via study website.

WS 12.1 Paper production worksheet (PaperMon.WS)

When: As soon as paper writing starts

Who: A person in the office of the chair or in the coordinating center

Purpose: To provide data for study leaders in monitoring paper production

Definitions

ancillary publication - A publication bearing on an ancillary aim of a research project; in the case of trials, usually publications from ancillary studies.

primary publication - A publication from a study considered essential in relation to the primary purpose or objective of a research project; in the case of trials, includes publications of primary results and publication on the design, methods, and baseline results of the trial; aka: mainline paper

secondary publication - A study publication related to a secondary study objective; in the case of trials, usually publications devoted exclusively to results for a secondary outcome measure or publications providing added information bearing on a primary result.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

B. Publications

4. Published papers including "in press"?
   ( ) None; skip to next section
   ( ) One or more
   Number . . . . . ____

5. Breakdown of publications represented by total number in item 4 by type
   Primary . . . . . Number ____
   Secondary . . . . . Number ____
   Ancillary . . . . . Number ____
   Total . . . . . Number ____

6. Breakdown of publications represented by total number represented in item 4 by place of publication

   Indexed medical journal . . . . . Number ____

   Book/book chapter . . . . . Number ____

   Other . . . . . Number ____

   Total . . . . . Number ____

7. For papers published (item 4)

   Time from commissioning to publication (if total number in item 4 ≥ 2 give median time) . . . . . _____ wks

   Range of times if total number in item 4 ≥ 2 . . . . . _____ wks _____ wks

8. Publications (including "in press") in last 12 months?
   ( ) None; skip to next section
   ( ) One or more
   Number . . . . . ____

9. For papers published in last 12 months

   Time from commissioning to publication (if number in item 8 ≥ 2 give median time) . . . . . _____ wks

   Time range if number in item 8 ≥ 2 . . . . . _____ wks _____ wks

C. Commissioning/de-commissioning process

10. Does the study have a process for commissioning papers for development?
    ( ) No
    ( ) Yes

11. Who is the commissioning authority (check one)
    ( ) Study chair/PI
    ( ) Study officers
    ( ) Executive committee
    ( ) Steering committee
    ( ) Sponsor
    ( ) Other (specify)

    _____

12. Is the commission for manuscripts time limited?
    ( ) No
    ( ) Yes

    Period of commission . . . . . _____ wks

13. Is there a process for de-commissioning manuscripts?
    ( ) No
    ( ) Yes
    If "yes"
    Does the de-commission involve a formal written notice to manuscript chair?
    ( ) No
    ( ) Yes
    If "yes" does the notice indicate that the manuscript may be reassigned within the study investigatorship for production?
    ( ) No
    ( ) Yes

WS 12.2 Authorship policy worksheet (Author.WS)

When: Early in the course of the trial, well before any paper writing activities

Who: A principal study leader or study officer

Purpose: To lay out policy for authorship attribution on study papers prior to initiation of paper writing activities

Paper types

ancillary paper: A publication related to an ancillary aim of a research project; in the case of trials, usually publications from ancillary studies.

primary paper: A publication considered essential in relation to the primary objective of the study; in the case of trials, includes publications of primary results and publications on the design, methods, and baseline results of the trial.

secondary paper: A paper dealing with a secondary objective of the study

Authorship formats

corporate

corporate author citation: A form of citation with authorship attributed exclusively to a corporate entity; a citation absent the means of identifying the person or persons responsible for authoring the work and a masthead author listing involving only a corporate name (e.g., in a multicenter trial: The XYZ Research Group).

modified corporate author citation: A form of corporate author citation in which names of persons responsible for authoring a work appear in a footnote to the title page or in the credits or acknowledgments section of the work.

conventional

conventional author citation: A form of author citation with authorship attributed exclusively to named persons; an author masthead listing not containing a corporate name.

modified conventional author citation: A form of conventional author citation in which, in addition to named persons, the name of the corporate entity under which the work was done is listed in the masthead listing (e.g., Nancy Jones and Harry Brown for the XYZ Research Group).

Reminders and comments

- Assume that everyone in a research group is concerned about authorship
- When discussing authorship policy among investigators do not assume absence of comment means agreement
- Do not propose and vote on an authorship policy in the same deliberative session
- Policy should be discussed at least twice, separated in time by > 30 days before voting
- Vote by closed ballot
- Review policy at periodic intervals over the trial and modify as necessary

WS 12.2 Authorship policy worksheet

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—_____

B. Paper writing plans

4. Likely start of paper writing activities
   - ( ) During enrollment
   - ( ) End of enrollment, during followup
   - ( ) After end of trial

5. Papers planned (check all that apply)
   - ( ) Baseline results
   - ( ) Design and methods
   - ( ) Design and methods and baseline results
   - ( ) Primary results
   - ( ) Secondary results
   - ( ) Ancillary results
   - ( ) Other (specify)

_____

C. Authorship

6. Primary papers (check one)
   - ( ) Corporate
   - ( ) Modified corporate
   - ( ) Conventional
   - ( ) Modified conventional
   - ( ) Other (specify)

_____

7. Secondary papers (check one)
   - ( ) Corporate
   - ( ) Modified corporate
   - ( ) Conventional
   - ( ) Modified conventional
   - ( ) Other (specify)

_____

8. Ancillary papers (check one)
   ( ) Corporate
   ( ) Modified corporate
   ( ) Conventional
   ( ) Modified conventional
   ( ) Other (specify)

   _____

9. If "modified corporate" checked in any item above indicate policy for where writing committee is listed:
   ( ) Title page
   ( ) Credits section of manuscript
   ( ) Other (specify)

   _____

10. If "modified conventional" checked in any item above indicate whether the attribution to the study research group will be:
    ( ) "for" (e.g., R Jones, B Simth, and A Anderson **for** the XYZ Research Group)
    ( ) "and" (e.g., R Jones, B Simth, and A Anderson **and** the XYZ Research Group)
    ( ) "on behalf of" (e.g., R Jones, B Simth, and A Anderson **on behalf of** the XYZ Research Group)

11. Indicate how authors are chosen for study publications

    Primary papers
    ( ) Study chair/PI
    ( ) Study officers/executive committee
    ( ) Self-selection/volunteers
    ( ) Other (specify)

    _____

    Secondary papers
    ( ) Study chair/PI
    ( ) Study officers/executive committee
    ( ) Self-selection/volunteers
    ( ) Other (specify)

    _____

    Ancillary papers
    ( ) Study chair/PI
    ( ) Study officers/executive committee
    ( ) Self-selection/volunteers

( ) Other (specify)

_____

12. For papers with authors listed in publications, indicate policy on order of listing:

Primary papers

( ) Alphabetic
( ) 1st author then alphabetic order
( ) As ordered by study officers
( ) As specified by senior author
( ) By order of contribution to writing effort
( ) By order of contribution to study
( ) Other (specify)

_____

Secondary papers

( ) Alphabetic
( ) 1st author then others in alphabetic order
( ) As ordered by study officers
( ) As determined by senior author
( ) By order of contribution to writing effort
( ) By order of contribution to study
( ) Other (specify)

_____

Ancillary papers

( ) As determined by senior author
( ) By order of contribution to writing effort
( ) By order of contribution to the ancillary study
( ) Other (specify)

_____

13. Bounds on numbers of persons listed as authors?

Primary papers

( ) No limit
( ) Limit . . . . . Lower ___ Upper ___

Secondary papers

( ) No limit
( ) Limit . . . . . Lower ___ Upper ___

Ancillary papers

( ) No limit

( ) Limit . . . . . Lower ___ Upper ___

D. Review and acceptance procedure

14. Name of study reviewing and accepting body of authorship rules
    ( ) Steering committee
    ( ) Executive committee
    ( ) Study officers
    ( ) Other (specify)

    _____

15. Date of 1st review . . . . . __–__–____

16. Date of 2nd review . . . . . __–__–____

17. Date of official acceptance . . . . . __–__–____

WS 12.3 Paper proposal worksheet (Proposal.WS)

When: Mid course in the trial when plans for paper writing start to jell

Who: Study leaders

Purpose: To provide plans for monitoring the production of papers

Definitions

ancillary publication - A publication bearing on an ancillary aim of a research project; in the case of trials, usually publications from ancillary studies.

commissioned manuscript - A manuscript commissioned by study leaders

investigator-proposed manuscript - A manuscript proposed by a study investigator

primary publication - A publication from a study considered essential in relation to the primary purpose or objective of a research project; in the case of trials, includes publications of primary results and publication on the design, methods, and baseline results of the trial; aka: mainline paper

secondary publication - A study publication related to a secondary study objective; in the case of trials, usually publications devoted exclusively to results for a secondary outcome measure or publications providing added information bearing on a primary result.

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __ __—__ __ __—__ __ __ __

B. The proposal

4. Initiative (check one)
   - ( ) Commissioned by study leaders
   - ( ) Investigator-initiated
   - ( ) Sponsor-initiated
   - ( ) Other (specify)

     _____

5. Type of manuscript (check one)
   - ( ) Primary treatment results
   - ( ) Secondary treatment results
   - ( ) Safety results

( ) Design, methods, and baseline results
( ) Natural history
( ) Ancillary study
( ) Other (specify)

_____

6. Tentative title

_____

7. Target journals

1 _____

2 _____

8. Proposed authorship format; see *Authorship policy worksheet* (WS 12.2) for definitions (check one)
( ) Conventional
( ) Modified conventional
( ) Corporate
( ) Modified corporate
( ) Other (specify)

_____

9. Summary of purpose of paper

_____

_____

_____

10. Data required from coordinating center?
( ) No
( ) Yes (specify types and amounts of data required)

_____

_____

11. Analytical and statistical help required from the coordinating center?
( ) No
( ) Yes

12. Approximate time from commission to first submission of manuscript for publication?
    ( ) 3 months
    ( ) 6 months
    ( ) 9 months
    ( ) Other (specify)

    _____

C. Commissioning and approval

13. Commissioning and approving authority (check one)
    ( ) Study chair/PI
    ( ) Study officers
    ( ) Executive committee
    ( ) Steering committee
    ( ) Other (specify)

    _____

14. Lead author/chair of writing committee

    _____

15. Other authors/members of the writing committee

	Name	Center	Discipline
1			
2			
3			
4			
5			
6			

16. Date of approval or of commissioning . . . . . ___—___—_____

17. Conditions of approval imposed by approving body listed in item 13 (check all that apply)
    ( ) Review and approval of manuscript prior to submission for publication
    ( ) Inclusion of study credit list in finished manuscript
    ( ) Listing of funding source in manuscript

( ) Other (specify)

WS 12.4 Study CV worksheet (CV.WS)

When: Early in the course of the trial

Who: A person designated by the study leadership

Purpose: To maintain a record of study history and accomplishments

Definition

study curriculum vitae - A document similar to that for a person but with the study being the subject of the vitae; giving particulars of the study including history, purpose, design, funding, mode of initiation, centers and related personnel, presentations, and publications, see https://jhuccs1.us/adapt/ for example.

Reminders and recommendations

- Assume need for study CV and proceed accordingly
- The time to produce a log of study activities is when the activities occur
- Study CVs have various uses including those related to renewal of funding and for details required when producing papers or presentations

A. Identifying information

1. Study name: _____

2. Completed by: _____

3. Date completed (day-month-year) . . . . . __-___-____

B. Content checklist

4. Information to be included in CV (check all that apply)
   - ( ) Funding history
   - ( ) Statement of study objectives
   - ( ) Study log/chronology of events
   - ( ) Design summary
   - ( ) Participating centers (past and present)
   - ( ) Committees (past and present)
   - ( ) Enrollment history
   - ( ) Publications
   - ( ) Presentations
   - ( ) Ancillary studies
   - ( ) Glossary of study abbreviations
   - ( ) Other (specify)

_____

C. Maintenance

5. CV custodian: _____

6. CV update frequency
   ( ) As needed
   ( ) At specified time intervals (specify time)

   _____

D. Availability and access

( ) Password-protected website
( ) Open access website
( ) Other (specify)

_____

E. Sign-off approval

7. Name of review and approving body: _____

8. Date of sign-off: . . . . . __—__—____

CL 12.1 Content checklist for results papers (Paper.CL)

A. Identifying information

1. Study name: _____

2. Title of paper

_____

3. Form completed by: _____

4. Date completed (day-month-year) . . . . . __—___—_____

B. Title page checklist

5. Title ≤ 10 words
   ( ) Yes
   ( ) No (shorten)

6. Title form
   ( ) Neutral
   ( ) Declarative

7. Design and methods descriptive terms in title (check all that apply)
   ( ) Trial
   ( ) Randomized
   ( ) Controlled
   ( ) Placebo-controlled
   ( ) Mask/blind
   ( ) Other (specify)

_____

8. Population descriptors
   ( ) No
   ( ) Yes
   Check all that apply
   ( ) Adults
   ( ) Adolescents
   ( ) Children
   ( ) Infants
   ( ) Elderly
   ( ) Males
   ( ) Females
   ( ) Pregnant females
   ( ) Other (specify)

_____

9. Disease/treatment descriptors
   ( ) No
   ( ) Yes (list)

   _____

10. Author-selected key words
    ( ) No
    ( ) Yes (list)

    _____

11. Masthead author listing
    ( ) Conventional
    ( ) Modified conventional
        ( ) **and** the XYZ Research Group
        ( ) **for** the XYZ Research Group
        ( ) **on behalf of** the XYZ Research Group
    ( ) Corporate
    ( ) Modified corporate
        ( ) Writing committee listed as footnote to title page
        ( ) Writing committee listed in credits section of manuscript

12. Order of authors in conventional formats
    ( ) Alphabetic
    ( ) Reverse alphabetic
    ( ) Modified alphabetic (1st author followed by others in alphabetic order)
    ( ) Modified reverse alphabetic (1st author followed by others in reverse alphabetic order)
    ( ) As determined by 1st author
    ( ) As determined by commissioning body
    ( ) Other (specify)

    _____

13. Name and address of corresponding author provided?
    ( ) Yes
    ( ) No (provide)

C. Abstract section

14. Structured?
    ( ) Yes
    ( ) No (required in most journals)

15. Content of abstract (check all that apply)
    ( ) Purpose of trial

( ) Primary outcome measure
( ) Test treatment(s)
( ) Control treatment(s)
( ) Level of treatment masking
( ) Number of persons enrolled
( ) Method of treatment assignment
( ) Conclusion(s)
( ) Registration number and registration site

D. Introduction section

16. Rationale for publication of results
    ( ) End of trial
    ( ) Treatment stopped because of harm
    ( ) Treatment stopped because of benefit
    ( ) Other (specify)

    _____

17. Rationale for publication stated in paper?
    ( ) Yes
    ( ) No (revise to state)

18. Content (check all that apply)
    ( ) Historical background of trial
    ( ) Rationale for trial
    ( ) Objective(s) of trial
    ( ) Rationale for choice of test and control treatment(s)
    ( ) Literature review
    ( ) Other (specify)

    _____

E. Methods section

19. Study population and enrollment
    ( ) Eligibility and exclusion criteria
    ( ) Method of patient recruitment
    ( ) Enrollment start and end date
    ( ) Consent process
    ( ) Other (specify)

    _____

20. Study treatments
    ( ) Test treatments
    ( ) Control/comparison treatment
    ( ) Treatment dosage

( ) Method of treatment administration
( ) Level of treatment masking
( ) Treatment contraindications and proscriptions
( ) Other (specify)

_____

21. Outcome measure focused upon in paper (specify)

_____

22. Design specifications (check all that apply)
    ( ) Method of randomization
    ( ) Description of safeguards to ensure the integrity of the assignment process
    ( ) List of stratification variables
    ( ) Blocking specifications
    ( ) Description of procedures for packaging and dispensing study medications (in masked drug trials)
    ( ) Primary outcome measure and rationale for choice
    ( ) Planned length of patient followup and rationale
    ( ) Planned recruitment goal
    ( ) Type I and II error protection levels for planned recruitment goal
    ( ) Other (specify)

_____

23. Patient safeguards
    ( ) Outline of steps for obtaining consent
    ( ) Method of updating consent (especially for long-term followup trials)
    ( ) Measures taken to protect patient confidentiality
    ( ) Description of procedures used to monitor study results for evidence of treatment effects
    ( ) Other (specify)

_____

24. Data collection schedule
    ( ) Sequence of baseline and followup visits
    ( ) Definition of missed visits and dropouts
    ( ) Other (specify)

_____

25. Data processing
    ( ) Cut-off date for data included in manuscript

( ) Description of approach and supporting rationale for dealing with missing data and departures from the treatment protocol
( ) Literature references for analysis methods
( ) Description of any special analysis procedures not already described in existing literature
( ) Methods for judging statistical importance of differences observed (e.g., nominal and adjusted *p*-values; confidence intervals)
( ) Other (specify)

_____

26. Quality control procedures
( ) General data editing
( ) Quality control of laboratory tests and for special reading and coding procedures
( ) Checks on data entry, programming, and analysis
( ) Other quality controls, such as site visits to clinics, training and certification, etc.
( ) Other (specify)

_____

27. Treatment effects monitoring
( ) Frequency of interim analyses for treatment monitoring
( ) Group responsible for monitoring
( ) Methods used to carry out interim analyses
( ) Procedures for implementing protocol changes based on results from interim analyses
( ) Masking
( ) Other (specify)

_____

28. Organizational structure
( ) Number and location of participating centers
( ) Location of data center
( ) Location of other resource centers
( ) Mode of funding (e.g., grant or contract; individual or consortium award)
( ) Other (specify)

_____

29. Other items
( ) Notation and language conventions in manuscript
( ) Addition or deletion of a treatment
( ) Addition or separation of study clinics
( ) Data purges because of questions concerning data reliability or accuracy
( ) Major modifications of data collection forms or coding procedures during the course of the trial

( ) Other (specify)

F. Results section

30. Enrollment and followup
    - ( ) Number of persons enrolled by treatment group
    - ( ) Number of ineligible persons enrolled by treatment group
    - ( ) Assessment of the comparability of the treatment groups with regard to important baseline characteristics
    - ( ) Number of deaths by treatment group
    - ( ) Visit completion rate by treatment group
    - ( ) Numbers of dropouts and person lost to followup by treatment group
    - ( ) Count of persons by treatment group not receiving the assigned treatment
    - ( ) Count of persons receiving an alternative treatment by treatment group
    - ( ) Person years of followup by treatment group
    - ( ) Other (specify)

---

31. Treatment comparisons
    - ( ) Comparison of treatment groups for primary and secondary outcome measures using various analytic techniques, including simple comparisons of proportions, as well as lifetable methods, etc.
    - ( ) Treatment group comparisons for differences in occurrence of serious side effects, rate of hospitalization, and other general health indicators
    - ( ) Treatment comparisons by selected baseline characteristics
    - ( ) Multiple regression analyses using baseline characteristics to provide adjusted treatment comparisons
    - ( ) Treatment comparisons by clinic (multicenter trials)
    - ( ) Other (specify)

---

32. Subgroup analyses
    - ( ) By disease state
    - ( ) By age
    - ( ) By gender
    - ( ) By ethnic origin
    - ( ) Other (specify)

---

33. Tables and figures
    - ( ) Adequately titled?
    - ( ) Column labels for treatment groups consistent across tables?

( ) Totals consistent across tables and figures?
( ) Values in tables decimal aligned?
( ) Other (specify)

_____

G. Discussion and conclusion sections

34. Discussion (check all that apply)
    ( ) Discussion of how reported findings relate to previous studies, paying particular attention to those considered to be new and those that are not consistent with findings of previous studies
    ( ) Discussion of the implications of the findings
    ( ) Enumeration of questions or areas needing further analysis or research
    ( ) Other (specify)

    _____

35. Conclusion (check all that apply)
    ( ) Succinct statement of conclusion
    ( ) Limits on generalization of the conclusions
    ( ) Discussion of observed statistical power if no treatment difference is detected
    ( ) Other (specify)

    _____

H. Referencing and supporting documentation

36. Unconnected references?
    ( ) No
    ( ) Yes (delete references not cited or fix the problem by citing the reference in text)

37. References in order of citation?
    ( ) Yes
    ( ) No (rearrange so in order of citation)

38. Reference format as per journal instruction?
    ( ) Yes
    ( ) No (revise)

39. Referencing for (check all that apply)
    ( ) Previous work
    ( ) Data analysis methods
    ( ) Laboratory methods
    ( ) Coding or reading procedures for abstracting information from special records or documents
    ( ) Treatment methods

( ) Other (specify)

_____

40. Supporting documents available on study website or on request (check all that apply)
    - ( ) Study protocol
    - ( ) Study handbook/manual of operations
    - ( ) Study data forms
    - ( ) Data listing
    - ( ) Analysis dataset
    - ( ) Study website address
    - ( ) Description of special procedures needed to understand results, but too detailed to be included in the body of the publication
    - ( ) Special analyses and tabulations
    - ( ) Other (specify)

_____

I. Credit roster and acknowledgments

41. Study credit roster? (see Form WS 6.3)
    - ( ) Full study credit roster
    - ( ) Partial study credit roster
    - ( ) No study credit roster

42. Acknowledgments and disclosures (check all that apply)
    - ( ) Funding sources
    - ( ) Supplier of study drugs
    - ( ) Grant/contract numbers
    - ( ) Conflict of interest disclosures
    - ( ) Other (specify)

_____

13 Management tables, worksheets, and checklists

Table 13.1 Document production and distribution sites (Produce.Tab)

When: Early in the course of planning

Who: A study officer

Purpose: To identify documents needed for the trial and to specify where they are produced and where distributed from

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

Instructions

Check at left if document exists and then indicate in the check spaces at the right where the document is produced and where distributed from.

Legend

CC = coordinating center
OC = Office of study chair
S = Sponsor
Oth = Other; if checked specify site

4. Study documents	Production site				Distribution site			
	CC	CO	S	Oth	CC	CO	S	Oth
( ) Protocol	( )	( )	( )	( )	( )	( )	( )	( )
( ) Prototype consent	( )	( )	( )	( )	( )	( )	( )	( )
( ) Study handbook	( )	( )	( )	( )	( )	( )	( )	( )
( ) Study manual of operation	( )	( )	( )	( )	( )	( )	( )	( )
( ) Data collection forms	( )	( )	( )	( )	( )	( )	( )	( )
( ) Data entry manual of operations	( )	( )	( )	( )	( )	( )	( )	( )
5. Study reports								
( ) Performance monitoring reports	( )	( )	( )	( )	( )	( )	( )	( )
( ) Treatment effects monitoring reports	( )	( )	( )	( )	( )	( )	( )	( )

Table 13.1 Document production and distribution sites

	Production site				Distribution site			
	CC	CO	S	Oth	CC	CO	S	Oth
6. Other documents								
( ) Investigator's brochure	( )	( )	( )	( )	( )	( )	( )	( )
( ) Policy and procedures memoranda	( )	( )	( )	( )	( )	( )	( )	( )
( ) Data dictionaries	( )	( )	( )	( )	( )	( )	( )	( )

WS 13.1 Integrity preservation procedures (Fraud.WS)

When: Before the start of data collection

Who: Senior study personnel

Purpose: To establish procedures for ensuring integrity in the processes and procedures of the trial

Definitions

fabrication - 1. The act or process of fabricating. 2. The product of fabricating; lie; falsehood.

falsification - The deliberate act of making something false.

fraud - Broadly, deceit or trickery; specifically, a deception deliberately practiced to secure unfair or unlawful gain; an act of deceiving or misrepresenting; intentional perversion of the truth to induce another to part with something of value or to surrender a right. ***Usage note***: Avoid as an accusation, absent evidence of intent. To be fraudulent, an act has to be motivated by an intent to deceive. The element of intent is evident in the definitions of fraud, as given in the *Oxford English Dictionary*[12] and *Black's Law Dictionary*.[3] Even acts of omission can be fraudulent if intended to deceive. Oxford English Dictionary: *1. The quality or disposition of being deceitful; faithlessness, insincerity. 2. Criminal deception; the using of false representations to obtain an unjust advantage or to injure the rights or interests of another. 3. An act or instance of deception, an artifice by which the right or interest of another is injured, a dishonest trick or stratagem. 4. A method or means of defrauding or deceiving; a fraudulent contrivance; in modern colloquial use, a spurious or deceptive thing.* Black's Law Dictionary: *An intentional perversion of truth for the purpose of inducing another in reliance upon it to part with some valuable thing belonging to him or to surrender a legal right. A false representation of a matter of fact, whether by words or by conduct, by false or misleading allegations, or by concealment of that which should have been disclosed, which deceives and is intended to deceive another so that he shall act upon it to his legal injury. Anything calculated to deceive, whether by a single act or combination, or by suppression of truth, or suggestion of what is false, whether it be by direct falsehood or innuendo, by speech or silence, word of mouth, or look or gesture.*

plagiarism - An act or an instance of plagiarizing; something plagiarized. ***Usage note***: Use with caution as an implied or explicit charge or accusation, especially in the absence of specific factual information supporting the charge or accusation.

scientific misconduct - 1. Willful disregard of norms and standards for conduct of research. 2. Any act or representation by a person in the conduct of research that violates accepted norms or standards for integrity. 3. Fraud, falsification, fabrication, or plagiarism in relation to the design, conduct, analysis, or reporting of research, or in relation to credentialing or documentation. 4. research misconduct

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Integrity training

4. Persons exposed to integrity training
   - ( ) No integrity training planned
   - ( ) All study personnel
   - ( ) Selected personnel (check all that apply)
     - ( ) Center directors
     - ( ) Study physicians
     - ( ) Study nurses
     - ( ) Center coordinators
     - ( ) Data collectors
     - ( ) Data keyers
     - ( ) Other (specify)

       _____

5. Mode of exposure (check all that apply)
   - ( ) No integrity training planned
   - ( ) Didactic lectures and discussion
   - ( ) Case studies
   - ( ) Online course and examination
   - ( ) Other (specify)

     _____

6. Will study leaders instruct study personnel in regard to (check all that apply):
   - ( ) Definition of scientific misconduct and examples thereof
   - ( ) Definitions of fraud, fabrication, and falsification and examples thereof
   - ( ) Definition of plagiarism and examples thereof
   - ( ) Consequences of misconduct to persons found guilty of misconduct
   - ( ) Consequences of misconduct to the study
   - ( ) Responsibilities of study personnel for integrity
   - ( ) Whom persons should report suspected cases of fraud to
   - ( ) How charges of misconduct are investigated and disposed of

C. Practices aimed at detecting aberrant data (check all that apply)
- ( ) Site visiting
- ( ) Data auditing
- ( ) Checking for protocol departures
- ( ) Indelible randomization audit trail
- ( ) Eligibility checks
- ( ) Performance monitoring

( ) Data analyses to identify suspicious data patterns
( ) Other (specify)

WS 13.2 Meeting planning worksheet (Meet.WS)

Use form for planning specific meetings. Indicate the meeting or group to meet item 4.

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

4. Meeting
   ( ) Research group
   ( ) Steering committee
   ( ) Study officers
   ( ) Treatment effects monitoring committee
   ( ) Working committee (specify)

   _____

   ( ) Other (specify)

   _____

5. Meeting organizer/coordinator
   ( ) Office of study chair
   ( ) Coordinating center
   ( ) Sponsor
   ( ) Other (specify)

   _____

6. Purpose of meeting

   _____

7. Day(s) of meeting
   ( ) One day
   ( ) Multiple days . . . . . Number of days ___

8. Day of week (start date for multi-day meetings)
   ( ) Monday
   ( ) Tue, Wed, or Thu
   ( ) Friday
   ( ) Sat
   ( ) Sun

9. Meeting dates
   One day meeting; date . . . . . __—___—_____

   Multi-day meeting . . . . . Start: __—___—_____ End: __—___—_____

10. Meeting time
    Start time . . . . . __:__ am/pm

    End time . . . . . __:__ am/pm

11. Expected number of people attending . . . . . Number ___

12. Travel arrangements (hotel and plane reservations)
    ( ) None necessary (local meeting)
    ( ) By persons traveling
    ( ) By meeting coordinator
    ( ) Other (specify)

    _____

13. Meeting location
    ( ) Host institution
    ( ) Airport meeting room (specify)

    _____

    ( ) Hotel

        City . . . . . _____

        Hotel name . . . . . _____

        Address . . . . . _____

    ( ) Other (specify)

    _____

14. Meeting date picked to coincide with a society meeting?
    ( ) No
    ( ) Yes (specify)

    _____

15. Meeting materials
    ( ) Distributed prior to meeting via hard copy

( ) Distributed via e-mail
( ) Distributed hard copy at meeting

WS 13.3 Conference phone meeting planning worksheet (ConfCall.WS)

Use form for planning conference calls for a group. Indicate the group meeting in item 4.

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—___—____

4. Conference call meeting
   ( ) Research group
   ( ) Steering committee
   ( ) Study officers
   ( ) Treatment effects monitoring committee
   ( ) Working committee (specify)

   _____

   ( ) Other (specify)

   _____

5. Call organizer/coordinator
   ( ) Office of study chair
   ( ) Coordinating center
   ( ) Sponsor
   ( ) Other (specify)

   _____

6. Purpose of call

   _____

7. Time of conference call
   Day of week . . . . . _____

   Time of day . . . . . __: __ am/pm

   Date . . . . . __—___—____

8. Meeting time
   Start time . . . . . __: __ am/pm

   End time . . . . . __: __ am/pm

WS 13.3 Conference call meeting worksheet

9. Number of people on the call . . . . . Number ___

10. Arrangement
    ( ) Call in (number provided by call coordinator)
    ( ) Persons called by operator
    ( ) Other (specify)

    _____

11. Call materials
    ( ) Distributed via hard copy
    ( ) Distributed via e-mail
    ( ) Distributed both hard copy and via e-mail

CL 13.1 Checklist of forms, worksheets, and checklists to be completed (Formlist.CL)

A. Identifying information

1. Study name: _____
2. Form completed by: _____
3. Date completed (day-month-year) . . . . . __—__—____

B. Tables to be completed

C. Worksheets to be completed

D. Checklists to be completed

CL 13.1 Checklist of forms, worksheets, and checklists to be completed

CL 13.2 Log of completed forms, worksheets, and checklists (LogList.CL)

A. Identifying information

1. Study name: _____

2. Form completed by: _____

3. Date completed (day-month-year) . . . . . __—__—____

B. Tables completed

C. Worksheets completed

D. Checklists completed

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