

DESIGNING,  
PREPARING  
AND  
DELIVERING  
RESEARCH  
DIETS



A TRAINING  
WORKSHOP

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Pennington Biomedical  
Research Center  
Baton Rouge, Louisiana

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# PLANNING STUDIES TO ANSWER SCIENTIFIC QUESTIONS

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Research studies as varied as cell culture studies and ecological studies contribute to a body of knowledge on issues of diet and human health. Human feeding studies are a unique line of research that contribute to establishing cause and effect relationships. Typically, a human feeding study is preceded by epidemiologic studies and animal studies that ask closely related research questions. Human feeding studies define a relationship between dietary intake and changes in an outcome, typically a risk factor for disease. Promising results from human feeding studies may be followed by clinical intervention trials. These trials may document that a change in dietary intake alters prevalence of a disease or disease endpoint. Together, various lines of research produce a body of knowledge that is tapped by imminent organizations to make dietary recommendations for the public.

Among human studies, the model producing the highest degree of control is the residential study, also known as the metabolic ward or in-patient study. In addition to strict dietary compliance, other variables, such as exercise, can be controlled. However, residential studies are expensive, and confinement to a metabolic ward is a major interference with the life-style of research subjects. When this degree of control is not critical, free-living subjects can be studied under controlled diet conditions. Participants continue their normal activities but eat only food provided within the context of the study. Food items are typically weighed in proportion to calorie needs, and subjects commonly eat a predetermined number of meals at the study facility.

Human feeding studies are typically planned by a team of researchers including the principal investigator, co-investigators and collaborators who have expertise concerning the research topic. These may include a study coordinator, dietitian and statistician. Depending on the complexity of the study, one or a series of planning meetings are held to clarify the research question, design the study and assign responsibilities to team members.

A research question or hypothesis dictates all aspects of study design. Therefore, the research question must be clearly stated and agreed upon by all team members before a study is designed. The research question identifies the subject population, nutrient of interest, endpoints to be measured and the confounding variables to be controlled. A good research question is specific, testable, biologically plausible and likely to produce an unequivocal answer. If a single study is designed to answer several research questions, the research questions should be prioritized.

The study design typically begins as a diagram that identifies the treatments and treatment order for each group of subjects. Common designs for human feeding studies are the crossover design, the parallel arm design and the longitudinal design. The statistician on the research team can provide valuable input on design as well as procedures for randomizing subjects and for data management. In the crossover design,

each subject receives all treatments in random order. This arrangement makes studies long and increases subject burden. However, the within-subject variability associated with subjects serving as their own controls is small, so fewer subjects are needed to detect statistical differences among treatments. In the parallel arm design, different groups of subjects receive different treatments. The sample size is large to compensate for a large among-subject variability, but the study duration is comparatively short. In the longitudinal design, each subject receives each treatment in a set order. A disadvantage of the longitudinal design is that outcome variables can be inadvertently influenced by uncontrolled changes that occur across time; for example, seasonal changes.

Once a design is agreed upon, a study protocol is written. The protocol documents the specific aims of the study and describes dietary treatments, the subject population, recruitment procedures, eligibility criteria, outcome variables, laboratory methods, statistical approaches and other pertinent issues for conducting the study including quality assurance. The protocol may identify individuals responsible for subject recruitment, data management and authorship for anticipated manuscripts. The protocol may include a budget, a description of the facility and CV's of investigators; in short, a mini grant proposal.

It is desirable to complete research studies with the minimum number of subjects needed to detect a true difference in the endpoint of interest. The number of subjects required in a study is best estimated by working with a statistician to conduct a power calculation. Sample size increases when 1) subject variability is high due to uncontrolled variables or design of the study, 2) measurement error is high due to lack of assay precision, 3) changes to be measured are small, or 4) changes in nutrient intake or bioavailability are small.

The length of feeding periods and the amount of the nutrient to be fed are dictated by the research question. Often, the research question seeks to establish consequences of a long-term change in a dietary variable. This necessitates feeding the nutrient in question long enough for the outcome variable of interest to stabilize. Feeding high levels of a nutrient, levels above those attainable through use of normal foods, can facilitate detecting small differences in an outcome variable, whereas smaller changes in nutrient intake can model realistic dietary changes in a population.

Cost, a major factor in conducting human feeding studies, is determined in part by the number of subjects to be fed and the length of feeding. The cost of operating feeding facilities varies greatly. Our non-residential studies currently cost about \$60 per subject per day, excluding expenses involved in sample collection and analysis. In estimating cost one must consider fixed costs (e.g., salaries, space charges, utilities, equipment expenses, medical coverage), funds for food and paper goods, temporary employees and, if applicable, subject payment.

Studies are often blinded to avoid bias. Blinding of participants prevents variation in compliance based on knowledge of the treatment. During information meetings, subjects are told what the treatment variables are, and if the study is blinded, they are told that

they will not know which diet they are eating. Diets can be coded by color, number or letter designations. It is common to have the statistician rather than the investigator assign subjects to dietary treatments to avoid selection bias. Blinding can be extended to the data collector to avoid bias in laboratory analysis; biological samples are sent to the lab without identifying subjects by name or treatment. As an added precaution, data can be sent directly from the data collector to the statistician without passing through a principal investigator who is not blinded.

Insightful and detailed planning of studies pays off by producing accurate, definitive data that contribute to the body of knowledge linking diet to disease prevention.

## NOTES

## **CONSIDERING ETHICAL ISSUES IN STUDY PARTICIPANT MANAGEMENT**

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The guiding principle for all plans and decisions concerning the conduct of human studies is that all investigators are responsible for the welfare of participants and staff, before, during and for a limited time after the completion of the study. When decisions are made from the standpoint of “taking responsibility” the ethical issues are distinguished and the decisions can be more clearly made. We will walk through a typical controlled feeding study and discuss various ethical issues that may arise at each point in the study’s progress.

Ethical issues arise at the beginning with the design of the study. Study designs seek to maximize the variance in the independent variables in order to insure obtaining an effect in the outcome variables. Studies must be designed to produce better health as a study outcome. To protect the well-being of study subjects, three factors should be taken into consideration: 1) invasiveness of the specific procedures, 2) malaise promotion due to the summation of procedures, and 3) subject burden through the requirement of too many measurements, activities or restrictions. Any research involving human subjects must be approved by an Institutional Review Board.

Recruitment and screening prospective study subjects should be done straightforwardly. Advertising should clearly describe the type of participants desired and generally what will be required as part of study participation. Since the foundation to the ethical conduct of human studies is “informed consent”, a full and truthful description of all the study details is mandatory. This includes helping the subject understand the ramifications of study requirements which may include: 1) time and money necessary to come to the study site on a daily basis, 2) family and social contact, 3) difficulty in rearranging financial agreements concerning food with dormitories, room-mates, etc., and 4) interference with field trips, vacations, meetings, home emergencies and leisure activities. A full discussion of these and similar issues helps to prevent study drop-out. Each study sets up a set of inclusions and exclusions that are rigidly followed in order to avoid selection bias. There are additional safety issues that must be considered in addition. These include pregnancy tests and PAP smears for premenopausal women and whether it is ethical to screen for HIV and Hepatitis B infections.

A surprising number of circumstances can arise during the course of a study which require ethical decisions. The longer the study the greater the number of circumstances. Illnesses presumably unrelated to the study raise issues as to who will pay for treatment and what medications may be allowed. Life events such as accidents, funerals, etc., must be handled with compassion, flexibility and innovative solutions. On long studies participants may undergo emotional problems and stress that are not necessarily connected to the study. Study subjects are unlikely to declare that they no longer wish to participate in the study. Rather they will miss appointments, meals, eat non-study food

and let you know about it, etc. Ways must be found to allow them to leave the study with their self-esteem intact. The semi-adherent participant who wishes to stay in the study is more of a problem. Such individuals are often seen as “problem subjects” by study staff and investigators. Confrontation and denial can lead to ethical dilemmas and should be dealt with promptly in such a way to leave study subjects with their self-respect. Study participants may also develop abnormal laboratory values such as high blood pressure, low hemoglobin, etc. It is the obligation of the investigators to take these values seriously, find out whether they are accurate via prompt retesting, or take a person out of the study. Investigators are ethically responsible for providing nutritious and wholesome food to study participants. This includes rigorous attention to food temperatures, especially in packed meals, and the cleanliness of the food storage and preparation areas.

Financial remuneration for study participation is an important symbolic recognition of the extra time and effort required of subjects, but such payments should be kept low enough that subjects remain in a study solely because they are dependent upon the remuneration for their maintenance. Arrangements should be made to have payments ready at milestones in the study, and a single large payment only at the completion of the study should be avoided.

Because of the great deal of cooperation between participants and staff, anonymity of study subjects is out of the question. Confidentiality can be somewhat preserved by referring to all data and specimens collected from subjects by subject number, keeping all subject-related data in a locked location with limited access to staff members, and encouraging a profound respect for subjects and their confidentiality.

The end of a study also raises some ethical issues. Often promises are made to study participants, for example, sharing of results, follow-up nutrition education, etc. Ethically these promises must be kept, but often the resources or personnel are not available to accomplish this when the study is completed. Promises should be kept to the absolute minimum. Study investigators should check with their Human Subjects Review Board as to how long they must keep records concerning study participants after the study is completed. Informed consents and other legal documents may need to be retained for several years.

Ethical considerations in running a well-controlled feeding study may seem overwhelming. Many of the considerations will apply to some studies and not others. Getting the ethics right is consistent with running a study with scientific merit and decisions are made from just using good common sense. They should not deter the dedicated investigator from undertaking human feeding studies.

## NOTES

# **FACILITY DESIGN AND STAFFING**

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The unique design, equipment and staffing concerns of the research kitchen are identified in this session. Approaches and guidelines are presented for establishing a new facility or redesigning an existing layout.

Planning considerations include defining the project scope, facility requirements, equipment needs, space and budget guidelines. Future needs are considered during this “design phase” to allow for realistic growth and expansion.

## **Project Scope and Complexity**

Mapping out the scope and complexity of the kitchen design or redesign project is the initial step in the planning process. Outlining specific parameters and resources is all-important at the onset.

## **Facility Requirements**

The basis for facility requirements is forecasts for food production and menu requirements. Therefore, equipment needs are accurately identified.

## **Space Versus Function**

Equipment placement and functionality are important aspects of designing floor plans that work well. (See work sheet for accurately estimating space requirements.) Actual space and configurations of workstations should be considered to save steps and optimize work flow.

## **Costs**

Costs are predicted based on the aforementioned criteria. It is important to justify realistic expenses.

## **New Versus Remodeling Projects**

A key step is to identify and revise existing design drawbacks. “Don’t make the same mistakes twice.” Space and cost efficiency will be maximized. Considering future expansion during the design or remodeling phase is advisable. “Flexible designs” can amount to a considerable cost savings in the future. Suggestions include incorporating movable equipment, table tops and modular furniture. Also, equipment contracts can include arrangements for future upgrades.

The complexity of the project and facility specific resources will dictate which design team members will participate in the proposed project. Potential design team members include the following:

Architect and General Contractors- Subcontractors may be advised for smaller projects. In addition to project planning and coordinating, may act as health department advocates.

Equipment Dealers- Lends the resources from parent companies, input regarding price competitive equipment options and realistic design considerations.

Health Inspector- Addresses health regulations and installation specifications.

Lead Nutrition Staff- Prepares needs assessment, identifies production and menu requirements, logistical problems and budget issues.

Advisory Board Member- Maintains awareness of current projects and resource utilization.

Criteria for kitchen layout include work flow, area specific function, floor, storage and counter space, and efficient arrangements. Space and function requirements of specific work stations dictate these priorities. Guidelines for planning the most efficient work station arrangements include 6-9 ft. of counter space for food preparation and 3-6 ft. in the cook area (per 5-10 participants). Additional space is required for “to go” meal preparation. Equipment space must be considered for the main kitchen areas. Ventilation, climate control, atmosphere and office space also need to be accommodated.

Work area configurations include straight line (best utilizes space and time), parallel (space efficient; provides ample work surfaces and two-sided access), U-shaped (provides a large surface area, but adds more steps for staff), L-shaped (uses limited space), and islands (6 x 9 foot are functional; enhances the efficiency of a work area).

Work areas need sufficient electrical access for major and minor equipment requirements. Multiple studies can be accommodated via two or more L- or U-shaped workstations. Each “bay” may be similar or specialized for the food preparation function.

“Research food” needs to be maintained separately from “regular food” to maintain the integrity of nutrient specific information per specific brands. Metabolic studies requiring batch food purchases can seriously impact food storage requirements.

Storage requirements for all aspects of food production are summarized in the work sheet for calculating capacity and space requirements. Other storage considerations include dry (mainly contingent on lot size and par values), refrigerator (raw ingredient and short-term food service dictate refrigerator storage), freezer (frozen food requirements hinge on lot size, advanced food preparation, prepared food and baked goods) and non-food (separate storage is required, away from food and perishables). Bulky items can be stored adjacent to the kitchen or “off-site.”

Space savers include deep pull-out drawers, tray cabinets, drawer dividers and lazy susans. Solutions for “tight space” situations include obtaining long-term storage for large lots from a local butcher or purveyor. Mobile locked cages can be utilized especially when space is shared.

## **Staffing Guidelines**

Conducting a “staffing needs assessment” is a requirement to forecast full-time equivalents (FTE’s). A “Protocol Intensity Ranking Guide” helps to prioritize and synchronize multiple research protocols occurring simultaneously.

Worksheets for quantifying required effort for protocol design and methods, and for estimating nutrition staff requirements, are useful. These can be amended to gauge specific functions of an individual unit. Protocol requirements that impact staffing include research diet design, resident or non-resident study, number and length of study period, number of subjects, nutrients to be controlled, nutritional care to be provided, data collection instruments, and quality assurance procedures. Functional time analyses identify nutrition time requirements for differing aspects of new and on-going protocols.

## A WORK SHEET FOR CALCULATING CAPACITY AND SPACE REQUIREMENTS

### Capacity-

Number of Participants	X	_____
Projected meal requirements per day		_____
	Total	_____

### Space Requirements for Kitchen Work Stations (1)

Storage Area- (1.0-2.0 sq. ft./meal)		
Dry: (.33 - 0.5 sq. ft./meal)		_____
Walk-in:		
• Refrig (0.5 - 1.0 sq. ft./meal)	+	_____
• Freezer (0.75-1.5 sq. ft./meal)	+	_____
Non-food: (.09 sq. ft./meal) (may be increased for carry out containers and disposables)	+	_____
Preparation (includes refrigeration) (may be increased for multiple ovens and other large equipment)		
1.1 - 1.5 sq. ft./meal	+	_____
Serving Area (2)		
.57 sq. ft./meal	+	_____
Dishwashing and Sanitation Areas (2)		
.58 sq. ft./meal	+	_____
Dining Area		
12-14 sq. ft./participant per seating	+	_____
	Total	_____

(1) Factors to estimate storage for a large research kitchen, those facilities feeding 25-100 participants, underestimate actual requirements.

(2) The figures for estimating serving and dishwashing areas may be inflated to calculate needs of large feeding programs. Less space is required when dishwashing and meal service is done in shifts.

Adapted from: VanEgmond-Pannell, D. 1081 School Foodservice, 2nd edition The AV1 Publishing Company, Inc. Connecticut.

## NOTES

# **SPECIFYING AND PROCURING FOODS FOR RESEARCH DIETS**

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## **Food Procurement and Specifications**

The guiding philosophy of procuring foods for research diets is to meet the nutrient specifications of the experimental diets and to minimize nutrient variability, especially in target nutrients. Decisions about central or local procurement of food items are based on control of target nutrients. Developing well-defined food specifications and estimating amounts needed are also very important. Food specifications should include a complete description of the food items, size and type of packaging and amounts needed, as well as, a delivery schedule. The amount of individual food items ordered should reflect actual needs plus losses and wastage. Contingency plans that are designed to deal with emergency situations are essential.

### **Local/central procurement**

Food items for well-controlled experimental diets can be procured either centrally or locally. In general, food items that contain significant amounts of the target nutrient(s) should be procured centrally to minimize nutrient variability. In the DELTA Study, since total fat, saturated fat and/or cholesterol were the dietary constituents of interest, all food sources of fat, saturated fat and/or cholesterol were procured centrally. As a general rule, food sources that are needed for the entire study should be procured all at once a few weeks prior to the beginning of the study (except when the shelf life of the food is shorter than the duration of the study). This approach greatly minimizes, if not eliminates, nutrient variability of the target nutrient(s). For instance, the fat, fatty acid and cholesterol content of many natural and processed foods vary with the season, lot number and brand name. Olive oil is one such example. The oleic acid content varies widely among different brands. Even within the same brand there is still some variability from lot to lot. By obtaining all amounts needed for the entire study of each fat source from a single lot, the variability is minimized. All foods that are not significant sources of the target nutrient(s) can be procured locally.

After making a decision about what food items to procure centrally or locally, potential sources, vendors and brand names need to be identified. More than one potential source and brand for each centrally procured item should be identified. If the brand name for any locally procured item is not available, another brand name with the same nutritional specifications may be used.

### **Food specifications**

A complete, accurate and concise description of food items is one major criteria for developing good food specifications. Using catalogues from different food vendors and manufacturers could come in handy, especially when several variations of a single food item might be available. For example, there are at least 4 varieties of V-8 juice. These

include regular, picante, spicy and low salt. Also, white bread may be regular, low fat, fat free, thin-sliced or extra thin-sliced. Describing meat, fish and poultry could be more challenging since most lay persons are not familiar with the standard terminology used to describe these products. It is advisable to work closely with a meat scientist or at least cross check items with a nutrient database. Other important criteria include specifying the type and size of the food packages (#10 vs. 4 oz fruit cans; 10 lb. cheese block vs. 10 1 lb. shredded cheese bags), the amounts needed and the exact dates of delivery.

Precise food specifications help prevent many problems related to receiving the wrong food items, returning them and trying to get the right ones.

### **Estimating the amounts of foods needed**

The amount of each food item needed (AFN) for the entire study can be estimated by using the following formula:

AFN = Amount of food needed for a participant on 2500 Kcal (average Kcal required)/menu cycle x potential number of participants x number of menu cycles.

A “fudge factor” (FF) is added to the AFN to add a margin of safety that accounts for any waste and potential accidents leading to loss. The FF for most foods is x 2. The FF may be higher for food items where substantial waste is expected such as untrimmed meat and lower for food items where virtually no losses are anticipated such as PC items.

### **Logistics of Food Deliveries**

Great care and planning are required to identify the logistics of food deliveries, especially for centrally procured foods. The first consideration is having appropriate and ample storage space. Ideally, deliveries should be made 2-4 weeks prior to the beginning of the study. It is important to specify exactly where the foods are to be delivered and when someone will be available to receive them. A contact person is also a necessity, especially to deal with problematic situations.

With centrally procured items, packaging is very important. Most bulk food vendors and large food companies package food in units that are quite large and therefore, difficult to handle, such as 30 lb. packages of pork and 200 lb. barrels of oil. The size of the packages needs to be specified and sometimes negotiated. It is frequently easier to obtain smaller units of certain foods that are locally procured.

### **Other considerations: Examples from DELTA**

-Portion control items (PC): The use of PC's for nonfat sources is very convenient, simplifies food production efforts and minimizes waste. However, PC's are more expensive than bulk packages and are not always appealing when served in the original container at a meal. As a compromise, PC's were used for take-out meals because they are convenient and minimize spillage. Weighed food items were used for on-site meals.

-Egg products: Due to the variability in the cholesterol content of fresh eggs purchased from different farms and the impracticality of purchasing fresh eggs centrally, frozen whole eggs were obtained from a single source and lot. Egg yolk powder also was obtained from a single lot. Egg yolk powder is more convenient to use.

## **Food Donations**

In many feeding studies there may be an opportunity to use donated foods. While on the surface it may appear that donated foods would save some money, the decision to solicit food donations must be carefully considered. For example, the process of soliciting food donations is quite time consuming and costly as it involves many phone calls and faxes that sometimes are unsuccessful. Before seeking food donations, several issues need to be carefully considered to determine whether it is worthwhile to initiate this often elaborate process. First, the potential foods that need to be donated must be identified and the costs of purchasing, shipping and storing them should be determined. With this information the economical feasibility of requesting a donation can be assessed. Secondly, potential donors must be identified to determine whether they are willing to donate foods and if they have a mechanism in place to do so. It is also very helpful to have personal contacts with key individuals in these companies.

Once all the above issues have been clarified, an initial letter is sent to each company in which the study is briefly described and a food donation is requested. It is very important to fully describe each food item and to clearly specify the amounts needed. This letter is followed by a phone call. Some companies may need further information about the study or need to be reassured that their food will not be singled out in any future publications. Thus, an executive summary of the study may be sent to the company.

It is rare that the requested food items are sent shortly after the first contact. In about 80% of the cases, many more phone calls and faxes are needed before the final decision is made (which may be positive or negative). In other instances, a final decision may not be made until 2-3 months have elapsed. In general, if no information is available about the reputation of the potential donor company, and the study is scheduled to start in a few weeks, at least some of the food should be purchased, if not all, unless there is a decision to still pursue the donation.

In some situations a company may donate certain food items, but will not cover the shipping charges or will ship all food for all centers to one center (in the case of a multicenter study). The center receiving the food will be responsible for repackaging and shipping the items to the other centers. The shipping charges may be more expensive than the food items themselves.

## **Emergency Situations**

Having a backup plan for emergency situations is highly advisable. For locally procured items, more than one vendor and brand name must be identified for each product. For centrally procured frozen and refrigerated food items, the temperature of the storage units needs to be monitored daily and the storage units need to have backup power supplies. If possible, each item should be divided among more than one storage unit so that if one unit fails, some of the food will be salvaged. This will allow enough time to replenish the lost food item(s) without interfering with the flow of the study.

## NOTES

## **DETERMINATION OF CALORIC LEVELS AND SUBSEQUENT MONITORING TO ACHIEVE WEIGHT MAINTENANCE**

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Clinical trial research diets require the calculation of appropriate calorie levels to 1) maintain the weight level of each participant to eliminate an extraneous or unwanted variable that might affect the experimental outcome, 2) provide an intake that satisfies hunger without overfeeding, and 3) meet nutritional adequacy requirements within the confines of the research diet prescription. Meeting caloric requirements and achieving weight maintenance of the research participant often involves adjustments in caloric levels throughout the study feeding periods.

Determination of an appropriate calorie level is based on establishment of a target weight. Target weight can be defined as that weight which is usual to the subject and will become the weight that is considered suitable for monitoring purposes throughout the study. The target weight should be based on several factors to assure that the study is neither in the position of maintaining a short-term weight evaluation nor perpetuating a brief drop in weight. Setting a target weight that is not a usual weight for a given participant will either promote inability to eat all food provided by the research diet or result in ongoing problems with hunger. For diet adherence purposes, it is essential that participants are able to eat all food provided and have a feeling of fullness upon completion of the meals.

Determination of target weight should include the following factors: 1) standardized weight measurements taken at each eligibility visit, 2) a weight history of no less than the past year and preferably spanning the past several years, and 3) consensus with the participant on the target weight level. A target weight level should be carefully determined and assigned to the participant with the knowledge and agreement that caloric adjustments will be made as necessary throughout the study diet periods.

Energy requirements vary according to age, gender, body size and composition, physical activity and climate. Various methods of estimating individual calorie needs have been recommended. Malgalko and Johnson compared eight methods of estimating energy needs and found that none of the methods were satisfactory for long-term use. Follow-up and adjustment were essential for weight maintenance of + or - 2 percent. Long-term use was defined as at least ninety days. Basal Metabolic Rate (BMR) is influenced by a number of considerations. Age, body surface area, and gender are the most crucial factors. A younger person will have a higher BMR due to the increased activity of cells. After growth stops, BMR decreases by about 2 percent per decade of life. Research has shown that body surface area rather than weight influences BMR. The greater the amount of body surface area, the higher the BMR. Gender also influences BMR. Males generally have a faster metabolic rate than females, due to the higher percentage of lean tissue in the male body. Muscle tissue is highly active even when it is resting, whereas fat tissue is comparatively inactive. Cunningham reported a multiple

regression analysis of several factors influencing BMR using data from the classic metabolism studies published by Harris and Benedict. Factors in his analysis included gender, age, height, body mass, and estimated lean body mass. Lean body mass (LBM) was found to be the single largest predictor of BMR, accounting for 70% of the variability of BMR. This analysis suggests that estimations of BMR based on body surface area are accurate largely due to its correlation to LBM within each gender. Cunningham's analysis supports the work of Harris and Benedict; that is, active body mass determines BMR. Calculation of individual calorie needs using the Harris Benedict Equation or the linear equation for determination of BMR from lean body mass is appropriate. Additional calories are then added to allow for the energy expenditure of activity. To estimate the energy spent on muscular activities, lifestyles are classified as sedentary, lightly active, moderately active, or very active/heavy work. The following figures are approximations of energy expenditure for each classification: sedentary--add 20% of BMR, lightly active--add 30% of BMR, moderate activity--add 40% of BMR and very active/heavy work--add 60% of BMR.

Following the calculation of a calorie requirement for each participant, adjustments may be required dependent upon the calorie levels provided within the research diet. Research diet menus designed for large scale feeding studies generally provide a range of calories at set intervals. The range of caloric levels is based on an estimate of the lowest and the highest caloric requirements of the population to be studied. The utilization of calorie intervals serves as a means of categorizing the research diet menus to result in greater efficiency and accuracy in menu preparation and assembling procedures. Small scale metabolic studies may not have a need for calorie intervals or may have small intervals of only 100-200 calories. Larger scale studies may include caloric intervals of as large as 500 calories (i.e.: 1500, 2000, 2500, 3000, 3500). A caloric requirement falling between the set calorie interval can be met through the use of unit foods. Unit foods are specially designed food items that reflect the composition of the diet and are used to increase caloric load by small increments. Therefore, unit foods may be used to supplement a caloric interval to reach a higher calorie requirement.

Weight should be measured on a continuing basis throughout the diet period(s). Measuring weight daily under standard conditions is most prudent, with a weekly weight average calculation to be compared to the assigned target weight. Careful attention must be paid to possible fluid retention, activity deviation, clothing differences and normal weight fluctuations to minimize unnecessary caloric adjustments. A change in calorie level is indicated if weight increases or decreases persist. Most often, a caloric adjustment will not result in actual weight change within a seven-day period.

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## NOTES

## **RECRUITING TECHNIQUES AND CONSIDERATIONS**

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Effective recruitment of study subjects is an important part of a successful feeding study. There are many activities that are integral in planning and implementing the recruitment effort. Ample planning is essential and adequate resources must be allocated to all recruitment activities to ensure that the goals of the study are achieved. In addition, methods for recruiting and selecting potential subjects must be carefully considered. The scope of these activities will be governed by the size and complexity of the study. Thus, all recruitment activities will reflect the inherent and unique characteristics of each study.

Successful recruitment of study subjects requires considerable planning. An effective recruitment effort must include a realistic timeline, development of all necessary forms, consideration of staffing needs, an adequate budget, appropriate equipment, facilities, and resources, advertising strategies, a well-controlled monitoring system in place, and a back-up plan ready to implement. A major goal of recruitment is to identify the required number of subjects necessary for the study within a projected timeline with the resources available. The amount of time that should be allocated to recruiting subjects depends on the type and complexity of the study as well as the eligibility criteria that have been defined. For example, a demanding study with narrowly defined eligibility criteria will require more time, effort and resources than less intensive studies with broadly defined eligibility criteria. For a typical well controlled feeding study, approximately two (to four) months should be sufficient to recruit up to forty subjects. A lengthy recruitment period may cause some potential subjects to lose interest in the study. Thus, the timeline goal is to recruit subjects expediently. Different forms will be needed to screen subjects and monitor the recruitment efforts. Well-designed forms that have been pilot-tested are essential to assure that the recruitment process is organized, efficient and monitored effectively. Adequate resources including staff, space, and equipment (such as an ample number of telephone lines) will ensure that the recruitment proceeds smoothly. In addition, a well-trained staff will enhance recruitment efforts. A monitoring system that clearly communicates the status of recruitment also is essential to maintain efficiency and professionalism. Lastly, the success of recruitment is dependent upon effectively reaching potential subjects. There are various recruitment strategies that have been shown to work well: radio/television/newspaper advertising, mailing (including e-mail), flyers and posters, word of mouth, physician referrals, and others (e.g. recruitment meetings). To progress efficiently with recruitment, it is preferable to employ more than one technique.

To recruit special populations such as the elderly, minority groups, and women, the recruitment activities must be targeted to these groups. Elderly subjects can be recruited from senior citizen centers and through materials designed specifically for them. Minority groups can be recruited through churches and professional associations at the worksite and within the community. Women's organizations, the PTA/PTO, and other volunteer groups provide an excellent conduit for reaching both women and families.

During the recruitment process, it is very important to monitor the progress being made and assure that recruitment goals and timelines are being met. In addition, it is essential to maintain close contact and good rapport with all potential subjects. Their questions and requests should be addressed in a timely manner. A back-up recruitment plan is also important to have ready to implement. Should recruitment not be progressing as anticipated, then the back-up plan can be implemented promptly. It is advisable to offer small incentives (e.g. a mug, T-shirt, diet analysis, etc.) to potential subjects during recruitment to encourage their full cooperation at this time. However, the incentives should not be so generous that they encourage individuals only to go through screening, but not the actual study.

Once a pool of eligible subjects has been recruited, they should be interviewed carefully so they are fully apprised of the expectations of the study. At this time potential subjects can review the menus and obtain any additional information about the study. This meeting gives investigators an opportunity to assess a potential subject's commitment to the study. Lastly, a run-in period (e.g., a "trial run" of key experimental procedures such as being on the test diet) is highly recommended at least for several days. Collectively these procedures help minimize the drop-out rate which typically is ~10-15% in controlled feeding studies. (This necessitates overrecruiting subjects for clinical trials).

In summary, a successful recruitment effort requires careful planning and adequate resources. The scope of this effort will vary depending on the study objectives; for some studies, recruiting subjects may be straight-forward and relatively easy, whereas for other studies, this can be very challenging. Lastly, flexibility is of utmost importance in dealing with many unanticipated issues that arise when recruiting subjects into a well-controlled feeding study. With adequate attention to all aspects of recruiting subjects into a feeding study, recruitment goals will be achieved and contribute significantly to the success of the study.

## Recruitment Strategies for Well-Controlled Clinical Nutrition Studies

Strategy	Strengths	Limitations
Newspaper	Large display ads in specific sections reach a wide audience; Smaller ads in classifieds are inexpensive	Can be costly Reaches a limited audience
Radio and Television	Generally as public service announcements; reaches a wide audience	Can be costly; stations not always willing to broadcast
Mailings	Very informative; letters describing the study can be sent to target population; lists generated from organizational directories and membership rosters	Time intensive and can be costly; extensive description of study might not be read
Flyers/Posters	Inexpensive	Not effective when used alone; must be posted in high visibility areas
Physician Referrals	Increases study credibility and “encourages” participation of target group	Slow rate of referrals
Word-of-Mouth/Networking	Presentations to clubs or professional organizations whose members are part of the target population; can tap into source of reliable volunteers	Small yield
Recruitment Meetings	Personal contact and large audience sizes are obtained when holding informational meetings	Requires participant “effort”; time intensive for staff
Electronic Mail/Bulletin Board	Inexpensive and reaches a broad audience	May be discarded as junk mail; news group may not be widely read by target audience; may be limited to upper SES population
Health Fair/Information Booth	Personalized contact allows promotion of study to interested individuals and/or target group	Time intensive for staff
Databases from Previous Studies	Easily accessible, inexpensive; subject characteristics known	Must be updated; limits participant pool

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## NOTES

## MANAGING AND ENCOURAGING STUDY PARTICIPANTS

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Study participants are truly volunteers and that makes them very special people. They are co-participants in the research processes and, in many ways, are co-investigators. Having this point of view as an underlying operating paradigm communicates the respect and high regard in which they should be held throughout the study and even after the study is over. All investigators and staff should approach each activity and request made of or by study participants from the point of view of "unconditional positive regard". It is impossible to describe completely how the study is going to be for participants, and it is often much more difficult than they anticipated. The more that is requested of them and the longer the study, the more difficult is adherence and maintaining a positive attitude.

Knowing what motivated participants to volunteer and then adhere to a study protocol is of prime importance in planning how to manage and encourage their continued participation. Three main reasons why our subjects say they participate in studies are 1) the money, 2) finding out about themselves and others, and 3) contributing to science and their fellowman. Therefore, management must make sure that all three of these issues are addressed on a continuing basis.

Other issues also become very important since participants are giving over responsibility for their lives for a short period of time into the hands of the study investigators and staff. They must have complete confidence in the investigators and study staff throughout the study. Confidence is built in the following ways: 1) they must perceive that they are in good and responsible hands, which is often understood as a well-organized study where everything is spelled out at the beginning, and everything is well prepared, done on time and communicated; 2) study demands on their time must be minimized and completely organized, but at the same time staff must be able to accommodate participants' emergencies and mistakes; and 3) the study atmosphere must be up-lifting and the activities, food or food presentation must be interesting yet comprehensible. For study investigators, all of the above is accomplished by paying attention to staff training and staff morale. For staff, whether the study goes well scientifically and whether full participation is obtained from subjects is entirely dependent on them.

Investigators and staff set the mood and adherence of study participants. Non-adherent participants are always present in studies to a greater or lesser extent. They are particularly problematic because they destroy the morale of staff and other participants if not dealt with quickly. The approach is always in the context of concern for the non-compliant behavior and what can be done to support the subject in protocol compliance. There is always "unconditional positive regard" for the study participant themselves.

Finally, although studies are very hard work for all concerned, they should be a lot of fun with fellowship for everyone. Celebrations of participation by all engaged in the endeavor should be a part of all study plans.

## NOTES

## **EVALUATION OF DIET COMPLIANCE/MONITORING ADHERENCE**

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Participant adherence to the research diet and guidelines is critical to the successful completion of the study. Monitoring and compliance expectations should be included in the recruitment phase when all requirements involved in the study participation are discussed with prospective participants. Adequate time must be taken during eligibility visits to thoroughly inform each individual of the study purpose, implementation and the crucial role of the study participant. Recruitment goals should be set generously enough to allow for careful subject selection.

Following selection of eligible and interested candidates, a 'diet run-in' should be utilized to allow chosen individuals to experience the feeding center atmosphere, menus, limitations and expectations. Individuals completing the run-in phase should be evaluated regarding degree of commitment and adherence to feeding-center protocol. When participant selection and randomization has been completed, every effort should be made to promote cooperation and enhance commitment throughout the study feeding periods.

Participants should be provided with adherence guidelines in written form during the recruitment visits and subsequently for their continued reference throughout the study. Such guidelines should clearly state information regarding limitations of any allowed self-selected food and/or beverages, restrictions on use of medications, expectations for dining room attendance, activity level maintenance expectations, etc.

Feeding study participants agree to eat all food provided by the feeding center and to not eat any food which has not been provided by the center. A designated number of meals each day are generally served at the feeding center, allowing for direct observation of participant attitudes toward compliance and also allowing a tray inspection to be completed following each meal. It is helpful to place a name card on each tray to be certain that trays are being accurately assessed at the completion of a meal. Waste containers should be removed from the dining area to prevent any omission of food or containers from the tray evaluation. Individual spatulas may be provided at each meal to serve as a reminder of the need to consume all food served, and to facilitate the consumption of sauces, gravies, oils and remnants of food remaining on plates or in containers.

A daily intake record to be completed by each participant assures that an ongoing effort to record and track any deviation and enforce complete adherence is in place. The daily record should include information regarding the consumption of the experimental diet as well as any food or beverage consumed in addition to the experimental diet. Information regarding possible use of caffeinated or alcoholic beverages, adjustment of calories by unit foods, use of medication, changes in or record of activity level, or any

other information pertinent to a particular study could be included on such a tracking form. Scoring of the tracking sheet can provide information on self-reported adherence daily, weekly, and throughout the entire period.

Body weight measurement can provide a daily assessment of caloric level adequacy as well as basic information which might suggest gross deviation from the experimental diet. Additionally, daily weight monitoring allows for ongoing individualized participant contact and exchange of information. Ideally, the weight measurement scale should be located adjacent to the dining room, away from the direct comment and discussion of dining participants thereby allowing private conversation. Communication regarding the day to day rigors of restricted eating can provide valuable insight into attitude and how the participants function in real-life situations demanding decisions affecting study adherence.

Further evaluation of compliance is dependent on participant contact with study staff. Ability to communicate with study staff for questions, problems or concerns both in and out of the dining room setting should be available. Use of telephone information cards can provide the participant with ongoing easy access to selected staff members. Frequent interaction between study staff and participants allows for valuable exchange of information regarding acceptance of study limitations and degree of difficulty with ongoing compliance concerns. Deviations from the protocol should be handled discreetly with a sincere interest in understanding the situation causing the deviation and counseling regarding alternative future adherence behavior. Care must be taken to secure accurate information without shaming or embarrassing the participant, which could promote a cover-up of similar behavior in the future. Designated study staff should be readily available to answer questions, reinforce protocol issues, and solve problem situations. Use of a trained staff person as a dining room monitor during meal service hours allows continued observation of participants and can facilitate awareness of problem areas, diffuse negativism that is likely to evolve as the result of limited food choices over time, steer conversations that could be possibly offensive to a more positive level and, in general, promote a beneficial research-oriented perspective.

## NOTES

## PREPARING AND DELIVERING RESEARCH DIETS

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The effective use of dietary control and its appropriate application is a vital component of the clinical research process in order to assure maximal patient compliance and accurate data collection.

Well controlled dietary studies are designed to study the metabolism or physiological effect of food constituents and/or specific nutrients or chemical elements. By controlling dietary intake, outcome variables can be more effectively measured, monitored, and evaluated.

Numerous types of methodologies are employed in controlled feeding studies. Which methods are used must be thought out very carefully in the initial study design in order to blend the need for accurate scientific data collection and outcome with patient compliance, food production and delivery, facilities and staffing, and cost.

A classification system for research diets was developed in 1973 by Sachiko de St. Jeor and published in the Journal of the American Dietetic Association. Accurate dietary intake can only be achieved when subjects are provided with all their foods, required to eat all the food provided, and not allowed to eat or drink anything else. Dietary methodology used in clinical feeding studies usually falls within the classification of the controlled nutrient diet, constant diet, and metabolic balance diet. This latter would also include formula diets. Some methods offer an advantage to the investigator because more reliable data are available, while others offer more flexible patterns of eating and more acceptable food choices for the subject. Each has its place, effectiveness and use as long as the inherent advantages and disadvantage of each are recognized and evaluated thoroughly.

Research diets are designed based on nutrient analysis of sophisticated databases usually using a combination of USDA data and manufacturer's data. When necessary, laboratory analyses of particular food items are conducted specifically for a study. Factors to consider in determining the methodology to use include an assessment of the following needs: constant food source and standardized food preparation techniques, individual or batch recipe preparation, use of fresh fruits and vegetables, distilled water vs. local water, single menu vs. rotation, number of subjects, duration of study, food storage and procurement, kitchen size and staffing, inpatient vs. outpatient, and cost.

Accuracy is the foundation for calculating the research diet and for its ultimate weighing, preparation, service, distribution, and monitoring. It is necessary that all procedures are defined, written out, and followed by the entire staff in exactly the same manner. Continuous monitoring and checking systems are important to minimize errors.

**Food Preparation Techniques** vary depending upon dietary methodology. For the most accurate solid food diets, all foods should be procured from the same supplier, used from the same lot for the duration of the study, and prepared individually for each subject. Fresh fruits and vegetables are frequently avoided due to variation in nutrient composition. However, if there is little effect on the nutrients being studied, they are a welcomed addition which adds to patient satisfaction. Distilled water may or may not be necessary depending upon elements being studied. All foods are weighed on electronic balances into the container in which they will be served or cooked. Meats are calculated and weighed raw so that changes in cooking time and weight will not add an additional variable. Guidelines for weighing vary; however, a common guideline is foods > 10 gm may have a variance of +/- 0.5 gm and foods < 10 gm a variance of +/- 0.1 gm.

The use of portion-controlled food items from the manufacturer may sometimes be incorporated. This helps to reduce labor and staffing. Also, batch recipes using weighed ingredients and standardized food preparation and cooking techniques can be developed and used in specified weighed amounts.

**Unique Equipment Necessary For a Research Kitchen** includes items such as electronic balances, a distilled water system, an automated packaging system, and an institutional blender.

Considerations for an electronic balance include capacity/weighing range necessary for weighing serving dishes plus the food item, food composites, TPN solutions, and formulas, readability to 0.1 gm, pan size and dimensions, stabilization time, ease of use, calibration, and price.

Distilled water systems can be incorporated into the kitchen water supply using undercabinet tanks. Systems can be purchased or rented and service contracts can be set up for routine regeneration.

Automated packaging systems such as an autobagger or heat sealer can facilitate food sealing and packaging for both dry goods and cooked foods.

An institutional blender with a minimum capacity may be necessary for preparing formula diets and foods aliquots.

**Food Service To Inpatients** is usually typical of conventional tray service. Name tags which identify the type of research diet or a simple command such as "FINISH" are helpful. Special individual dishes for food service are also usually required as well as small spatulas for subjects to use in cleaning their dishes.

**Food Service For Outpatients** can use all disposable containers and packaging, returnable food containers, or a combination. Containers for carrying the day's food home include brown shopping bags, large plastic bags with handles, or coolers with ice packs. Food safety is a necessary consideration. Availability of refrigerated or frozen food storage at home or at work must be assessed in addition to mode of transportation and transport time. For subjects traveling a distance or having to store their food in a

heated car, insulated coolers may be necessary. Temperature indicators are available to put on refrigerated foods to monitor food safety.

## NOTES

# **DEVELOPING MENUS USING NUTRIENT DATABASE PROGRAMS**

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Two important considerations when selecting nutrient database programs to calculate research diets are 1) the reliability of the database, and 2) the functionality of the program. Both aspects are important, but it would be hard to argue that anything would be more important than reliability of the data. No matter how easy a program is to use or how well the output from a program supports kitchen management, if the data is wrong, the research objective is not met.

Data from the USDA National Nutrient Databank forms the basis for most, if not all, dietary calculation packages used in the U.S. and has served researchers well. Therefore, it is important for the researcher to understand how USDA data is organized.

USDA provides nutrient data in a variety of formats. The printed version is called USDA Handbook 8, with 21 sections representing 21 food groups. There are also currently five provisional tables providing information about nutrients where valid data is available for only a limited number of foods.

Electronic versions of USDA data are primarily of two types: a “standard reference” which contains analytical values for 77 components, with fields left blank if no acceptable analytical values are available; and a “survey database” which contains analytical and imputed values for foods required for calculating the composition of food records and recalls from national surveys, each containing 30 components (with NO missing values). Each of these two general databases involve numerous supporting files.

Other sources of data used for research include Pennington and Church’s “Food Values of Portions Commonly Used,” data for specific products provided by the manufacturer, and data derived by individual investigators to support their own studies. For an example of the latter, at the University of Iowa we have calculated diets using carnitine and biotin data provided by local laboratories.

If desired nutrients are not included on the USDA database, developers must either search the literature for additional data or omit the nutrient from their database. When research centers need data not on the USDA tables, they often must manually add the needed nutrients to their database. This effort requires considerable time and knowledge of database development procedures to ensure the new data is appropriate. Attempts to keep pace with the addition of new foods in grocery stores and restaurants present another challenge to database development. This is a greater problem for population studies than it is for metabolic studies. For many database developers, keeping up with new products has meant that partial data is added to the database; for example, a manufacturer of a new product may only analyze for the nutrients required on the label, so only this information will be available when the food is added to the database. When

new foods with data for only a few nutrients is entered onto the database, we can call this an incomplete database, or a database with missing values. Information about the completeness of nutrient data on a database is often difficult to obtain, so the user must beware.

Calculating research diets and managing the production of the food and menus can be greatly facilitated by the appropriate computer software. There is not one single “best” computer application for this task. Many research centers have developed applications for their own operation. Few of these applications are packaged in a way to facilitate their distribution. For example, the USDA human study unit at Beltsville, MD uses SAS for manipulating the USDA nutrient data and for developing their own research diets. SAS is a common statistical package which facilitates sharing the data, but the application is not robust, and documentation is generally lacking.

A D-Base application developed at the University of California General Clinical Research Center (GCRC) uses the USDA Standard Reference Data and is packaged for limited distribution within the GCRC. A FOXPRO system is also being developed at the Pennington Biomedical Research Center with their own database that also has limited distribution.

Commercial software calculation systems are used in many research centers, and several of the programs offer features very helpful in research diet design. For example, the CBORD Diet Analyzer screen facilitates tracking the composition of a meal or a total menu as it is entered and altered to achieve a stated nutrient goal. Nutritionist III and IV provide a food selection screen which previews the composition of a food and gives the source of the data. ESHA’s Genesis program offers a recipe calculation system which facilitates adjustments to recipes to account for fat and moisture gain and loss during preparation. These features are very helpful to the research dietitian for selected uses.

While the above features facilitate research diet design, they fall short of providing the full potential of a computerized system designed specifically for research. For example, a project currently underway to design a comprehensive system for research diet design, service and reporting includes 8 major functions: 1) Diet creation and editing, with system manipulation of diet to meet target, 2) Study protocol design and tracking, 3) Investigator and subject records, 4) Kitchen management, 5) Data tracking and analysis, 6) Anthropometry, 7) Forms and reports, and 8) Tools. This system recognizes the significant management component involved in research diet design.

Typical tasks involved in diet design and calculation include developing the protocol, calculating the diet, selecting foods and recipes that are acceptable to the subject population and whose preparation make efficient use of study facilities and staff, scheduling meal service and delivery and documenting consumption. Advanced planning facilitates efficient use of human and equipment resources.

The first step to the actual design and calculation of research diets is developing the diet prescription. Typical diet prescriptions may involve 1) a “standard” diet identical for all subjects, 2) a standard diet proportional to the calorie value of the diet or to the

subject's body weight, or 3) a diet that varies with appetite or other variables unique to the study design. The actual prescription may consider the composition of the total diet, or the composition of each meal may be prescribed. If the total caloric level of the diet is flexible, but the proportional composition is set, units of the diet may be devised that match the overall composition to be eaten ad lib (sometimes called "unit foods").

During implementation of the diet, an important consideration is how much latitude should be allowed to accommodate a subject's food preferences. Modifying the diet does two things; first, the composition of the diet will change as foods are substituted that may not exactly match the original item, and second, making frequent dietary changes puts an additional burden on study personnel. It is important to balance the added workload involved in frequent diet changes with subject satisfaction and successful completion of the study.

After the diet has been completed and consumed, the computer is helpful for calculating the composition of the actual food consumed. Planning data collection and analysis strategies during this phase simplifies data summarization and analysis. If data is organized to permit direct import to a statistical package, summarization and analysis of the dietary data is greatly facilitated. A well-designed computer application can contribute significantly to this process.

## NOTES

# COMPOSITING AND ASSAYING DIETS FOR NUTRIENT CONTENT

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In the past, controlled or metabolic diets may have consisted of a solution of purified nutrients such as sugars, amino acids, various lipids, vitamins and minerals. Today research subjects participate in their normal daily activities while consuming a prescribed diet. An array of customary foods can be used to deliver a defined nutrient pattern to subjects. Since the daily intake of any component will be the sum of the contributions of different foods in the day's diet, the research staff is challenged to provide an acceptable, varied menu and yet maintain the prescribed nutrient intake over the course of the study.

Initially, a food composition database may be used to develop the menu plan for the study. However, the calculation of component levels should be supplemented by chemical analysis of representative samples of diet composites or individual foods to establish specific and accurate values for levels of major components consumed during the study period. Generally, a food component database contains estimates which represent the approximate nutrient content of a food sampled across a national or regional supply rather than of individual lots of locally obtained food supplies used in the feeding study. Use of a single lot or source of a food will minimize the variability in component intake due to different brands, production dates, formulations, etc. In contrast, the usual food composition database will not contain values for specific sources of foods.

The analysis of foods and diets to determine accurate estimates of their composition requires a thorough knowledge of the measurement process and includes the development and testing of protocols for sample selection and handling, as well as the validation of analytical methods. The process begins with the selection of the representative sample and ends with the acceptance of quantitative estimates. Other critical points in the process include homogenization and analytical quality control. Each step in the process must be defined, tested, and monitored to achieve accurate and representative results. In addition, the cost of analyses for specific components will affect the development of the plan of analyses to be conducted.

Daily diets for humans are generally composed of 15 to 25 foods per day and represent several different food groups. For any component, values for multiple individual units of a food product will exhibit a statistical distribution characterized by a mean and/or median value and variability about that value. For this reason it is important to obtain representative samples of each of the individual foods for analysis as a composite or as individual samples. Representative samples of the foods will be identical in weight and physical description to the food portions used to feed subjects. Foods should be taken from the same brands and lots as those portions used for feeding. Particular attention should be paid to cuts of meat and complicated mixtures (such as stews) to assure the selection of the portion which is similar to the others.

Diet samples should be homogenized according to predetermined and tested protocol to minimize nutrient loss and sample contamination. Improper homogenization can cause changes in the sample matrix which affect component levels or lead to difficulties in sampling the mixture. Homogenization protocols will vary from component to component and matrix to matrix. The analyst should participate in the development of the homogenization and storage protocols to assure the stability of the samples. Following homogenization proper storage of samples according to predetermined protocol is required to maintain the stability of components. Samples may be individual aliquots or composites of daily diets or individual meals. Compositing individual units of a product is efficient in terms of the number of analyses required, but diminishes the amount of information about variability of the component.

The choice of analytical methods for the measurement of component levels is determined by the study objectives, the required level of specificity, the availability of expertise and instrumentation, the number of analyses required, and budget. As scientific knowledge evolves, objectives focus on the metabolic effects of specific vitamins or component forms. As public health priorities change, new methods must be developed to determine these components of new interest. Investigators must be knowledgeable about analytical methodologies required, as well as the necessary quality assurance protocol to achieve accurate and representative food composition data. The validation of analytical methods before the analysis of food/diet samples occurs should be documented and reviewed by the investigator. Reports of analytical results must be accompanied by quality control results in order to guarantee the quality of the data. Use of food composition data with unknown accuracy or variability can lead to erroneous conclusions about the diet-response relationship and subsequent conclusions.

## NOTES