Assessing the Effects of Food on Drugs in INDs and NDAs — Clinical Pharmacology Considerations

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2026
Clinical Pharmacology
Revision 1

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Contains Nonbinding Recommendations

Assessing the Effects of Food on Drugs in INDs and NDAs — Clinical Pharmacology Considerations Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides recommendations to sponsors planning to conduct food-effect (FE) studies for orally administered drug products as part of investigational new drug applications (INDs), new drug applications (NDAs), and supplements to these applications. This guidance revises part of the 2022 guidance for industry *Food-Effect Bioavailability and Fed Bioequivalence Studies* (June 2022).[2] Information on fed bioequivalence (BE) studies to be submitted in abbreviated new drug applications (ANDAs) is now found in the draft guidance for industry *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA* (August 2021).[3] Specific recommendations concerning fed comparability studies are now described in the guidance for industry *Bioavailability Studies Submitted in NDAs or INDs — General Considerations* (April 2022).

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Clinical Pharmacology in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-6821 (available at https://www.regulations.gov/docket?D=FDA-2017-D-6821). See the instructions in that docket for submitting comments on this and other Level 2 guidances.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[3] When final, this guidance will represent the FDA's current thinking on this topic.

II. BACKGROUND

Food-drug interactions can have a significant impact on the safety and efficacy of orally administered drug products. These effects can manifest in different ways. In some cases, co-administration of an orally administered drug with food can increase the systemic exposure of the drug, potentially leading to an increased pharmacologic effect impacting efficacy and/or safety findings. In other cases, administration of an orally administered drug with food can lower the systemic absorption of a drug, thereby reducing the efficacy. Hence, assessing the effect of food on the absorption of an orally administered drug contributes to the optimization of the safety and efficacy of the product and helps provide adequate instructions for drug administration in relation to food. Because diets vary with respect to the amount and type of food, and maintaining strict control over the daily content of food can be difficult, developing drug formulations that are not affected by food is strongly encouraged. However, when developing such formulations is not possible, well-conducted FE studies can inform how, when, and why drugs should or should not be administered with food. During new drug development, pharmacokinetic studies to assess the effect of food on the systemic exposure of the drug are conducted to determine: (1) if, and to what extent, food impacts the systemic exposure of the drug; (2) whether food changes the variability of the systemic exposure of the drug; and (3) if the effect of food is different across meals with different fat or caloric contents.

Understanding the exposure-response relationships of the drug can be informative in assessing the implications of FE studies. Additionally, the impact of various clinical dosing scenarios (e.g., under fed or fasted conditions, types of food, duration of fasting) is important to provide adequate instructions for use of the drug. In some cases, the clinical pharmacology characteristics of the drug could suggest that it should be administered only under fasted conditions (e.g., when higher exposures under fed conditions raise the risk of a clinically significant adverse reaction). In such cases, the drug should be administered without food in the clinical trials. In these trials, the sponsor should include a realistic interval between drug administration and food to include in the product labeling that patients can practically implement. In other examples, some drugs cause adverse reactions that can be alleviated when taken with a meal. For example, drugs that cause gastric irritation can adversely impact patient compliance or lead to loss of the administered dose from vomiting. In such cases, the drug could be administered with food. The sponsor should determine the impact of food, and when necessary, the impact of the type of food, on the pharmacokinetics (PK) of the drug. Lastly, in some circumstances, co-administration of a drug with food could be the only practical means of ensuring adequate systemic availability for the drug to be effective in patients (e.g., food could increase the absorption). In such cases, the drug should be administered with food, and the sponsor should determine the attributes of the food that will ensure adequate systemic availability to inform the labeling.

Sometimes, the observed increase or decrease in the systemic exposures of some drugs in the presence of food might not be clinically relevant based on exposure-response information. If appropriately conducted FE studies indicate that food does not have a clinically significant impact on the PK of the drug, the sponsor can conduct pivotal safety and efficacy trials

without regard to food, and the labeling can state that the drug can be taken with or without food.

The composition of the meal itself can influence the absorption of a drug. The physiological conditions induced by a high-fat meal generally provide the greatest effects on gastrointestinal physiology and the maximum effects on the systemic availability of the drug. The investigation of the effect of food on a new drug should include a study with a high-fat meal. For some drugs, the absorption can increase when the drug is given with a high-fat meal, but a low-fat meal could have inconsequential effects on the absorption of the same drug. To provide dosing instructions in relation to food, FE studies that include additional meal types that do not result in a clinically relevant effect of food can be beneficial and provide useful labeling information. When drug administration with a high-fat meal causes unacceptable increases in PK, toxicity, or a loss of drug efficacy, it is possible that a low-fat meal can have less or no impact on systemic exposures, improve patient compliance, and alleviate gastric irritation. In these circumstances, evaluating the effect of additional meal types on the PK of the drug can be helpful.

III. RECOMMENDATIONS FOR FE STUDIES

Generally, sponsors should conduct FE studies for new orally administered drug products including immediate-release products, modified-release products, and fixed-combination products of new, or in some cases, previously approved drugs. Sponsors are encouraged to engage FDA staff early in the development of a new drug regarding the strategy and details of FE studies. The general recommendations for these FE studies are as follows:

- Sponsors should assess the effect of a high-fat meal on the PK of a new drug product early in development to inform the appropriate dose and administration throughout clinical development and product labeling. If an important drug-food interaction is seen with a high-fat meal, assessing the interaction with a lower-fat meal could be useful.

- Sponsors should test the effect of food on a new drug product in clinical trials (see section IV) *before* conducting the pivotal safety and efficacy trials to provide rational decisions regarding dosing with respect to food. Preliminary assessments of the effects of food on a new drug in pilot studies (e.g., as part of the first-in-human trials (see section IV)) help determine whether a drug should be administered with food in clinical trials until a to-be-marketed formulation is identified.

- The sponsor should conduct a definitive FE study using the final to-be-marketed oral formulation. In cases where the clinical trial formulation had no significant effect of food, and the to-be-marketed formulation is not significantly different from the clinical trial formulation (see the guidances for industry *SUPAC-MR: Modified Release Solid Oral Dosage Forms Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing and In Vivo Bioequivalence Documentation* (October 1997) and *SUPAC-IR: Immediate-Release Solid Oral Dosage Forms: Scale-Up and Post-Approval Changes: Chemistry, Manufacturing and Controls, In Vitro*

Dissolution Testing, and In Vivo Bioequivalence Documentation (November 1995)), an FE study with the to-be-marketed formulation might not be necessary. Further, an FE study with the to-be-marketed formulation might not be necessary in a situation where a biowaiver is accepted for a formulation change (see the guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers* (May 2021)). The sponsor should discuss the approach with the relevant FDA review division. In cases where the clinical trial formulation is significantly different from the final to-be-marketed formulation, the sponsor should conduct a relative bioavailability study to compare the systemic exposures and an FE assessment using the to-be-marketed formulation, if appropriate (for more information refer to the guidance for industry *Bioavailability Studies Submitted in NDAs or INDs — General Considerations* (April 2022)).

- When the efficacy or safety of a new drug is adversely impacted by food, and fasted dosing is necessary, the sponsor should conduct FE studies to determine a practical interval of time between drug administration and food. The choice of the interval of time for dosing should be guided by the pharmacokinetic characteristics of the drug.

IV. CONSIDERATIONS FOR DESIGNING FE STUDIES

This section provides general considerations for designing FE studies. Sponsors can propose alternative study designs and data analyses. The sponsor should provide the scientific rationale and justifications for any alternative study designs and data analyses in the study protocol.

A. Pilot Studies

Early in development, the sponsor should consider conducting a pilot study to provide a preliminary assessment of the effect of a high-fat meal on the systemic exposure of the drug. To ensure the safety of the subject population, sponsors should carefully choose the dose for the FE assessment to account for any potential significant effects of food on the exposure of the drug that might increase the number or severity of adverse events.

B. Definitive Studies

The sponsor should generally use a randomized, balanced, single-dose, two-treatment (i.e., fed versus fasted), two-period, crossover design to study the effects of food on the orally administered drug product. A three-way crossover study can be conducted if the bioavailability of two formulations is being assessed in the same study (refer to the guidance for industry *Bioavailability Studies Submitted in NDAs or INDs — General Considerations* (April 2022)). The formulation to be tested should be administered on an empty stomach during one period and with the high-fat test meal during the alternate period. For other types of food, see section C below. A washout period of three to five elimination half-lives of the drug should separate the treatments in the FE study.

For drugs with long elimination half-lives (i.e., longer than 24 hours), a randomized single-dose, parallel study design can be more practical. In these studies, the sponsor should administer each treatment (i.e., fasted and fed) to a separate group of subjects with similar demographics.

The sponsor should enroll an adequate number of subjects to sufficiently characterize the effect of food on the PK of the drug. The sample size for each group will depend on the pharmacokinetic variability of the drug.

C. Types of Meals to Evaluate

For all orally administered drugs under development, an FE study with a high-fat meal should be conducted. Sponsors should also consider FE studies with a low-fat meal when administration of the oral product with a high-fat meal in the indicated patient population cannot be tolerated. Table 1 provides the definition of various test meals:

Table 1. Test Meal Definitions

Meal Type	Total Kcal	Fat		
		Kcal	Grams	Percent
High-Fat[4]	800-1000	500-600	55-65	≥50
Low-Fat[5]	400-500	100-125	11-14	25

The sponsor should provide a description of the meal as well as the caloric and content breakdown (carbohydrates, proteins, and fat) in the study report. Data collected on the type of fat (e.g., percent saturated fat and percent unsaturated fat) can be helpful. Examples of high- and low-fat meals are provided in the Appendixes and can help guide study design and product labeling.

D. Subject Selection

Sponsors can conduct FE studies in healthy adult subjects. Subjects from the patient population can also be appropriate if safety concerns preclude the enrollment of healthy subjects, or if differential effects of food on the drug are expected in the target patient population as compared to healthy subjects because of the underlying disease condition.

The sponsor should enroll both male and female subjects in the FE study unless the indication is specific to one sex (e.g., oral contraceptives), or if safety concerns preclude the enrollment of one sex (e.g., if the drug is a teratogen, women of childbearing age should be excluded). Subjects in FE studies should have normal renal and hepatic function. Sponsors should exclude subjects if they cannot refrain from using concomitant drugs that could confound the results of

[4] See Appendix 1: Composition of a High-Fat Meal. The definitions of "high-fat" and "low-fat" presented in this guidance are intended only for purposes of this guidance.

[5] See Appendix 2: Composition of a Low-Fat Meal. The definitions of "high-fat" and "low-fat" presented in this guidance are intended only for purposes of this guidance.

the FE study (e.g., drugs that can alter the absorption of other drugs by affecting gastrointestinal motility or by changing the gastric pH as well as drugs that can increase or decrease the metabolism and excretion of the investigational drug).

E. FE Study Doses

The sponsor should use the clinically recommended dose in the definitive FE study. When several doses of a drug that exhibit linear PK will be marketed, the sponsor should use the highest clinically recommended dose unless safety concerns necessitate a lower dose. When it is unsafe to administer the highest dose to healthy subjects, the sponsor can conduct the study in patients or test the highest strength of the drug product in lieu of the highest dose in healthy subjects, as long as the PK of the drug over the therapeutic range is linear. For drugs with nonlinear PK across the therapeutic dose range, the sponsor should conduct single-dose FE studies using both the high and low doses listed in the proposed product labeling.

F. Administration

1. Fasted Conditions

Following an overnight fast of at least 10 hours, investigators should administer the drug product to study subjects with 240 mL (i.e., 8 fluid ounces) of water. Additional water is permitted ad lib except for the period 1 hour before until 1 hour after administration of the drug product. The study subjects should not consume any food for at least 4 hours after the dose. Subjects should receive standardized meals scheduled at the same time throughout the study.

2. Fed Conditions

Following an overnight fast of at least 10 hours, the study subjects should start the recommended meal 30 minutes before administration of the drug product. Study subjects should eat this meal in 30 minutes or less. The study subjects should take the drug product with 240 mL (8 fluid ounces) of water. Additional water is allowed ad lib except for the period 1 hour before until 1 hour after drug administration. No food is allowed for at least 4 hours after the dose.

3. Modified Fasted Condition

When fasted dosing is necessary because food can significantly increase or decrease the exposure of the drug, the standard, overnight, fasted test condition might not be practical for patient treatment. Furthermore, the results of the overnight, fasted condition might not be applicable to shorter periods of fasting in patients. To provide food-drug labeling instructions (e.g., do not consume food within *X hours before* or *Y hours after* drug administration) for such products, the sponsor should conduct FE studies with appropriate separation times between drug administration and food consumption. The sponsor should provide pharmacokinetic data to support pragmatic labeling instructions to prevent food-drug interactions, taking into consideration the frequency of dosing, the patient demographics, the disease condition, and any other relevant factors.

G. Sample Collection

For both fasted and fed treatment periods, the sponsor should collect samples in a suitable biological matrix (e.g., plasma) from the study subjects. To characterize the complete concentration versus time profile for the drug, the total duration of sampling should cover at least three to five elimination half-lives (e.g., 12 to 18 samples per subject per period). The sponsor can use different sample collection times for the fasted and fed treatments when co-administration of a drug with food is expected to alter the time course of drug concentrations. To determine whether to measure other moieties in addition to the parent drug in the biological matrix, such as active metabolites, sponsors should refer to the guidance for industry *Bioavailability Studies Submitted in NDAs or INDs — General Considerations* (April 2022).

V. OTHER CONSIDERATIONS

A. FE Study Waivers

Biopharmaceutics Classification System class 1 (BCS class 1) drug products are highly soluble, highly permeable, and rapidly dissolving products that are in most cases unaffected by food. Based on FDA experience, more than 80 percent of BCS class 1 immediate-release drug products are not affected by high-fat meals; therefore, the labeling for these drug products states that they can be administered with or without food. The remaining BCS class 1 drug products are subject to high first-pass metabolism effects or luminal degradation and can be affected by meals. The FDA may waive an FE study for drug products that are designated as BCS class 1 (i.e., high solubility, high permeability), immediate-release drug products as defined in the guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers* (May 2021) that also have a high bioavailability ($F \geq 0.85$). Sponsors should consult the FDA regarding the feasibility of an FE study waiver.

B. Model-Informed Drug Development Approaches

In conjunction with FE data in subjects, physiologically based pharmacokinetic (PBPK) analyses can sometimes be used to further assess the effects of food on a drug. For example, PBPK models can guide in vitro experimental designs to generate data that can be used to further support PBPK model development, and to identify and optimize parameters that are important to understanding and predicting food-drug interactions in conjunction with FE data. PBPK approaches can also be useful to guide clinical study designs. However, PBPK modeling is still evolving, and new applications of PBPK simulation are continuously being evaluated by the FDA. Sponsors are encouraged to consult the appropriate review division for advice.

C. Drug Products Intended for Administration With Soft Foods

The labeling of some orally administered drugs (e.g., oral granules, or extended-release capsules) include recommendations for use of the drug product with qualified soft food vehicles (e.g., applesauce, pudding). Soft foods for use as vehicles should be identified and qualified by in vitro

assessments to demonstrate a lack of potential physicochemical interactions between the soft food and the drug product (intact or manipulated), including interactions of the drug substance or excipients with the vehicle. For recommendations on in vitro assessments to select appropriate soft food vehicles for drug administration, refer to the draft guidance for industry *Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments* (July 2018).[6] In vitro assessments are used to identify and qualify potential vehicles but do not replace the need for an in vivo evaluation to permit instructions for drug administration with qualified soft food vehicles in labeling. For the labeling to indicate that the drug can be sprinkled on soft foods, the sponsor should perform additional in vivo, relative bioavailability studies using the soft foods listed as vehicles in the proposed labeling. A sponsor should provide in vitro study results for all proposed soft food vehicles and should discuss with the relevant FDA review division to determine if relative bioavailability assessment of one soft food vehicle can be extended to similar soft food vehicles (see Pediatrics Section below).

D. Drug Products Intended for Intact Administration

Some drug products should be swallowed without chewing. When the product is to be labeled for administration as an intact dosage form (e.g., tablets, capsules), a new formulation that is intended to be opened, diluted, chewed, or crushed should be compared to the original formulation administered as the intact form taken with food, if the effect of food on the formulation has not already be been tested.

E. Drug Products Intended for Administration With Liquids as Vehicles

The labeling of certain oral products (e.g., cyclosporine oral solution) recommends that the product be mixed with a liquid vehicle (e.g., beverage) before administration. The bioavailability of these products can change when mixed with different liquid vehicles because of the formation of complex mixtures and other physical, chemical, or physiological factors. The qualification of liquids for their use as vehicles should include an assessment and demonstration of lack of a potential interaction between the liquid and the drug product (intact or manipulated), including interactions of the drug substance or excipients with the vehicle. For recommendations on in vitro assessments to select appropriate liquid vehicles for drug administration, refer to the draft guidance for industry *Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments* (July 2018).[7] Sponsors should contact the FDA to determine what data should be submitted to support proposed labeling instructions regarding the use of specific liquids as qualified vehicles for drug administration.

[6] When final, this guidance will represent the FDA's current thinking on this topic.

[7] When final, this guidance will represent the FDA's current thinking on this topic.

F. Specific Populations

1. Geriatric Patients

The FDA does not recommend a dedicated FE study in geriatric patients (i.e., patients aged 65 years and over). The prevalence of certain diseases (e.g., gastro-esophageal reflux disease) that can alter the bioavailability of drugs increases with age. However, these diseases do not influence the effect of food on the bioavailability of the drug in an age-dependent manner.

2. Pediatric Patients

When a new age-appropriate pediatric formulation is developed, the sponsor should conduct a new FE study with the pediatric formulation in adults. These results can then be applied to the pediatric population. Sponsors can use foods and quantities of food that are commonly consumed with drugs in a particular pediatric population (e.g., formula or milk for infants as well as jelly, pudding, or applesauce for toddlers). The outcomes of FE studies conducted with one soft food vehicle could be extrapolated to other similar soft food vehicles (e.g., same fat, protein, and carbohydrate content) and could support proposed labeling instructions. However, such extrapolation should be supported by in vitro data which demonstrates a lack of interaction between the drug product (intact or manipulated), including lack of interaction with the drug substance or excipients, with other similar soft food vehicles (see section V(C)). For products intended to be used in pediatric populations with modified diets, discuss plans with the relevant FDA review division prior to undertaking a FE study.

Small quantities of liquids or soft foods (e.g., 5-15 mL) used as vehicles for pediatric drug delivery should adhere to the principles described in the draft guidance for industry *Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments* (July 2018).[8]

When a formulation that is approved for use in adults is approved for use in a pediatric population ≥12 years old, a separate FE study is not necessary. Furthermore, a separate FE study might not be necessary if a pediatric formulation is very similar to the adult formulation, and if the pediatric formulation is approved based on a biowaiver approach.

G. Fixed-Combination Drug Products

Fixed-combination drug products are products with two or more active ingredients combined at a fixed dosage in a single dosage form. Such fixed-combination drug products can exhibit different effects of food compared to when each active drug ingredient is administered alone. Therefore, the sponsor should assess the effect of food on the various active ingredients of the fixed-combination drug product after administration of the combination drug product. An FE study might not be necessary if neither drug product when given alone is affected by food, and

[8] When final, this guidance will represent the FDA's current thinking on this topic.

the sponsor can provide an adequate justification that the fixed-combination drug product would be unaffected by food.

VI. DATA ANALYSIS AND LABELING

A. Data Analyses

The following exposure measures and pharmacokinetic parameters should be derived from all FE studies and reported:

- The total exposure of the drug or area under the concentration-time curve ($AUC_{0\text{-}INF}$, $AUC_{0\text{-}t}$)
- The peak concentration of the drug (C_{max})
- The time to the peak concentration of the drug (T_{max})
- The time taken for the drug to appear in the systemic circulation following administration (T_{lag}), when applicable
- The elimination half-life of the drug ($t_{1/2}$)
- The apparent clearance (Cl/F)
- The apparent volume of distribution (Vd/F)

Individual subject measurements as well as summary statistics (e.g., group averages, standard deviations, coefficients of variation, ranges) should be reported.

For new orally administered drugs, the exposure-response relationships for safety and efficacy should be considered when available to assess the clinical impact of the effect of food. When a fed bioavailability study is conducted to assess changes in formulations, an equivalence approach is recommended (refer to the guidance for industry *Bioavailability Studies Submitted in NDAs or INDs—General Considerations* (April 2022)). To include a statement in the labeling of no effect of food, the data should be analyzed using an average criterion, with the fasted treatment arm serving as the reference.

Exposure measurements (AUC and C_{max}) should be log-transformed before statistical analysis. The 90 percent confidence interval for the ratio of the population geometric means between the fed and fasted conditions should be provided for $AUC_{0\text{-}INF}$, $AUC_{0\text{-}t}$, and C_{max}. An absence of an effect of food on bioavailability is established if the 90 percent confidence interval for the ratio of the population geometric means between fed and fasted treatments, constructed based on log-transformed data, is contained in the equivalence limits of 80-125 percent for $AUC_{0\text{-}INF}$ ($AUC_{0\text{-}t}$ when appropriate) and C_{max}, unless other criteria based on the established exposure-response relationships for the drug are more appropriate (refer to the guidance for industry *Statistical*

Approaches to Establishing Bioequivalence (February 2001)). When the 90 percent confidence interval for the ratio of the population geometric means of either $AUC_{0\text{-}INF}$ ($AUC_{0\text{-}t}$ when appropriate) or C_{max} between fed and fasted treatments fails to meet the limits of 80-125 percent, the sponsor should provide specific recommendations on the clinical significance of the effect of food based on what is known about the exposure-response relationships of the drug and the totality of the clinical information. The clinical relevance of any difference in T_{max} and T_{lag} should also be indicated by the sponsor.

B. Labeling Recommendations

Labeling should include a summary of essential information pertaining to the effect of food on the PK and pharmacodynamics of an orally administered drug (if known) that is needed for the safe and effective use of the drug. See the guidance for industry *Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (December 2016) for more information. The effect of food on the absorption of orally administered drugs should be described under a subheading called "Effect of Food" under the "Absorption" heading in the *Pharmacokinetics* subsection of the CLINICAL PHARMACOLOGY section. The "Effect of Food" subheading should include detailed information that informs actionable recommendations. The specific dosing instructions related to food should be described in the DOSAGE AND ADMINISTRATION section of labeling with a cross-reference to the CLINICAL PHARMACOLOGY section.[9] Other FE information in labeling should be included in other sections of labeling as appropriate (e.g., WARNINGS AND PRECAUTIONS, PATIENT COUNSELING INFORMATION). Orally administered drugs that are unaffected by food should be labeled as take "with or without food" in the DOSAGE AND ADMINISTRATION section.

When the DOSAGE AND ADMINISTRATION section of labeling provides an actionable recommendation that is not the result of a pharmacokinetic or pharmacodynamic effect (e.g., dosing with food to reduce nausea), the rationale for the recommendation should be stated and the appropriate section with the rationale should be cross-referenced.

[9] See the guidance for industry *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023). When final, this guidance will represent the FDA's current thinking on this topic.

APPENDIX 1. COMPOSITION OF A HIGH-FAT MEAL*

Total Calories	800-1000
Calories from Protein	150
Calories from Carbohydrates	250
Calories from Fat	500-600
Percent Calories from Fat	≥50
An Example of a High-Fat Breakfast	• Two eggs fried in butter • Two strips of bacon • Two slices of toast with butter • Four ounces of hash brown potatoes • Eight ounces of whole milk

*50 percent of calories are derived from fat. Substitutions can be made to this meal if the content, volume, and viscosity are maintained.

APPENDIX 2. COMPOSITION OF A LOW-FAT MEAL*

Total Calories	400-500
Calories from Fat	100-125
Percent Calories from Fat	25
An Example of a Low-Fat Breakfast*	• Eight ounces milk (1 percent fat) • One boiled egg • One packet flavored instant oatmeal made with water

*This low-fat breakfast contains 387 calories and has 10 grams of fat.