

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

DDM
Display Date 5-30-07
Publication Date 5-31-07
Certifier D. Jenkins

[Docket No. 2007D-0168]

**Draft Guidances for Industry Describing Product-Specific Bioequivalence
Recommendations; Availability**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: This notice announces the availability of draft guidances for industry that describe recommendations on how to design bioequivalence (BE) studies for 200 specific drug products to support abbreviated new drug applications (ANDAs). These draft guidances are being made available concurrently with the publication of a draft guidance for industry entitled "Draft Guidance for Industry—Bioequivalence Recommendations for Specific Products" (product specific BE recommendations). This draft guidance describes the new process for making available guidance on product-specific BE studies. Under the process described in the draft guidance, draft and final product-specific BE study guidance will be made available on the FDA Web site. FDA believes that making this information available on the Internet will streamline the guidance process and provide a meaningful opportunity for the public to consider and comment on product-specific BE study recommendations. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of a related guidance document entitled "Draft Guidance for Industry—Bioequivalence Recommendations for Specific Products."

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NAD 1

DATES: Submit written or electronic comments on the draft guidances by [*insert date 120 days after date of publication in the Federal Register*]. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of draft product-specific BE study guidances to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Doan T. Nguyen, Center for Drug Evaluation and Research (HFD-600), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-827-0495.

SUPPLEMENTARY INFORMATION:

I. Background

To receive approval for an ANDA, an applicant generally must demonstrate, among other things, that its product has the same active ingredient, dosage form, strength, route of administration and conditions of use as the listed drug, and that the proposed drug product is bioequivalent to the reference listed drug (21 U.S.C. 355(j)(2)(A); 21 CFR 314.94(a)). Bioequivalent drug products show no significant difference in the rate and extent of absorption of the therapeutic ingredient (21 U.S.C. 355(j)(8); 21 CFR 320.1(e)). BE studies are undertaken in support of ANDA submissions with

the goal of demonstrating BE between a proposed generic drug product and its reference listed drug. The regulations governing BE are provided at 21 CFR in part 320.

The draft guidance entitled “Bioequivalence Recommendations for Specific Products” describes the following process for making available draft and final product-specific BE recommendations:

- FDA will develop product-specific BE recommendations and post them on the Center for Drug Evaluation and Research (CDER) guidance page (<http://www.fda.gov/cder/index.html>) in draft to facilitate public consideration and comment. The recommendations can be viewed by clicking on the URL associated with the “Bioequivalence Recommendations for Specific Products” guidance on the CDER guidance page or on the Office of Generic Drugs Page (see www.fda.gov/cder/ogd/index.htm). Users can also search for a specific product BE recommendation using the search tool on the CDER guidance page.
- Newly posted draft and final BE recommendations will be announced in the “Newly Added Guidance Documents” list, which is posted monthly on the CDER guidance page.
- The agency will issue a notice in the **Federal Register** announcing the availability on the FDA web site of new product-specific draft and final BE recommendations. The notice will identify a comment period for the recommendations.
- Comments on product-specific BE recommendations will be considered in developing final BE recommendations.
- The BE recommendations will be revised as appropriate to ensure that the most up-to-date BE information is available to the public.

FDA is making the first group of draft product-specific BE recommendations available concurrently with the issuance of the draft guidance document describing the process.

II. Drug Products for Which Draft Product-Specific BE Recommendations Are Available

The FDA is making available draft recommendations for drug products containing the following active ingredients:

A

Abacavir Sulfate
 Abacavir Sulfate; Lamivudine; Zidovudine
 Acamprosate Calcium
 Acitretin
 Acyclovir
 Almotriptan Malate
 Alosetron HCl
 Alprazolam
 Amlodipine Besylate
 Amlodipine Besylate; Benazepril HCl
 Amoxicillin; Clavulanate Potassium
 Anagrelide HCl
 Anastrozole
 Aprepitant
 Atazanavir Sulfate
 Atomoxetine HCl
 Atorvastatin Calcium

B

Benzonate
 Benzphetamine HCl
 Bicalutamide
 Bisoprolol Fumarate
 Bisoprolol Fumarate; Hydrochlorothiazide

C

Candesartan Cilexetil
 Candesartan Cilexetil; Hydrochlorothiazide
 Carbamazepine
 Carbidopa; Entacapone; Levodopa
 Carvedilol
 Cefditoren Pivoxil
 Celecoxib
 Cetirizine HCl
 Cevimeline HCl
 Cilostazol
 Cinacalcet HCl
 Clarithromycin
 Clonidine HCl
 Clopidogrel

D

Danazol
 Dantrolene Sodium
 Darifenacin HBr
 Deferasirox
 Desloratadine
 Dextromethorphan Polistirex
 Diclofenac Sodium; Misoprostol
 Dicloxacillin Sodium
 Didanosine (multiple dosage forms)
 Digoxin
 Dipyridamole
 Divalproex Sodium
 Dofetilide
 Donepezil HCl
 Doxazosin Mesylate
 Drospirenone; Estradiol
 Duloxetine HCl (multiple dosage forms)
 Dutasteride

E

Efavirenz (multiple dosage forms)
 Emtricitabine
 Entacapone
 Entecavir

Eplerenone
 Erlotinib HCl
 Escitalopram Oxalate
 Esomeprazole Magnesium
 Etidronate Disodium
 Exemestane

F

Famotidine (multiple dosage forms)
 Felbamate (multiple dosage forms)
 Fenofibrate
 Fexofenadine HCl (multiple dosage forms)
 Flavoxate HCl
 Fluconazole
 Fluoxetine HCl; Olanzapine
 Fosamprenavir Calcium
 Fosinopril Sodium; Hydrochlorothiazide

G

Gabapentin (multiple dosage forms)
 Galantamine HBr
 Ganciclovir
 Gemifloxacin Mesylate
 Glimepiride
 Glipizide; Metformin HCl
 Glyburide; Metformin HCl
 Granisetron HCl

H

Hydrochlorothiazide
 Hydrochlorothiazide; Lisinopril
 Hydrochlorothiazide; Losartan Potassium
 Hydrochlorothiazide; Moexipril HCl
 Hydrochlorothiazide; Olmesartan Medoxomil
 Hydrochlorothiazide; Valsartan

I

Ibandronate Sodium
 Ibuprofen; Pseudoephedrine HCl
 Indinavir Sulfate
 Irbesartan
 Isosorbide Mononitrate
 Isradipine (multiple dosage forms)
 Itraconazole

L

Lamivudine
 Lamivudine; Zidovudine
 Lamotrigine (multiple dosage forms)
 Leflunomide
 Liothyronine Sodium
 Losartan Potassium

M

Mefloquine HCl
 Meloxicam (multiple dosage forms)
 Mercaptopurine
 Mesalamine
 Metaxalone
 Metformin HCl
 Metformin HCl; Pioglitazone HCl
 Miglustat
 Mirtazapine
 Modafinil
 Moexipril HCl
 Montelukast Sodium
 Morphine Sulfate
 Mycophenolate Mofetil
 Mycophenolate Mofetil HCl

N

Nabumetone
 Nateglinide
 Nelfinavir Mesylate
 Nevirapine

O

Olanzapine
 Olmesartan Medoxomil
 Olsalazine Sodium
 Omeprazole (multiple dosage forms)
 Omeprazole Magnesium
 Ondansetron (multiple dosage forms)
 Oxcarbazepine (multiple dosage forms)

P

Pantoprazole Sodium
 Perindopril Erbumine

Pilocarpine HCl
Pravastatin Sodium

Q

Quetiapine Fumarate
Quinapril HCl

R

Raloxifene HCl
Ramipril
Ribavirin (multiple dosage forms)
Rifampin
Riluzole
Risedronate Sodium; Calcium Chloride
Risedronate Sodium
Risperidone
Ritonavir
Rizatriptan Benzoate
Rosiglitazone Maleate
Rosuvastatin Calcium

S

Sertraline HCl
Sibutramine HCl
Sildenafil Citrate
Simvastatin
Sirolimus
Stavudine
Sulfamethoxazole; Trimethoprim
Sumatriptan Succinate

T

Tacrolimus
Tadalafil
Tamsulosin HCl
Telithromycin
Telmisartan
Terbinafine HCl
Testosterone
Ticlopidine HCl
Tizanidine HCl
Tolterodine Tartrate
Topiramate (multiple dosage forms)
Torsemide
Tramadol HCl
Tramadol HCl; Acetaminophen
Trandolapril
Triamterene

V

Valacyclovir HCl
Valsartan
Vardenafil HCl
Venlafaxine HCl
Verapamil HCl (multiple dosage forms)
Voriconazole

Z

Zaleplon
Zidovudine (multiple dosage forms)
Ziprasidone HCl
Zolpidem Tartrate

These draft guidances are available on the CDER guidance page and may be viewed by clicking on the URL associated with the draft “Bioequivalence Recommendations for Specific Products” guidance on the CDER guidance page or on the Office of Generic Drugs Page (see www.fda.gov/cder/ogd/index.htm). Users can also search for a specific product BE recommendation using the search tool on the CDER guidance page.

These draft guidances are being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidances represent the agency's current thinking on the design of product-specific bioequivalence studies to support ANDAs. Guidance does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the draft guidance. Two copies of mailed comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the draft product-specific BE recommendations at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: 5/22/07
May 22, 2007.

Jeffrey Shuren,
Assistant Commissioner for Policy.

[FR Doc. 07-????? Filed ??-??-07; 8:45 am]

BILLING CODE 4160-01-S

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Dawn P. Hawkins