enterocolitis caused by *Staphylococcus aureus* (including methicillin-resistant strains) and antibiotic-associated pseudomembranous colitis caused by *Clostridium difficile*. Vancocin oral capsules are designated the reference listed drug (RLD) and therefore any ANDA for generic vancomycin HCl oral capsules must demonstrate BE to Vancocin prior to approval. There are no approved ANDAs for vancomycin HCl capsules.

Vancomycin acts locally in the lower gastrointestinal (GI) tract. After oral administration, a vancomycin capsule releases the drug in the stomach and upper GI tract, the released drug is completely solubilized in GI fluids, and it is transported along with GI fluids to its site of action in the lower GI tract. As set forth in the Clinical Pharmacology section of the approved product labeling for Vancocin, vancomycin is poorly absorbed after oral administration and does not usually enter the systemic circulation. Thus, plasma and urine concentrations of vancomycin are generally undetectable following oral administration, and traditional BE studies with pharmacokinetic (PK) measurements are of limited utility. Accordingly, in 1996, FDA recommended an in vivo BE study with clinical endpoints in patients to demonstrate BE of generic vancomycin HCl oral capsules.

In October 2004, FDA asked its Advisory Committee for Pharmaceutical Science to consider when dissolution testing could be used to establish BE for locally-acting GI drugs. The committee concluded that dissolution testing along with PK studies should be acceptable to establish BE for such products. In light of the committee's conclusions, after obtaining data showing that vancomycin HCl is highly soluble at pH conditions encountered in the GI tract and expected to be in solution long before it reaches the site of action in the lower GI tract, the FDA revised its recommendation in early 2006 to include in vitro dissolution studies to demonstrate BE of generic vancomycin HCl oral capsules. This approach would provide FDA's Office of Generic Drugs with information about drug availability at the site of action and would be more sensitive than clinical trials in detecting differences in product performance. In accordance with its practice prior to publication of the draft guidance ''Bioequivalence Recommendations for Specific Products,'' FDA provided its 2006 revised BE recommendations to those parties that had requests pending with FDA for this information. In March 2006, Viropharma, Inc., the manufacturer of the RLD Vancocin, filed a petition for stay of action (PSA) challenging FDA's revised recommendation (Docket No. FDA–2006–P–0007).[1]

In the draft ''Bioequivalence Recommendation for Vancomycin HCl,'' FDA further clarifies its recommendations on the design of BE studies to support ANDAs for vancomycin HCl capsules. Because generic applicants may use different inactive ingredients, which may affect the transport, absorption, and/or effectiveness of the drug, FDA is currently recommending in vitro dissolution studies only for test formulations that are qualitatively (Q1) and quantitatively (Q2) the same as the RLD with respect to inactive ingredients. For test formulations that are not Q1 and Q2 the same as the RLD with respect to inactive ingredients, FDA is recommending in vivo BE studies with clinical endpoints. The draft BE recommendation for vancomycin HCl capsules is consistent with the 2004 advisory committee's conclusion. PK studies are not appropriate in this case, however, because vancomycin levels are generally not detectable in the plasma or urine due to very limited absorption.

Comments on this draft guidance will also be considered by FDA as it addresses the complicated issues raised in Viropharma, Inc.'s PSAs. FDA will carefully consider such comments before responding to the petition and finalizing its BE recommendation for vancomycin HCl. Because of the lengthy history of FDA's consideration of bioequivalence methodologies for vancomycin HCl capsules, the pendency of the PSAs, and the complexity of the issues involved, the availability of this draft guidance is being announced in a drug product-specific notice, and the recommendations include a significant amount of background information and explanation of the reasons for the bioequivalence recommendations.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on the design of BE studies to support ANDAs for vancomycin HCl. It 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.

[1] This PSA was originally assigned Docket No. 2006P–0124. The number was changed to FDA–2006–P–0007 as a result of FDA's transition to its new docketing system (Regulations.gov) in January 2008. This docket also includes a second PSA and numerous supplements filed by ViroPharma.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at *http://www.regulations.gov*.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.regulations.gov*.

Dated: December 8, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–29692 Filed 12–15–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–D–0614]

Draft Guidance for Industry on Changes to Approved New Animal Drug Applications—New Animal Drug Applications Versus Category II Supplemental New Animal Drug Applications; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry #191 entitled ''Changes to Approved NADAs—New NADAs vs. Category II Supplemental NADAs''. This guidance is intended to assist sponsors who wish to apply for approval of changes to approved new animal drugs

that require FDA to reevaluate safety and/or effectiveness data. The goal of this guidance is to create greater consistency in how such applications are handled by sponsors and by FDA's Center for Veterinary Medicine (CVM).

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit written or electronic comments on the draft guidance by February 17, 2009.

ADDRESSES: Submit written requests for single copies of the guidance to the Communications Staff (HFV–12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. 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.regulations.gov*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Suzanne J. Sechen, Center for Veterinary Medicine (HFV–126), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240–276–8105, e-mail: suzanne.sechen@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry #191 entitled ''Changes to Approved NADAs—New NADAs vs. Category II Supplemental NADAs''. In the past, applications for changes to approved new animal drugs may have been handled inconsistently by sponsors and the agency. Inconsistency in handling such applications has been confusing for sponsors and for CVM, particularly when reviewing and referencing the history of specific new animal drug applications (NADAs). This guidance is intended to improve consistency in the way applications for changes are handled. We believe that consistent handling of these types of applications also will help maintain clarity in the administrative record, which is an important part of protecting the public health.

When proposing a change to an approved new animal drug that may affect the safety and/or effectiveness of the drug, such changes generally must be submitted to FDA either as a new NADA or a supplemental application to the original NADA. Category II supplemental NADAs are the type of supplement that is used to propose changes that may require a reevaluation of certain safety or effectiveness data in the parent application. Specific changes meeting the requirements for a Category II supplemental NADA are described in 21 CFR 514.106(b)(2). This guidance provides examples and makes specific recommendations about when a change to an approved NADA that requires FDA to review safety and/or effectiveness data should be submitted as a new NADA and when such a change should be submitted as a Category II supplemental NADA. In addition, the guidance addresses how to handle submissions relating to certain types of proposed changes at the investigational stage.

II. Significance of Guidance

This level 1 draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on this topic. It 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. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information have been approved under OMB Control No. 0910–0032.

IV. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at *http://www.regulations.gov*.

V. Electronic Access

Persons with access to the Internet may obtain the draft guidance at either *http://www.fda.gov/cvm* or *http://www.regulations.gov*.

Dated: Decmeber 8, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

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BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2008–D–0610]

Draft Guidance for Industry on Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During an Influenza Pandemic; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During an Influenza Pandemic.'' The draft guidance discusses FDA's intended approach to enforcement of adverse event reporting requirements for drugs, biologics, medical devices, and dietary supplements during the Federal Government Response Stages of an influenza pandemic. The agency makes recommendations to industry for focusing limited resources on reports related to influenza-related products and other specific types of reports indicated in the draft guidance.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit written or electronic comments on the draft guidance by February 17, 2009.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire