made in the Yesavage study. I find the Center's arguments to have merit.

A comparable issue was adjudicated in the Commissioner's Decision on Mysteclin. Therein, it was ruled, ''(E)ven if the subgroups and multiple endpoints had been identified in the protocol, * * * some downward adjustments in the p values should have been made to correct for the analyses of multiple subgroups and endpoints.'' (Commissioner's Decision on Mysteclin, slip op. at 43; see also Commissioner's Decision on Deprol, 58 FR 50929 at 50933.) Similarly, in the Commissioner's Decision on Deprol, it was noted that, ''if enough pair-wise comparisons are made, some comparisons will be 'statistically significant' by chance alone.'' (Commissioner's Decision on Deprol, 58 FR 50929 at 50933.) When multiple comparisons are made, corrections in the p values are needed to maintain the correct Type I error rate because the likelihood of a Type I error increases with the number of individual comparisons. (Commissioner's Decision on Deprol, 58 FR 50929 at 50933.) In other words, as one great author more expressively observed, ''Fortune brings in some boats that are not steered.'' (Shakespeare, *Cymbeline*, IV, iii, 46.)

For these reasons, I find that in weighing the adequacy of the Yesavage study, it is proper to consider the fact that numerous statistical analyses were employed, and to consider that the particular outcome of interest was not specified in advance, nor were adjustments to the p value made. Accordingly, I find no error in the ALJ's ruling on this point.

h. *Adequacy of the Yesavage study*. In sum, I find that the Yesavage study was not adequate and well-controlled. In making this determination, I have considered the aggregate effect of the protocol violations. I base my ruling upon these findings: (1) That the selection of patients for the study was flawed by the inclusion of patients with the concomitant condition of Parkinson's disease, and by the inclusion of outpatients, who were to be excluded under the protocol; (2) that the failure to show that stroke patients were included in both the drug and the placebo arms of the clinical trial can be considered as a flaw in the study; (3) that the fact that a statistically significant difference between test and control groups existed on the BMT was a proper consideration; (4) that the uncontrolled use of concomitant medication and the poor documentation of concomitant medication use weighs against finding the Yesavage study to be adequate and well-controlled; (5) that the small sample size was a proper factor to be considered in reviewing the results of the study, and can be weighed against the adequacy of the study; (6) that the improvement of patients on SCAG Factor 1 was not clinically significant; and (7) that the fact that numerous statistical analyses were employed and that the particular outcome of interest was not specified in advance, nor were adjustments to the p value made, can be weighed against the adequacy of the study.

II. Conclusion and Order

The foregoing opinion in its entirety constitutes my findings of fact and conclusions of law. Based on the foregoing discussion, findings, and conclusions, I affirm the ALJ's Initial Decision in all respects, except where specifically stated otherwise. I find that there is a lack of substantial evidence that Cyclospasmol® will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its labeling. Accordingly, under 21 U.S.C. 355(e)(3), the NDA for Cyclospasmol® must be withdrawn. I further find that, by reason of the lack of substantial evidence of its effectiveness, Cyclospasmol® is a ''new drug'' within the meaning of 21 U.S.C. 321(p).

Therefore, under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355(e), and under authority delegated to me by the Secretary (§ 5.10(a)(1)), the new drug application for Cyclospasmol® and all amendments and supplements thereto, are hereby withdrawn, effective January 2, 1997.

Dated: November 12, 1996.

Michael A. Friedman,

Deputy Commissioner for Operations.

[FR Doc. 96–30648 Filed 12–2–96; 8:45 am]

BILLING CODE 4160–01–P

[Docket No. 96D–0334]

Procedures for Issuance of and Review and Response to Materials Submitted in Response to Clinical Hold for Investigational New Drug (IND) Applications; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of two documents entitled ''Centerwide Policy on Issuance of and Response to Clinical Hold Letters for Investigational New Drug Applications'' (OD–R–8–96, Center for Biologics Evaluation and Research (CBER)) and ''IND Process and Review Procedures'' (MAPP 6030.1, Center for Drug Evaluation and Research (CDER)). The documents specify the procedures for the issuance of and review and response to material submitted in response to a notice of clinical hold. It is intended that these documents will clarify the agency's policy in regard to responses to clinical holds. The documents are made available as part of the agency's commitment to review and respond to data submitted in response to a clinical hold within 30 days of receiving the submission, as stated in the November 1995, Presidential National Performance Review report entitled ''Reinventing the Regulation of Drugs Made from Biotechnology.''

ADDRESSES:

CBER Information: For additional copies of the documents submit written requests to the Manufacturers Assistance and Communication Staff (HFM–42), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests. The document may also be obtained by mail or FAX by calling the CBER FAX Information System at 1–888–CBER FAX, or 301–827–3844. Persons with access to the Internet may obtain the document using FTP, the World Wide Web (WWW), or bounce-back e-mail. For FTP access, connect to CBER at ''ftp://ftp.fda.gov/CBER/''. For WWW access, connect to CBER at ''http://www.fda.gov/cber/cberftp.html''. For bounce-back e-mail send a message to ''INDHOLD@a1.cber.fda.gov''.

CDER Information: For additional copies of the documents contact the Drug Information Branch (HFD–210), Division of Communications Management, Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–1012. The form may also be obtained by calling the CDER FAX–ON–DEMAND System at 1–800–342–2722, or 1–301–827–0577. An electronic version of the documents is also available via Internet using FTP, Gopher, or the World Wide Web (WWW). For FTP, connect to the CDER anonymous FTP server at cdvs2.cder.fda.gov and change to the ''guidance'' directory. For Gopher, connect to the CDER Gopher server at

gopher.cder.fda.gov and select the ''Industry Guidance'' menu option. For WWW, connect to the FDA home page at http://www.fda.gov.

Submit written comments on the documents to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Corporations should submit two copies of any comments and individuals may submit one copy. Requests and comments should be identified with the docket number found in brackets in the heading of this document. Copies of the documents and received comments are available for public examination in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT:

Timothy W. Beth, Center for Biologics Evaluation and Research (HFM–630), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–594–3074, or

Murray M. Lumpkin, Center for Drug Evaluation and Research (HFD–2), Food and Drug Administration, 1451 Rockville Pike, Rockville, MD 20852–1420, 301–594–5417.

SUPPLEMENTARY INFORMATION: The President's November 1995 report, ''Reinventing the Regulation of Drugs Made from Biotechnology,'' outlined changes to the biologics regulations designed to reduce the burden of FDA regulations on industry without reducing public health protection. One of the recommended modifications was to have investigational new drug (IND) reviewers respond within 30 days whether newly submitted information supports the initiation or continuation of a human investigation that the agency has put on clinical hold.

Companies or individuals that intend to study IND's or biologics in humans generally are required first to submit an IND application to the agency. They may proceed with the study 30 days after the agency receives the application unless FDA puts the study on clinical hold (§ 312.42 (21 CFR 312.42).) Section 312.42(a) describes a clinical hold as an ''order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation.'' Section 312.42(d) states that the hold may be relayed to the sponsor by telephone or other rapid means of communication and that FDA will provide a written explanation of the basis of the hold to the sponsor no more than 30 days following the hold. Though § 312.42(d) allows for communication of the reasons for a hold within 30 days following the placement of the hold, both CBER and CDER provide this notification in even shorter timeframes, consistent with the procedures set forth in the CBER and CDER documents. Thus, a researcher or company that intends to begin testing a biologic or new drug in humans, may not begin or continue the study until FDA releases the clinical hold. Removal of the hold may be relayed by telephone or other rapid means of communication unless FDA notified the sponsor in writing that once a correction or modification was made they could proceed as outlined in § 312.42(e).

In the past, FDA had no internal operating procedures regarding how much time it may take to evaluate data submitted by the sponsor in response to the clinical hold. FDA is committed to promptly reviewing and responding to data submitted in response to a clinical hold and to do so within 30 days of receiving the submission. FDA believes that the 30-day period meets the needs of sponsors, will prevent delays during review of data, and will prevent unnecessary delays in the start or continuation of clinical studies. These procedures are contained in CBER's Policy and Procedure Guide, OD–R–8–96, ''Centerwide Policy on Issuance of and Response to Clinical Hold Letters for Investigational New Drug Applications,'' dated August 20, 1996, and in CDER's Manual of Policies and Procedures, MAPP 6030.1, ''IND Process and Review Procedures,'' dated June 20, 1996.

Although these documents do not create or confer any rights for or on any person and do not operate to bind FDA or the public, they do represent the agency's current thinking on time periods for the review and response to materials submitted in response to clinical hold for IND's.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the procedure documents. FDA will review the comments received and, if appropriate, consider preparing revised documents based upon that review. Corporations should submit two copies of any comments and individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Copies of the documents and received comments are available for public examination in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

Dated: November 19, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 96–30770 Filed 12–2–96; 8:45 am]

BILLING CODE 4160–01–F

Health Resources and Services Administration

Agency Information Collection Activities: Proposed Collection: Comment Request

In compliance with the requirement of Section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995 for opportunity for public comment on proposed data collection projects, the Health Resources and Services Administration (HRSA) will publish periodic summaries of proposed projects being developed for submission to OMB under the Paperwork Reduction Act of 1995. To request more information on the proposed project or to obtain a copy of the data collection plans and instruments, call the HRSA Reports Clearance Officer on (301) 443–1129.

Comments are invited on: (a) whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) ways to enhance the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology.

Proposed Project

Voluntary Customer Surveys of ''Partners'' of the Health Resources and Services Administration—NEW

In response to Executive Order 12862, Setting Customer Service Standards, the Health Resources and Services Administration (HRSA) is proposing to conduct voluntary customer surveys of its ''partners'' to assess strengths and weaknesses in program services. HRSA partners are typically State or local governments, health care facilities, health care consortia, health care providers, and researchers. Partner surveys to be conducted by HRSA might include, for example, surveys of grantees to determine satisfaction with the technical assistance, or surveys of providers who receive training from HRSA grantees to measure satisfaction with the training experience. Results of