HIV–1 transmission through transfusions of blood and blood products. To further address direct viral detection methods, FDA brought the issue of donor screening for HIV–1 antigen to a public meeting of the Blood Products Advisory Committee (BPAC) in June 1995. After hearing the most recent available data on HIV–1 risk in the blood supply, the estimated efficacy of antigen screening, and other issues bearing on a risk/benefit assessment, 9 of the 15 BPAC members present were of the opinion that donor screening for HIV–1 antigen by candidate test kits is not likely to provide a significant public health benefit which outweighs the potential risks. After considering the available information and the opinions of the BPAC members, FDA recommended that blood establishments should implement donor screening for HIV–1 antigen using licensed tests that are approved for this indication. FDA recommended implementation of HIV–1 antigen screening because of the benefit that it will provide to a small number of blood product recipients, as a partial preventive measure against the possibility of any increase in HIV–1 ''window period'' donations and to decrease the virus burden in plasma pools for fractionation.

FDA recommended that the screening for HIV–1 antigen(s) be implemented within 3 months of the commercial availability of the first such test approved for donor screening for all donations of Whole Blood, blood components, Source Leukocytes and Source Plasma, and all such inventoried units available for release. FDA also recommended that consigned within-date units intended for transfusion and still in the consignee's inventory be either replaced with screened units or tested for HIV–1 antigen(s) as soon as feasible. The memorandum included additional recommendations and information on the following: (1) Disposition and labeling of units; (2) donor deferral; (3) Public Health Service recommendations for donor notification and counseling; (4) exclusion/retrieval of potentially contaminated units from prior collections and notification of consignees; and (5) notification of consignees of neutralization test results.

Because HIV–1 antigen testing will reduce, but not eliminate, the residual risk of HIV–1 from transfusion, FDA regards such screening as an interim measure pending the availability of better technology for this purpose. FDA encourages continued development of new methods to further reduce the risk of HIV transmissions in the ''window period.''

As with other memoranda, FDA does not intend this document to be all-inclusive and cautions that not all information may be applicable to all situations. The memorandum is intended to provide information and does not set forth new requirements. The procedures cited in the memorandum are recommendations. FDA anticipates that blood and plasma establishments may develop alternative procedures and discuss them with FDA. FDA may find those alternative procedures acceptable. FDA recognizes that the scientific technology for controlling the risk of transmission of HIV by blood and blood products may continue to advance and that this document may become outdated as those advances occur. The memorandum does not bind FDA and does not create or confer any rights, privileges, or benefits on or for any private person, but is intended merely for guidance.

Interested persons may, at any time, submit to the Dockets Management Branch (address above) written comments on the memorandum. Two copies of any 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. A copy of the memorandum and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Received comments will be considered in determining whether further revisions to the memorandum are warranted.

Dated: January 22, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–1657 Filed 1–29–96; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 93D–0398]

Microbiological Testing for Antimicrobial Food-Animal Drugs; Final Guidance; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance document entitled ''Microbiological Testing of Antimicrobial Drug Residues in Food.'' The availability of the draft guideline was announced on January 6, 1994; this final guidance document addresses the comments submitted on the draft guideline. The final guidance document, which was prepared by the Center for Veterinary Medicine (CVM), addresses human food safety issues that may be associated with food-animal antimicrobial drug products. This guidance document also provides points to consider when determining which antimicrobials may require supplemental testing and recommends test procedures for establishing that antimicrobial drug residues will not cause intestinal microflora perturbations in the consumer.

DATES: Written comments on the guidance document may be submitted at any time.

ADDRESSES: Submit written requests for single copies of the final guidance document ''Microbiological Testing of Antimicrobial Drug Residues in Food,'' to the Communications and Education Branch (HFV–12), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1755. Send two self-addressed adhesive labels to assist that office in processing your requests. Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. Requests and comments should be identified with the docket number found in brackets in the heading of this document. A copy of the guidance document and received comments may be seen at the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Haydee Fernandez, Center for Veterinary Medicine (HFV–154), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1684.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of the final guidance document entitled ''Microbiological Testing of Antimicrobial Drug Residues in Food.'' In evaluating the safety of new animal drugs, the agency must determine, among other things, their cumulative effect in man or other animal as required by section 512(d)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360b(d)(2)(B)). The guidance document describes the testing that may be necessary to establish that antimicrobial drug residues in food will be safe and will not cause intestinal microflora perturbations in the consumer.

In the Federal Register of January 6, 1994 (59 FR 754), FDA issued a notice of availability of the draft guideline entitled ''Microbiological Testing of

Antimicrobial Drug Residues in Food.'' The draft guideline was made available for public comment to provide the agency with views to be considered in the development of the guideline. Comments were requested specifically on: (1) Recommendations for additional microbiological testing for antimicrobial drug residues that seek a safe concentration higher than 1 part per million (ppm) of microbiologically active residues in the total diet; (2) how the proposed guideline should relate the effect of low doses of antibiotics observed in model systems to potential adverse biological effects in humans; and (3) appropriate endpoints for monitoring the effects of the different classes of antibiotics. Interested persons were given until April 6, 1994, to comment on the draft guideline.

The agency received comments from university faculty members and the animal drug industry. FDA has revised the draft guideline as a result of these comments. In addition, FDA is reviewing its approach to the development of guidance documents. In order to eliminate confusion caused by use of different nomenclature for guidance documents (e.g., ''guidelines,'' ''points to consider'') and to make it clear that this document is not being issued under current § 10.90(b) (21 CFR 10.90(b)). FDA is issuing this document as ''guidance,'' not as a ''guideline.''

I. General Comments on the Draft Guideline

1. There was general consensus among the comments that microbiologically inactive metabolites and rapidly absorbed antimicrobials would not produce any adverse effect on the intestinal microflora of humans.

CVM agrees that the compounds that are most likely to raise human food safety concerns are those that are microbiologically active. Microbiologically inactive metabolites and rapidly absorbed antimicrobials are not the focus of this guidance document.

2. Industry commented that the sponsor of a compound should identify the active residues and conduct the appropriate microbiological endpoints in consultation with the agency.

FDA agrees that, under the act, it is the sponsor's responsibility to identify the microbiological activity of its product and to monitor the appropriate microbiological endpoint(s) to establish the antimicrobial no observed effect level (NOEL). As with all studies with animal drugs, the sponsor is encouraged to discuss the protocol with CVM representatives prior to initiating the study.

II. Comments Regarding Model Systems

3. The agency received several comments on the use of model systems to evaluate the effect of active residues on the human intestinal microflora. The model systems proposed in the comments were mainly in vitro systems using continuous flow. According to the comments, continuous flow systems allow the study of the effect of ''low levels'' of antimicrobials on human intestinal microflora by studying the selection for antibiotic resistance, the change in colonization resistance, the determination of anaerobic population counts, and the detection of virulence enhancement.

The agency agrees that in vitro models may offer a valid test system for assessing the effect of ''low levels'' of antimicrobials on the human intestinal microflora.

4. A trade association stated that it would be very difficult for the sponsors to undertake de novo development and validation of test procedures. The comment suggested that before requiring testing, CVM should have some experience with the model systems that could be used to study the microbiological endpoints. This could be done by funding research studies to develop and, if possible, validate the test procedures.

CVM is not aware of any validated model system for the testing of all antimicrobial agents. CVM does intend to initiate research which will lead to the development of validated model systems for evaluating the effect of low levels of antimicrobials on the human intestinal microflora.

III. Comments Regarding the Proposed Upper Limit of 1 ppm Antimicrobial Activity

5. Most comments agreed with FDA that 1 ppm was a level of microbiologically active residues that would be unlikely to produce any adverse effect on the human intestinal microflora and would, therefore, be safe. Because there was some confusion about how 1 ppm in the total diet should be interpreted in practice, the guidance document states CVM's belief, based on available data, that for antimicrobial drug residues in edible tissues from food-producing animals the acceptable daily intake (ADI) should be 1.5 milligrams per person per day (mg/person/day). Sponsors may demonstrate through additional specific testing that an ADI for drug residues in excess of 1.5 mg/person/day is safe.

6. One comment expressed concern that 1 ppm might not be a ''very low level'' for all antibiotics, mainly for new and more active molecules (per unit of weight) than current antimicrobials.

CVM disagrees based on the majority of scientific opinion. CVM has concluded that 1 ppm (or 1.5 mg/person/day) is a conservative level for determining whether or not antibiotic residues will produce an adverse effect on the human intestinal microflora. However, as the guidance makes clear, CVM may request information on microbiological activity of any new animal drug.

7. One comment from industry agreed that studies should be conducted by sponsors to establish microbiological activity, but disagreed with CVM's proposed use of microbiological activity as a valid endpoint for establishing tolerances for antimicrobial drugs. The comment argued that the predictive value of microbiological activity in determining the no effect level for the health and safety of individuals and the public has not been established. Therefore, according to the comment, microbiological activity should not be used to set the safe concentration but should only help to evaluate a NOEL established by classic toxicology. Instead, the comment stated that ''if there is a microbiological effect at a safe concentration higher than 1 ppm microbiologically active residue, then the regulated toxicological no adverse effect level for total residue will need to be adjusted downward accordingly, taking into account the percentage of microbiologically active residue in the total residue and the nature of the observed microbiological effect.''

CVM disagrees. It is well documented that high levels of antibiotics produce deleterious effects on intestinal microflora (see ''Symposium on Microbiological Significance of Drug Residues in Food,'' *Veterinary and Human Toxicology*, 35 (supplement 1), 1993). Therefore, CVM has concluded that microbiological activity is a valid endpoint for establishing the safe concentration for antimicrobial drugs. Thus, when scientifically appropriate, CVM will determine the no effect level and calculate the safe concentration based on the results of microbiological testing.

IV. Comments Regarding the Proposed Classification of Intestinal Microflora Changes

8. One comment suggested that FDA should classify the changes in the intestinal microflora as follows: (1) Changes in the number of microorganisms and composition of intestinal microflora; (2) changes in metabolic activity of the flora related to metabolism of exogenous and

endogenous compounds; and (3) changes in antimicrobial resistance patterns and resistant genetic elements within the microflora.

CVM generally agrees. CVM has identified the following areas for which microbiological residues represent a potential public health concern: (1) Changes in the metabolic activity of the intestinal microflora; (2) changes in antimicrobial resistance patterns of the intestinal microflora; (3) changes in the colonization resistance properties (barrier effect) of the microflora; and (4) changes in the number of microorganisms and composition of the intestinal microflora.

V. Conclusion

The Center specifically invites comments on how to relate the effect produced in the model systems to the identified public health concerns. In addition, information on the appropriate endpoints for monitoring the effects of the different classes of antibiotics is requested. The public has the opportunity to comment on this guidance document at any time. CVM will consider all comments for future modifications of this guidance document.

Guidelines are generally issued under §§ 10.85(a) (21 CFR 10.85(a)) and 10.90(b). The agency is now in the process of revising §§ 10.85(a) and 10.90(b). This guidance document does not bind the agency, and it does not create or confer any rights, privileges, or benefits for or on any person; however, it represents the agency's current thinking on microbiological testing of antimicrobial drug residues in food. A person may follow the guidance document or may choose to follow alternate procedures or practices. If a person chooses to use alternate procedures or practices, that person may wish to discuss the matter further with the agency to prevent an expenditure of money and effort on activities that may later be determined to be unacceptable to FDA.

Interested persons may, at any time, submit to the Dockets Management Branch (address above) written comments on the guidance document. Two copies of any 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 guidance document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Received comments will be considered to determine if further revision of the guidance document is necessary.

Dated: January 22, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–1579 Filed 1–29–96; 8:45 am]

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Health Resources and Services Administration

Proposed Data Collections Submitted for Public Comment and Recommendations

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 Projects

1. Evaluation of the Community Integrated Service System (CISS) Program—New—Data will be collected by mail and in person to assess demonstration effectiveness for program management purposes. Mail surveys will be conducted with four managers in each of 40 CISS grant funded programs: (1) Project director, (2) supervisor of intake/outreach, (3) medical director or closest equivalent, and (4) supervisors of care coordination. The purposes are to describe the organizational structure, service networks, and expected decision-making patterns prior to the more focussed on-site inquiries. Data subsequently will be collected in person from managers, staff, and clients of the 40 CISS grant-funded programs: (1) Project director and director of grant-receiving institution, (2) managers of each service in the program, (3) staff providing health services, (4) staff providing care coordination and services other than health care, and (5) a sample of clients who agree to participate. Numbers (3) and (4) will respond to focus group protocols. The purposes of the in-person data collection are to assess the day-to-day interaction of the service units, decision strategies employed by managers, and the effect on access for targeted clients. The study will provide the only evaluation to date of the effectiveness of the CISS program. The information will also be used to identify models with promise for replication. Because this data collection is targeted to a limited number of respondents, automated collection techniques will not be used. Burden estimates are as follows:

Respondent type	Number of respondents	Responses per respondent	Average burden per response (hours)	Total burden hours
Project Director	40	1	2	80
Intake/Outreach Supervisor	40	1	1.5	60
Medical Director	40	1	1.5	60
Supervisor of Care Coord	40	1	1.5	60
Proj. Dir./Inst. Dir	80	1	2	160
Service Managers	200	1	2	400
Health Service Staff	400	1	2	800
Care Coord./Other Service Staff	400	1	2	800
CISS clients	200	1	.3	60