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MASTER FILES

Guidance for Industry for the Preparation and Submission of Veterinary Master Files

1995

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR VETERINARY MEDICINE

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GUIDANCE FOR INDUSTRY[1]

FOR THE PREPARATION AND SUBMISSION OF VETERINARY MASTER FILES

I. INTRODUCTION

Purpose

This document is intended to provide guidance for the preparation and submission of master files to the Center for Veterinary Medicine. This document discusses the types of master files, information needed, submission format, procedures governing the review of master files, and obligations of the master file holder.

A master file (MF) is a voluntary submission to the Food and Drug Administration (FDA) that may be used to provide confidential, detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more veterinary drugs. We generally refer to master files on file with the Center for Veterinary Medicine as veterinary master files (VMF's). Whereas, those on file with the Center for Drug

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[1]This guidance has been prepared by the Office of New Animal Drug Evaluation, Division of Chemistry, Chemistry Manufacturing Controls review group of the Center for Veterinary Medicine (CVM), at the Food and Drug Administration. This guidance is an informal communication under 21 CFR 10.90(b)(9) that represents the best judgment of CVM employees at this time. This statement does not bind or otherwise obligate CVM employees at this time. This statement does not bind or otherwise obligate CVM to the views expressed. For further information about this guidance, contact William G. Marnane, Center for Veterinary Medicine, Office of New Animal Drug Evaluation, Division of Chemistry, HFV-143, 7500 Standish Place, Rockville MD 20855 (Phone: 301-594-0678; Fax: 301 594-2298)

Evaluation and Research (CDER) are referred to as drug master files (DMF's). There are no real differences between DMF's and VMF's other than their filing location. The differences in designation are used only for document and filing purposes to avoid confusion in possible numbering systems between the Centers. The information contained in a VMF or DMF may be used to support an investigational new animal drug application, a new animal drug application, an abbreviated new animal drug application, another VMF or DMF, an export application, or amendments or supplements to any of these.

A master file is NOT a substitute for an INADA, NADA, ANADA, or Export Application. The master file is used to provide support information and data for an NADA, ANADA, INADA, Export Application, or other master files. It is not approved or disapproved. Rather, the submission is found acceptable or deficient in support of an INADA, NADA, ANADA, Export Application, or other master file.

The submission of a master file is not required by law or FDA regulation. Master files are generally created to allow a party other than the holder of the master file to reference material without disclosing to that party the contents of the file. When an applicant references its own material, the applicant should reference the information contained in its own INADA, NADA, or ANADA directly rather than establishing a master file.

A master file is submitted solely at the discretion of the holder. The contents of a master file are reviewed by the Center only in conjunction with the review of an INADA, NADA, ANADA, or Export Application. All information submitted in a master file is considered confidential in accordance with 21 CFR 514.11 and is reviewed only when the master file holder provides appropriate authorization permitting the FDA to refer to it on behalf of an applicant or sponsor.

The Center for Drug Evaluation and Research (CDER) has defined five distinct categories of master file submissions that it will accept and maintain, and has designated these as Type I through Type V drug master files (DMP's), 21 CFR 314.420 (a)(5). The Center for Veterinary Medicine provided for the same five distinct categories of VMF's by referral to a guideline in Section 514.420 (c) of the New Animal Drugs; Proposed Rule

("NADA Rewrite") published in the FEDERAL REGISTER on December 17, 1991. However, the NADA Rewrite has not been published as a Final Rule and the referenced guideline was not issued by the Center for Veterinary Medicine. Consequently, master files on file with the Center for Veterinary Medicine have not officially been designated as Type I through Type V Veterinary Master Files. Rather, these submissions have been accepted and maintained under the general category of Master Files.

The recently published proposed rule (60 FR 34486, July 3, 1995) amends the human drug regulations (21 CFR 314.420) and eliminates Type I drug master files for CDER. Prior to eliminating Type I master files the FDA evaluated the usefulness of these submission. The agency determined that its inspectors were not using Type I DMF's to plan inspections and that they could be eliminated without adversely affecting inspections of manufacturing facilities. FDA also determined that its review divisions do not rely on Type I DMF's. Although Type I DMF's are often incorporated by reference, the information that the agency requested to be submitted under Type I DMF's is not required for chemistry, manufacturing, and controls (CMC) review. Additionally, the basic information (e.g. name and location of facilities used in the manufacture of the drug substance or product) is on file as part of the application. Therefore, Type I DMF's could be eliminated without adversely affecting the CMC review.

The Center for Veterinary Medicine concurs with these decisions. This information is already evaluated on site by FDA field activities, and a master file containing Type I information is of very limited value to either our review staff or the FDA field investigator.

Accordingly, this guidance document recognizes five distinct types of Veterinary Master Files (Type I - V), as well as public master files and eliminates Type I VMF's. The Center will no longer accept new Type I VMF's, or correspondence updating existing Type I VMF's. The information in Type I VMF's currently on file could no longer be incorporated by reference into new applications, amendments, or supplements, and the VMF’s would be transferred to the Federal Records Center, Suitland, MD. Further. comment regarding the mechanism by which this may be accomplished are provided below (see IV., A.,1., - Remarks).

The veterinary industry was informed of CVM's intent to eliminate Type I Veterinary Master Files in a Policy Letter dated July 26, 1995. This informal guidance document is intended to provide further clarification of this Policy Letter.

II. DEFINITIONS

For the purposes of this guidance document, the following definitions apply:

1. *Agency* - means the Food and Drug Administration.

2. *Agent or representative* - means any person who is appointed by a VMF holder to serve as the contact for the holder.

3. *Applicant* - means any person who submits an application or abbreviated application or an amendment or supplement to obtain FDA approval.

4. *Drug product* - means a finished dosage form, medicated article or medicated feed that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

5. *Drug substance* - means a material which is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the human body of man or other animals. The substance may be administered independently or as a component of a finished dosage form, medicated article or medicated feed.

6. *Export application* - means an application submitted under section 802 of the Federal Food, Drug, and Cosmetic Act to export a drug that is not approved for marketing in the United States.

7. *Holder* - means a person who owns a VMF.

8. *Intermediate* - means a pivotal, key or final intermediate whose process must be adequately controlled to assure the quality and purity of the drug substance.

a. Pivotal intermediate - means an intermediate which may be prepared by more than one manufacturing process to provide material of suitable quality for use in the production of a drug substance.

b. Key intermediate - means an intermediate in which an essential molecular characteristic(s) is first introduced into the structure and for which significant in-process controls are needed to ensure the purity of the drug substance.

c. Final intermediate - means the last intermediate isolated and controlled during the manufacturing process; prior to the final step which provides the crude drug substance.

9. *Letter of authorization* - means a written statement by the holder or designated agent or representative permitting FDA to refer to information in the VMF in support of another person's submission.

10. *Medicated Article* - means a Type A Medicated Article (21 CFR 558.3(b)(2) intended solely for use in the manufacture of another Type A medicated article or a Type B or Type C medicated feed. It consists of a new animal drug(s), with or without carrier (e.g., calcium carbonate, rice hulls, corn, gluten) with or without inactive ingredients.

11. *Medicated Feeds* - means Type B Medicated Feed or Type C Medicated Feed. A Type B Medicated Feed (21 CFR 558.3 (b)(3) is intended solely for the manufacture of other medicated feeds (Type B or Type C). A Type C Medicated Feed (21 CFR 558.3 (b)(4) is intended as the complete feed for the animal or may be fed "top dressed" or offered "free choice".

12. *Person* - includes individual, partnership, corporation, and association. (Section 201(e) of the Federal Food, Drug, and Cosmetic Act.)

13. *Sponsor* - means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution**,** private organization, or other organization.

III. TYPES OF MASTER FILES

There are six types of master files recognized by the Center for Veterinary Medicine. These master files cover the following information and data categories:

A. Veterinary Master Files (VMF's)

Type I Manufacturing Site, Facilities, Personnel and Operating Procedures.

Type II Manufacturing Information for finished dosage forms, medicated articles or medicated feeds, or manufacturing information for bulk drug substances or intermediates used in the further manufacture of bulk drug substance.

Type III Packaging Materials.

Type IV Excipient, Colorant, Flavor, Essence or material used in their preparation.

Type V FDA Accepted Reference Information.

Each VMF should contain only one type of information and all supporting data. Supporting information and data in a VMF may be cross-referenced to another VMF or DMF.

B. Public Master Files (PMF's)

These master files usually contain safety and efficacy data and information that has been generated with public funds.

IV. MASTER FILE CONTENTS

A. Types of Veterinary Master Files

1. Type I: Manufacturing Site, Facilities, Operating Procedures, and Personnel

[As discussed in the Introduction to this guidance document, the Center is eliminating the need to submit and maintain a Type I Veterinary Master File. The Center currently has a number of these submissions on file and is only providing a description of this type of master file to aid holders of these master files in their determination that these are recognized by the Center as Type 1 master files and will no longer be accepted or maintained.]

Manufacturing Site and Facilities - This information consists of a diagram of the general layout of the site and buildings and includes the various sections of all operations. A diagram of the major production and processing areas is usually outlined and a list of the makes and models of major pieces of equipment are described in terms of application and location. Equipment that is specific for the operations performed at the facility is also normally provided. This list includes manufacturing and laboratory equipment.

Operating Procedures - Information, such as, general validation information, as well as, other general operating procedures are normally contained in this type of file. Sufficient information is normally provided in the master file to cover the significant operating areas.

Personnel - This information includes the major corporate organizational elements, such as, key manufacturing, quality control and quality assurance positions. A detailed flowchart illustrating the specific line of command is normally provided. Key personnel are identified with their role and qualifications in the specific operations designated in the file.

Remarks:

While some of CVM's master files contain only Type I information and may be easily eliminated, we do have many that contain additional information. This additional information includes: sterilization processes validation information, environmental assessment information, actual manufacturing information for finished dosage forms, medicated articles and medicated feeds, manufacturing information for bulk drug substances and intermediates, etc.. These types of information are important for our chemistry/manufacturing/control (CMC) evaluation and must remain available for our review and comment (see below).

If a VMF holder believes that their master file, which contains some Type I information should be categorized as a specific type of VMF other than a Type I VMF, the VMF holder should submit a request to the Center for Veterinary Medicine, Office of New Animal Drug Evaluation, Division of Chemistry, HFV-140, 7500 Standish Place, Rockville MD. 20855. This request should be submitted by the responsible official or designated U.S. agent, should briefly identify the subject of the VMF, and should propose the VMF Type (e.g., Type II, III, IV, or V) to which the VMF, or components of, should be recategorized.

CVM would consider transferring an entire VMF containing Type I information to another type only if the VMF contains substantive information other than information concerning manufacturing site, facilities, operating procedures, and personnel.

CVM recognizes that some master files currently on file contain information concerning sterilization process validation and other information relevant to the review, evaluation, and assurance of sterility of sterile products. For sterile items that are not the subject of an INADA, NADA, ANADA, and that are sold to a second party (e.g., rubber closures that are sterilized by the manufacturer and sold to a second party), CVM would consider transferring product-specific and general

information concerning sterilization process validation to the type VMF (e.g., II through IV) under which manufacturing information for the specific item is filed. Contract manufacturers of sterile finished drug products, contract sterilization firms (e.g., ethylene oxide, gamma radiation), and manufacturers of sterile finished drug products that are the subject of a drug product application could request a transfer to a Type V VMF of nonproduct-specific information and procedures that are submitted to support a claim of sterility. Where applicable, the content and format of such transferred information should follow FDA's guidance entitled, "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products". The mechanism for requesting a transfer would be the same as the mechanism for recategorizing VMF's, as described above.

Likewise, manufacturing information for medicated articles, medicated feeds, finished dosage forms, bulk drug substance, and intermediates should be retained in Type II VMF's. In many cases, the master files on file with CVM contain the appropriate information. These master files simply need to be appropriately designated as Type II VMF's containing specific manufacturing information for finished dosage forms medicated articles or medicated feeds, or manufacturing information for bulk drug substances or intermediates used in the further manufacture of bulk drug substance.

2. Type II: Manufacturing Information for finished dosage forms, medicated articles or medicated feeds, or manufacturing information for bulk drug substances or intermediates used in the further manufacture of bulk drug substance.

A Type II VMF should, in general, be limited to a single drug intermediate, drug substance, finished dosage form, medicated article, medicated feed or type of material used in their preparation.

a. Drug Substance Intermediates, Drug Substances, and Material Used in Their Preparation

o Summarize all significant steps in the manufacture and control of the drug intermediates or substance. Detailed guidance on what should be included in a Type II VMF for drug substances and intermediates may be found in the following guidelines:

> Guideline for Submitting Support Documentation in Drug Applications for the Manufacture of Drug Substances, Center for Drugs and Biologics, February, 1987
>
> Center for Veterinary Medicine Stability Guidelines

In part, this information includes:

o Description, including physical and chemical characteristics and stability.

> Names - Provide the chemical names and the generic and proprietary names, synonyms, chemical abstracts service registry number, and code number.
>
> Structural formula - Provide the chemical structure (including stereochemistry), molecular formula, and molecular weight.
>
> Physical and chemical characteristics - Describe physicochemical characteristics including, where applicable, such information as physical description, solid-state form, solubility profile, melting point, pH, specific rotation, and refractive index.
>
> Elucidation of structure - Supply physical and chemical data collected to elucidate and confirm the chemical structure of the drug substance.

Stability - Describe fully the studies on the stability of the new animal drug substance and include the results. Reference to stability information from prior studies or the literature may be used, as appropriate, to meet some or all of these requirements. Also, stability-indicating analytical methods information should also be included.

o Manufacturer(s) - Provide the name and address of each facility, excluding the applicant, that participates in manufacturing the drug substance (e.g., performs the synthesis, isolation, purification, micronization, testing, packaging, or labeling). Describe the operation(s) that each will perform.

o Method(s) of Manufacture and Packaging - Provide a full description of the materials and method(s) used in the synthesis, isolation, and purification of the drug substance. This description should include a list of starting materials, reagents, solvents, and auxiliary materials with specifications or a statement of the quality of each. The description should include a diagrammatic flow chart of the synthesis and a detailed description of each step. Any alternate methods or variations in the synthesis should be included with an explanation of the circumstances under which they would be used.

Process controls - Provide a full description of the control checks performed at various stages of the manufacture, processing, and packaging of the drug substance. The description should include the specifications and tests for pivotal and key/critical intermediates. The description should include the impurity profile for the drug substance.

Container-closure system - Provide appropriate information about the characteristics of, and the test methods used for the container, closure, or other component parts to assure their suitability for shipment and storage of the drug substance.

If the drug substance is prepared by fermentation or by extraction from natural sources (plant or animal), provide a full description of the process.

o Specifications and Analytical Methods for Drug Substance - Provide a full description of the acceptance specifications and test methods used to assure the identity, strength, quality, and purity of the drug substance. The methods and standards of acceptance should be sufficiently detailed to permit duplication and validation by FDA laboratories. Adequate documentation should be submitted to support the precision, accuracy, specificity, and sensitivity of the methodology and the integrity of the reference standard.

Where test methods and specifications are included in an official compendium or other public standard, the standard used should be cited.

b. Drug Product

Manufacturing procedures and controls for finished dosage forms, medicated articles or medicated feeds should ordinarily be submitted in an INADA, NADA, ANADA, or export application. If this information cannot be submitted in an INADA, NADA, ANADA or export application, it should be submitted in a Type II VMF. When a Type II VMF is submitted for a drug product, the applicant/holder should follow the following guidance:

Animal Drug Manufacturing Guidelines, 1994 **(Revised)**

Center for Veterinary Medicine Drug Stability Guidelines

Code of Federal Regulations (21 CFR 514.1(4)&(5))

c. Environmental Assessment

An environmental assessment (EA) according to 21 CFR 25.31a which addresses the manufacture at each drug substance and drug product manufacturing site should be submitted, when applicable.

3. TYPE III: Packaging Material

Each packaging material should be identified by the intended use, components, composition, and controls for its release. The names of the suppliers or fabricators of the components used in preparing the packaging material and the acceptance specifications should also be given. Data supporting the acceptability of the packaging material for its intended use should also be submitted.

4. TYPE IV: Excipient, Colorant, Flavor, Essence or material used in their reparation

Each additive should be identified and characterized by its method of manufacture, release specifications, and testing methods.

Toxicological data, where necessary, should be included under this type of VMF, if not otherwise available by cross-reference to another document.

Usually, the official compendia for **excipients and FDA regulations** f or color additives (21 CFR Parts 70 through 82), direct food additives (21 CFR Parts 170 through 173), indirect food additives (21 CFR Parts 174 through 178), and food substances (21 CFR Parts 181 through 186) may be used as sources for release tests, specifications, and safety. The guidance documents suggested for the preparation of a Type II VMF may be helpful for preparing a Type IV VMF. The VMF should include any other supporting information and data that are not available by cross reference to another document.

5. TYPE V: FDA Accepted Reference Information

This type of master file should include reference information that is not covered by Type II through Type IV VMF's. Some examples of these types of information may include:

a. Sterilization Processes Validation Information - Contract manufacturers of sterile finished drug products, contract sterilization firms (e.g., ethylene oxide, gamma radiation), and manufacurers of sterile finished drug products that are the subject of a drug product application could provide their nonproduct-specific information and

procedures that are submitted to support a claim of sterility in this type of master file. Where applicable, the content and format of such information should follow FDA's guidance entitled, "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products".

b. Environmental Studies - Environmental information that is not appropriate for submission in a Type II through Type IV VMF may be provided in this type of master file.

c. Animal Effectiveness, Safety, Residue and Metabolism, or Toxicity Studies - Generally this information is contained in an INADA or NADA for a specific product under investigation. In instances where the information and data may be applicable to numerous submissions it may be advantageous to maintain the information in this type of master file.

d. List Master File - The reference list of feed mills for the manufacture of medicated feeds may be provided in this type of master file.

e. Other Reference Information - The Center discourages the use of Type V VMF's for miscellaneous information, duplicate information, or information that should be included in one of the other types of VMF's. If any holder wishes to submit information and supporting data in a Type V VMF that is not covered by a Types II through IV VMF, a holder should first submit a letter of intent to the Center for Veterinary Medicine, Division of Chemistry, HFV-140, 7500 Standish Place, Rockville, Maryland 20855. The Center will then contact the holder to discuss the proposed submission.

B. Public Master Files (PMF'S):

These files usually contain safety and efficacy information and data that has been generated with public funds. This information is available to the public without the concern for trade secret and confidentiality associated with other types of master files. Public master files do not usually contain manufacturing information. The existence of a public master file is made known through a notice of availability in the Federal Register.

V. SUBMISSIONS TO VETERINARY MASTER FILES

A. Format, Assembly of Master File Documents

The information in a master file may be used to support multiple applications (INADA's, NADA's, ANADA's, another VMF or DMF, an export application, or amendments or supplements to any of these).

Each veterinary master file submission should contain a transmittal letter, administrative information about the submission, and the specific information to be included in the VMF.

The master file should be written in the English language. Whenever a submission contains information in another language, an accurate certified English translation should also be included.

Each page of each copy of the VMF should be consecutively numbered. An updated table of contents should be included with each submission.

An original and duplicate are to be submitted for all VMF submissions.

Veterinary Master File holders and their agents/representatives should retain a complete reference copy that is identical to, and maintained in the same chronological order as, their submission to FDA.

The original and duplicate copies must be collated, fully assembled, and individually jacketed. Each volume of a VMF should, in general, be no more than 2 inches thick. For multivolume submissions, each volume should be numbered. For example, for a 3-volume submission, the volumes would be numbered 1 of 3, 2 of 3, 3 of 3. Additionally, U.S. standard paper size (8 1/2 by 11 inches) is preferred. Paper length should not be less than 10 inches nor more than 12 inches. However, it may occasionally be necessary to use individual pages larger than standard paper size to present a floor plan (for a facility manufacturing sterile drug products), synthesis diagram, etc. Those pages should be folded and mounted to

allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. The Center's system for filing VMF's provides for assembly on the left side of the page. The left margin should be at least three-fourths of an inch to assure that text is not obscured in the fastened area. The right margin should be at least one-half of an inch. The submitter should punch holes 8 1/2 inches apart in each page.

Veterinary Master File submissions and correspondence should be addressed to:

Document Control Unit
HFV-199
Food and Drug Administration
Center for Veterinary Medicine
Metro Park North 2 - Room N 403
7500 Standish Place
Rockville, MD 20855

Delivery charges to the above address must be prepaid.

The submission of an original master file will be acknowledged by letter with the designation of a document number, VMF-XXXX.

B. Transmittal Letter

1. Original Submission

The transmittal letter should contain the following:

Identification of submission: Original, the type of VMF (II-V), and its subject.

Identification of the applications, if known, that the VMF is intended to support, including the name and address of each sponsor, and relevant document numbers.

Signature of the holder or the authorized representative.

Typewritten name and title of the signer.

2. Amendments

The transmittal letter should contain the following:

Identification of submission: Amendment, the VMF number, Type of VMF, and the subject of the amendment.

A description of the purpose of the submission (e.g., update, revised formula, revised process, etc.).

Signature of the holder or the authorized representative.

Typewritten name and title of the signer.

C. Administrative Information

Administrative information should include the following:

1. Original Submissions: Administrative information for original submissions (Type II-V) should include the following names and addresses:

- o VMF holder
- o Corporate headquarters
- o Manufacturing/processing facility
- o Contact for FDA correspondence
- o Agents, if any
- o Statement of commitment - A signed statement by the holder certifying that the VMF is current and that the VMF holder will comply with the statements made in it.

2. Amendments: Administrative information for amendments (Type II-V) should include the following:

- o VMF holder
- o VMF number
- o Contact for FDA correspondence

- o Affected section and/or page numbers of the VMF
- o The name and address of each person whose INADA, NADA, ANADA, VMF or DMF, or Export application relies on the subject amendment.

VI. MASTER FILE REVIEW/HOLDER OBLIGATIONS

The contents of a master file (VMF or DMF) will be reviewed by the Center only when the master file holder provides appropriate authorization permitting the FDA to refer to it on behalf of the sponsor. Authorization must be in the form of a letter, a copy of which should be available in the application (INADA, NADA, ANADA, Export Application, or amendments and supplements to any of these).

Before making significant changes in processes covered in the master file (VMF or DMF), the master file holder must notify each sponsor. The sponsor is required by regulation to supplement or amend the affected application(s).

A Veterinary Master File will only be reviewed in conjunction with an application (INADA, NADA, ANADA, Export Application, or amendments and supplements to these applications). Previously, the Center routinely reviewed submissions (original and amendments to VMF's) that were not necessarily linked to a specific application, but for which authorization for FDA review were provided. In some instances, these master files were never referenced in support of a pending application. The Center has concluded that the routine review and evaluation of Veterinary Master Files not specifically referenced in applications may be a waste of resources. Therefore, the routine evaluation of updates and amendments to Veterinary Master Files will be discontinued. This change in the Center's review process only serves to emphasize that the affected applicants must be notified of significant changes in a Veterinary Master File that require the submission of an amendment or supplemental application. At that time, the Center (with appropriate authorization) will refer to the Veterinary Master File and evaluate the change in process, etc., and the impact of these changes on the affected application.

Acceptance of a master file is granted only upon the satisfactory review of the file contents. During the course of the review of a master file, should the information be considered deficient, the holder will be notified by the Center.Communications relevant to the contents of the master file are made by the Center directly with the responsible holder of the master file. At the same time, the Center will notify the person who relies on the information in a deficient DMF or VMF that additional information is needed in the supporting master file, and that separate communication detailing the deficiencies has been sent to the master file holder. While the general subject of the deficiencies may be identified, the details of the master file deficiencies are disclosed only to the master file holder. When the holder submits the requested information to the master file in response to the Center's deficiency letter, the holder should also send a copy of the accompanying transmittal letter to the affected persons relying on the master file. The transmittal letter will provide notice that the deficiencies have been addressed.

The master file should be routinely updated on an annual basis to assure that operations are current and information correct. A current list of authorized users of the file should be maintained.

VII. CONFIDENTIALITY OF INFORMATION

All information contained in a master file (DMF or VMF) is considered confidential. Further, it is Center policy not to make known the existence of specific master files. Rather, it is the responsibility of a sponsor to make sure that a master file (DMF or VMF) is available and request authorization for FDA referral.

VIII. AUTHORIZATION TO REFER TO A MASTER FILE

Letter of Authorization

Before FDA can review VMF or DMF information in support of an application, the holder must submit in duplicate to the master file a letter of authorization permitting FDA to reference the master file.

The letter of authorization should include the following:

- o Date of letter
- o Name of Veterinary Master File holder
- o VMF or DMF number
- o Name of persons authorized to incorporate information in the MF by reference.
- o Specific products covered by the master file
- o Sections, volumes and page numbers to be referenced
- o Statement of commitment that the master file is current and that the holder will abide with the statements made in it.
- o Signature of the authorizing official/agent
- o Typed name and title of the official authorizing reference to the file.

The holder should also send a copy of the letter of authorization to the affected applicant, sponsor or other holder who is authorized to incorporate by reference the specific information contained in the master file.

IX. OWNERSHIP TRANSFER/NAME CHANGE

To transfer ownership of a VMF to another party, the holder should notify the Center for Veterinary Medicine and authorized persons in writing.

The letter should include the following information:

- o Name of Holder/Transferee
- o Address of Holder/Transferee
- o Name of responsible official of the transferee
- o Effective date of transfer
- o Signature of the responsible transferring official
- o Typewritten name and title of the transferring official

The new holder should submit a letter of acceptance indicating the acceptance of the document and all existing responsibilities. The holder should provide an update of the information in the file, where appropriate, as soon as possible to indicate if any changes (e.g., plant location and methods) have or will take place.

X. REORGANIZATION OF THE VETERINARY MASTER FILE

A holder who plans a major reorganization of a VMF is encouraged to submit a detailed plan of the proposed changes and request its review and evaluation by the Division of Chemistry. All authorized users should also be notified when any changes are made in any operation that may affect the applicants products.

XI. CLOSURE OF A VETERINARY MASTER FILE

A holder who wishes to close a master file should submit a request to the Center citing the reason for the closure. The letter should include a statement that the holder's obligations have been fulfilled and all users have been notified.

The Center may close a VMF that does not contain an annual update and a list of changes made since the previous annual update. The holder will be notified of FDA's intent to close the VMF.