

UNDERSTANDING THE ROLE OF FLAVOR SUPPLIERS IN THE DRUG MASTER FILE SUBMISSION PROCESS

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A fundamental part of successful collaborations between pharmaceutical companies and flavor suppliers is the sharing of vital information. While this transfer of knowledge and expertise is necessary to driving innovation, there must be a clear understanding of upholding the integrity of intellectual property for both parties. When a pharmaceutical company submits a product to the Food and Drug Administration (FDA) for review, they may request confidential information like formulas from their flavor suppliers. To protect the supplier's intellectual property, the FDA created the Drug Master File (DMF) submission process that allows the flavor supplier to provide this sensitive information to the agency, while also ensuring intellectual property remains secure. But what exactly does the DMF process entail? And how would you work with your flavor supplier during this process?

The DMF Submission Process

Pharmaceutical companies submit their products to the FDA for review. These applications include Investigational New Drug Applications (IND), New Drug Applications (NDA), Abbreviated New Drug Applications (ANDA), or Export Applications. When flavors are used in these products, flavor suppliers voluntarily submit a DMF directly to the FDA, becoming DMF sponsors, or holders. These DMF submissions are cross-referenced with the corresponding pharmaceutical company's application. As the sponsor, flavor suppliers are responsible for tracking the progress of their DMF submissions through the review process.

There are 5 DMF types, but flavor suppliers focus on Type IV

- Type 1: Manufacturing sites, facilities, operating procedures
- Type II: Drug substance, drug substance intermediate, and material used in their preparation, or drug product
- Type III: Packaging material
- Type IV: Excipient, colorant, flavor, essence, or material used in their preparation
- Type V: FDA accepted reference information

Supplier Obligations as DMF Sponsor During FDA Review Process

FDA does not approve flavors for use in pharmaceutical products; instead, they approve the final product that uses a flavor. The initial FDA review determines whether the DMF meets minimum requirements for format and content. Once those standards are met, FDA assigns a DMF number and passes along for full review. Flavor suppliers should provide this DMF number to the pharmaceutical company as part of a Letter of Authorization submitted in the original application. FDA will only review information in the DMF when a pharmaceutical company submits an IND, NDA, ANDA, or Export Application and wishes to incorporate information from the flavor supplier DMF. Flavor supplier DMF sponsors will also provide an annual report for each DMF. This report includes updates such as a list of persons authorized to make edits to the DMF or any person whose authorization has been withdrawn in the last year.

Inactive Ingredient Guide

The Inactive Ingredient Guide (IIG) is the FDA database of inactive ingredients, such as flavors, and provides easily accessible information about those ingredients. This information includes route of administration (how the drug is administered to a patient, ex. oral) and dosage form (form in which a drug is made and dispensed, ex. capsule). Sometimes, when an inactive ingredient appears in the database, a less extensive review may apply when used in products reviewed by the FDA in the future; however, the IIG is not a list of approved flavors and does not replace the DMF submission. The review process always defers to the FDA reviewer's discretion. Importantly, flavors listed in the IIG may be exclusive to a certain pharmaceutical company and therefore not available for purchase.

Health Canada and Australian Therapeutic Goods Administration

Pharmaceutical companies making products for sale outside the USA should be aware that there are parallel processes to the DMF-submission in other countries. Let's talk about two common areas: Canada and Australia. For example, Health Canada focuses on two areas of registration. The first is Food and Drugs Regulations which encompasses all prescription drugs. The second area is the Natural Health Products Regulations that focuses on vitamins, minerals, herbal remedies, homeopathic and traditional medicines, and other supplements. Similarly, to the DMF process, flavor suppliers directly submit confidential information to Health Canada. Costs are incurred by the flavor supplier as DMF sponsor.

In Australia, the Therapeutic Goods Administration (TGA) regulates medical drugs including prescription medicines, vaccines, sunscreens, supplements, and blood products. Under the TGA system, the pharmaceutical company completes an initial set of questions. The flavor supplier then completes the remaining information, ensuring their intellectual property remains secure.

Updates to the DMF Submission Process

On May 5, 2018, the FDA required that new DMFs and any updated documents to existing DMFs must be submitted using the Electronic Common Technical Document (eCTD) system. With this new filing process, additional costs are incurred by flavor suppliers sponsoring DMFs.

Conclusion

Partnerships between a pharmaceutical company and their flavor supplier are vital to moving development and production forward. Collaborative flavor suppliers will work with your team to determine the best ways to support your FDA product applications. They will navigate the complexities of the FDA review and DMF process, so you can focus on delivering optimal products to your consumers.

We know this can be a lot to digest. Don't worry, we got your back. Our Regulatory experts can help with any questions you may have about the DMF process. Reach out to reg@fona.com today for more information.

References

- U.S. Food & Drug Administration Drug Master Files: <https://www.fda.gov/drugs/developmentapprovalprocess/formsubmissionrequirements/drugmasterfilesdmfs/default.htm>
- Contract Pharma Drug Master File: https://www.contractpharma.com/contents/view_glossary/2012-02-27/drug-master-file-dmf-