Factor #3: Check to see if your product meets the conditions set forth under a final monograph.

If you have found a final monograph that may cover your product, the next step is to see if your product conforms to the conditions set forth under that final monograph. These conditions include, but are not limited to, active ingredients and labeling.

Each monograph explains the conditions necessary for an OTC drug product covered by that monograph to be generally recognized as safe and effective, or GRASE, and not subject to the New Drug Application (NDA) provisions.

Monographs include a listing of suitable active ingredients, including combinations of active ingredients, which can be included in the OTC drug product intended for the use(s) covered by a particular monograph.

All your product’s active ingredients should be addressed by that monograph. Depending on the intended use(s) of the product, in some cases if the monographs explicitly allow the combination with other monographs, your product can be the subject of multiple monographs simultaneously and would need to meet the conditions set forth in each.

Labeling requirements are specified in final OTC drug monographs. A description of the intended uses for your OTC drug product must be consistent with the uses specified by the relevant final monograph(s). As part of the required labeling, final monographs specify the language that must be used for warnings and directions for use, including the frequency of administration and duration of treatment. Certain monographs even go so far as to specify testing requirements for active ingredients and finished products, in addition to the testing specified in the good manufacturing practice (GMP) regulations.

The OTC monograph also may detail the permitted dosage strength or concentration, and dosage forms. In many cases, final monographs may be silent on certain dosage forms, or merely allow dosage forms that are “suitable.” It is important to note, however, that an OTC drug product in a dosage form that was never marketed in the United States on or before the inception of FDA’s OTC Drug Review, nor considered under that review by either an advisory review panel or by FDA, may be a new drug and require NDA approval, especially because its suitability has never been reviewed by FDA.

If there is a final monograph that addresses your active ingredient(s), including combinations, and your intended use(s), then you should make sure your product is formulated and labeled to conform with all conditions set forth in that final monograph. This includes not only permitted active ingredients and indications, but concentrations, dosing directions, warnings, appropriate dosage form and route of administration, and any other conditions set forth under the final monograph. If your product deviates from any of these conditions, then it is likely your product requires an application or it will be considered misbranded, and may be illegal to market.
Let’s take a look at a sample OTC monograph-compliant drug label. Below on the left is an excerpt from the first page of the antacid final monograph as it appears in the CFR. On the right, you see the Drug Facts label for a product that complies with the final monograph.

§331.10 Active ingredients... Calcium, as carbonate or phosphate; maximum daily dosage limit 160mEq. Calcium (e.g., 8 grams calcium carbonate)

§331.30(b) Indications... “For the relief of” (optional, any or all of the following:) “heartburn,” sour stomach,” and/or “acid indigestion”

§331.30(c) Warnings... “Do not take more than (maximum recommended daily dosage) in a 24-hour period, or use the maximum dosage of this product for more than 2 weeks.”

The antacid final monograph, again like all monographs, starts by identifying the allowed active ingredients. One of the allowed active ingredients for antacids is calcium carbonate. You can see the product's Drug Facts label is in compliance. The required indication statement in the antacid final monograph states, “for the relief of (optional, any or all of the following) heartburn, sour stomach, and/or acid indigestion.” You can see that this indication statement does, in fact, appear on the label.

To comply with the warnings requirement, one of the warnings must be “do not take more than (maximum recommended daily dosage) in a 24-hour period, and “do not use the maximum dosage of this product for more than two weeks” - that does appear on the label.

So, complying with each of the requirements in the final monograph, as well as all other applicable requirements, this product may be legally marketed without prior approval from FDA. As shown by this example, OTC drug products must follow the Drug Facts labeling requirements, which are separate regulations and not duplicated in any of the monographs. It is important to review all pertinent labeling requirements in Part 210 of Title 21 of the CFR, including requirements for such things as the principal display panel, the name and place of business for the manufacturer, packer, or labeler, and salicylate-containing drug products.
References

- 21 CFR 201.128
- 21 CFR 211
- 21 CFR 210

Drug Facts Labeling links:

http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143551.htm

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm150436.htm