Add the following:

▲Fenofibrate Capsules

» Fenofibrate Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$).

Packaging and storage—Preserve in well-closed containers, and store at controlled room temperature.

Labeling—When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

USP Reference standards ⟨11⟩—*USP Fenofibrate RS. USP Fenofibrate Related Compound B RS.*

Change to read:

Identification—•(RB 1-Jul-2009) The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩**—**

TEST 1—

Medium: 0.05 M sodium lauryl sulfate in water; 1000 mL, deaerated.

Apparatus 2: 75 rpm.

Time: 40 minutes.

Buffer solution pH 2.9 and *Mobile phase*—Prepare as directed in the *Assay.*

Standard solution—Dissolve an accurately weighed quantity of USP Fenofibrate RS in *Mobile phase* to obtain a solution having a known concentration of about (0.001 × *L*) mg per mL, where *L* is the Capsule label claim, in mg.

Test solution—Pass a portion of the solution under test through a 0.45-µm polyvinylidene difluoride (PVDF) filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay.* Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 4000 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL for Capsules labeled to contain 67 mg and about 5 µL for Capsules labeled to contain 134 mg or 200 mg) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the amount of $C_{20}H_{21}ClO_4$ dissolved by the formula:

$$\frac{r_U \times C_S \times 1000 \times 100}{r_S \times L}$$

in which r_U and r_S are the peak responses for the *Test solution* and the *Standard solution,* respectively; C_S is the concentration, in mg per mL, of the *Standard solution;* 1000 is the volume, in mL, of *Medium;* 100 is the conversion factor to percentage; and *L* is the Capsule label claim, in mg.

Tolerances—Not less than 70% (*Q*) of the labeled amount of $C_{20}H_{21}ClO_4$ is dissolved in 40 minutes.

TEST 2—If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2.*

Medium: phosphate buffer pH 6.8 ± 0.1 containing 0.1% pancreatin and 2% polysorbate 80; 900 mL, deaerated with vacuum.

Apparatus 2: 75 rpm, with sinker (see *Dissolution* ⟨711⟩*, Figure 2a*).

Time: 120 minutes.

Standard solution—Prepare solutions of USP Fenofibrate RS in *Medium* to obtain a final concentration of *L*/1000 mg per mL, where *L* is the Capsule label claim. A volume of methanol, not exceeding 10%, can be used in the first dilution to solubilize fenofibrate.

Test solution—Pass 20 mL of the solution under test through a 0.45-µm PVDF filter, discarding the first 2 mL.

Procedure—Determine the amount of fenofibrate ($C_{20}H_{21}ClO_4$) dissolved by employing UV absorption at the wavelength of maximum absorbance at about 288 nm on the *Test solution* in comparison with the appropriate *Standard solution,* using *Medium* as the blank and a 0.1-cm flow cell. Calculate the amount of fenofibrate ($C_{20}H_{21}ClO_4$), in percentage, dissolved by the formula:

$$\frac{A_U \times C_S \times 900 \times 100}{A_S \times L}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and the appropriate *Standard solution,* respectively; C_S is the concentration of fenofibrate in the appropriate *Standard solution;* 900 is the volume, in mL, of *Medium;* 100 is the conversion factor to percentage; and *L* is the Capsule label claim, in mg.

Tolerances—Not less than 80% (*Q*) of the labeled amount of $C_{20}H_{21}ClO_4$ is dissolved in 120 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

PROCEDURE FOR CONTENT UNIFORMITY—

Buffer solution pH 2.9, Mobile phase, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay.*

Test solution—Place 1 Capsule in a suitable volumetric flask, add *Buffer solution pH 2.9* to 10% to 20% of the final volume, and stir for 20 minutes to disintegrate the Capsule. Fill the flask to about 80% with methanol, sonicate for 10 minutes, stir for 15 minutes, and dilute with methanol to volume to obtain a solution having a known concentration of about 0.4 to 0.7 mg of fenofibrate per mL, based on the label claim. Quantitatively dilute an aliquot with *Mobile phase*, to obtain a solution having a known concentration of about 0.06 to 0.07 mg per mL, and pass it through a 0.45-µm PVDF filter, discarding the first 5 mL.

Procedure—Proceed as directed in the *Assay,* except to inject the *Test solution* instead of the *Assay preparation.*

Change to read:

Related compounds—•[NOTE—Use *Test solution 2* for Capsules labeled to meet the requirements of *Dissolution Test 2.* For all other products, use *Test solution 1.*]•(RB 1-Jul-2009)

Buffer solution pH 2.9 and *Mobile phase*—Prepare as directed in the *Assay.*

System suitability solution—Dissolve an accurately weighed quantity of USP Fenofibrate RS and USP Fenofibrate Related Compound B RS in *Mobile phase* to obtain a solution having concentrations of about 0.67 mg per mL and 3.35 µg per mL, respectively. [NOTE—Fenofibrate related compound B is 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoic acid (fenofibric acid).]

Standard solution—Dissolve an accurately weighed quantity of USP Fenofibrate RS and USP Fenofibrate Related Compound B RS in *Mobile phase* to obtain a solution having known concentrations of about 3.35 µg per mL of each component.

Sensitivity solution—Quantitatively dilute an aliquot of the *Standard solution* with *Mobile phase,* to obtain a solution having concentrations of about 0.67 µg of each component per mL.

•*Test solution 1*• (RB1-Jul-2009)—Accurately weigh the contents of not fewer than 20 Capsules. Mix the contents, and transfer an accurately weighed portion of the powder, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask. Fill the flask to about 80% with *Mobile phase,* sonicate for 10 minutes, stir for 15 minutes, and dilute with *Mobile phase* to volume. Pass a portion of this solution through a 0.45-µm PVDF filter, discarding the first 5 mL. The final concentration is about 0.67 mg per mL.

•*Test solution 2* (For Capsules labeled to meet the requirements of *Dissolution Test 2*)—Accurately weigh the contents of not fewer than 20 Capsules. Mix the contents, melt in an oven at 80° for not less than 30 minutes, and homogenize. Allow the sample to solidify. Transfer an accurately weighed portion of the sample, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask, dissolve in 30 mL of methanol with the aid of a mechanical shaker for not less than 4 hours, and dilute with *Mobile phase* to volume. Pass through a 0.45-µm PVDF filter, discarding the first 1 to 2 mL. The final concentration based on the label claim is about 0.67 mg per mL.• (RB 1-Jul-2009)

Chromatographic system (see *Chromatography* ⟨621⟩)—Prepare as directed in the *Assay.* Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between fenofibrate and fenofibrate related compound B is not less than 3.0; the column efficiency for the fenofibrate related compound B peak is not less than 3000 theoretical plates; and the tailing factor is not more than 2.0. Chromatograph the *Sensitivity solution,* and record the peak responses as directed for *Procedure:* the signal-to-noise ratio is not less than 10 for the fenofibrate peak. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0% for each peak.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the •designated• (RB 1-Jul-2009) *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of fenofibrate related compound B relative to the fenofibrate labeled content in the portion of Capsules taken by the formula:

$$100(C_S / C_T)(r_i / r_S)$$

in which C_S is the concentration, in mg per mL, of fenofibrate related compound B in the *Standard solution;* C_T is the concentration, in mg per mL, of fenofibrate in the *Test solution,* based on the label claim; and r_i and r_S are the responses of fenofibrate related compound B obtained from the *Test solution* and the *Standard solution,* respectively. Calculate the percentage of any other impurity relative to the fenofibrate labeled content in the portion of Capsules taken by the formula:

$$100(C_F / C_T)(r_i / r_F)$$

in which C_F is the concentration, in mg per mL, of fenofibrate in the *Standard solution;* C_T is as defined above; r_i is the peak response of each impurity obtained from the *Test solution;* and r_F is the peak response of the fenofibrate, obtained from the *Standard solution.* Not more than 0.5% of fenofibrate related compound B is found; not more than 0.2% of any other impurity is found; and not more than 2.0% of total impurities is found.

Change to read:

Assay—•[NOTE—Use *Assay preparation 2* for Capsules labeled to meet the requirements of *Dissolution Test 2.* For all other products, use *Assay preparation 1.*]•(RB 1-Jul-2009)

Buffer solution pH 2.9—Dissolve 136 mg of monobasic potassium phosphate in 1000 mL of water, and adjust with dilute phosphoric acid (1 in 10) to a pH of 2.9 ± 0.05.

Mobile phase—Prepare a mixture of methanol and *Buffer solution pH 2.9* (80 : 20). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Fenofibrate RS in *Mobile phase* to obtain a solution having a known concentration of about 0.067 mg per mL.

•*Assay preparation 1*•(RB 1-Jul-2009)—Accurately weigh the contents of not fewer than 20 Capsules. Mix the contents, and transfer an accurately weighed portion of the powder, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask. Fill the flask to about 80% with *Mobile phase,* sonicate for 10 minutes, stir for 15 minutes, and dilute with *Mobile phase* to volume. Quantitatively dilute 5.0 mL of this solution to 50 mL with *Mobile phase,* and pass a portion of this solution through a 0.45-µm PVDF filter, discarding the first 5 mL. The final concentration based on the label claim is about 0.067 mg per mL.

•*Assay preparation 2* (For Capsules labeled to meet the requirements of *Dissolution Test 2*)—Accurately weigh the contents of not fewer than 20 Capsules. Mix the contents, melt in an oven at 80° for not less than 30 minutes, and homogenize. Allow the sample to solidify. Transfer an accurately weighed portion of the sample, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask, dissolve in 30 mL of methanol with the aid of a mechanical shaker for not less than 4 hours, and dilute with *Mobile phase* to volume. Quantitatively dilute a 5.0-mL aliquot of this solution to 50 mL with *Mobile phase*. Pass through a 0.45-µm PVDF filter, discarding the first 1 to 2 mL. The final concentration based on the label claim is about 0.067 mg per mL.• (RB 1-Jul-2009)

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 285-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 6000 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the •designated• (RB 1-Jul-2009) *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) in the portion of Capsules taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of fenofibrate in the *Standard preparation;* C_U is the concentration, in mg per mL, of fenofibrate in the *Assay preparation,* based on the label claim; and r_U and r_S are the peak areas obtained from the *Assay preparation* and the *Standard preparation,* respectively.▲*USP32*