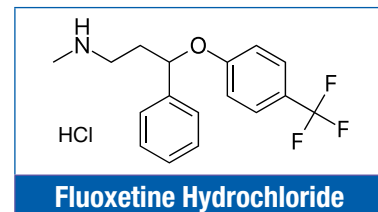


# APPLICATION

## Fluoxetine Hydrochloride and Related Substances

Ph. Eur. monograph 1104



### Overview

The Ph. Eur. Monograph 1104 outlines the separation of Fluoxetine from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.

### Ph. Eur. Monograph 1104 Details

**Reference Solution** Dissolve 22 mg of Fluoxetine Hydrochloride CRS\* in 10.0 mL of a 0.5 M sulfuric acid. Heat at about 85° C for 3 h. Allow to cool. The resulting solution contains considerable quantities of Impurity A and usually also contains 4-trifluoromethylphenol. To 0.4 mL of this solution add 28.0 mg of Fluoxetine hydrochloride CRS\*, about 1 mg of Fluoxetine Impurity B CRS\* and about 1 mg Fluoxetine Impurity C CRS\*, then dilute to 25.0 mL with mobile phase.

### Column

**Size** 150 x 4.6 mm  
**Stationary Phase** Octylsilyl silica gel for chromatography R (5 µm)  
**Mobile Phase** Mix 8 volumes of methanol R, 30 volumes of tetrahydrofuran R, and 62 volumes of a solution of trimethylamine R prepared as follows: to 10 mL of trimethylamine R, add 980 mL of water R, mix and adjust to pH 6.0 with phosphoric acid R (about 4.5 mL) and dilute to 1000 mL with water R.  
**Flow Rate** 1.0 mL/min  
**Detection** Spectrophotometer @ 215 nm  
**Injection** 10 µL  
**Run Time** 3 times the retention time of Fluoxetine

### Relative Retention with Reference to Fluoxetine (about 10-18 min)\*\*

**Impurity A** about 0.24  
**Impurity B** about 0.27  
**Impurity C** about 0.90

### System Suitability

**Peak-to-Valley Ratio** Minimum 11, where Hp = height above the baseline of the peak due to Impurity C and Hv = height above the baseline of the lowest point of the curve separating this peak from the peak due to Fluoxetine.

\* Fluoxetine hydrochloride CRS (F0253000), Fluoxetine Impurity B CRS (F0253020) and Fluoxetine Impurity C CRS (F0253030) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allée Kastner CS 30026F - 67081 STRASBOURG (France).

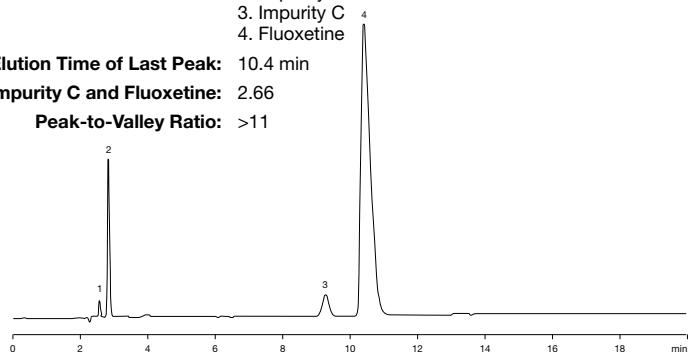
\*\* Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

### Method 1

#### Original Method as Described in the Monograph

**Column:** Luna® C8(2) 5µm Fully Porous  
**Dimensions:** 250 x 4.6 mm  
**Part No.:** 00G-4249-E0  
**Flow Rate:** 1.0 mL/min  
**Sample:** 1. Impurity A  
 2. Impurity B  
 3. Impurity C  
 4. Fluoxetine

**Elution Time of Last Peak:** 10.4 min  
**Rs Impurity C and Fluoxetine:** 2.66  
**Peak-to-Valley Ratio:** >11

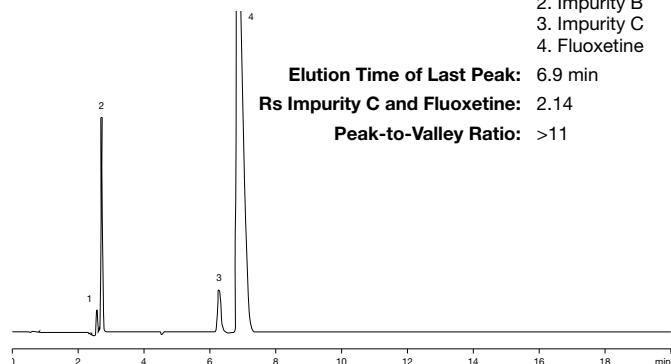


### Method 2

#### Faster Method Within Allowable Adjustments

**Column:** Kinetex® Core-Shell C8 5µm  
**Dimensions:** 250 x 4.6 mm  
**Part No.:** 00G-4608-E0  
**Flow Rate:** 1.0 mL/min  
**Sample:** 1. Impurity A  
 2. Impurity B  
 3. Impurity C  
 4. Fluoxetine

**Elution Time of Last Peak:** 6.9 min  
**Rs Impurity C and Fluoxetine:** 2.14  
**Peak-to-Valley Ratio:** >11



### Adjustments for Meeting System Suitability

(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1	Method 2
Mobile Phase pH	± 0.2 units	6 (as specified)	As specified
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1104 Details Table	As specified
Composition of the Mobile Phase	± 30% of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1104 Details Table	As specified
Wavelength of Detector	No deviations permitted	215 nm (as specified)	As specified
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	10 µL (as specified)	As specified
Column Temperature	± 10 °C	Ambient (as specified)	As specified
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octylsilyl silica gel for chromatography (as specified)	As specified
Column Length	± 70 %	250 mm (as specified)	As specified
Column Internal Diameter	± 25 %	4.6 mm (as specified)	As specified
Particle Size	-50 %	5 µm (as specified)	As specified
Flow Rate	± 50 %	1.0 mL/min (as specified)	As specified

## Kinetex® Ordering Information

5 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges <sup>‡</sup>
Phases	30 x 2.1	50 x 2.1	100 x 2.1	150 x 2.1	3/pk
C8	—	00B-4608-AN	00D-4608-AN	—	AJO-8784 for 2.1 mm ID

5 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges <sup>‡</sup>
Phases	50 x 3.0	100 x 3.0	150 x 3.0	3/pk
C8	00B-4608-Y0	00D-4608-Y0	—	AJO-8777 for 3.0 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges <sup>‡</sup>
Phases	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	3/pk
C8	00B-4608-E0	00D-4608-E0	00F-4608-E0	00G-4608-E0	AJO-8770 for 4.6 mm ID

<sup>‡</sup>SecurityGuard ULTRA Cartridges require holder, Part No.: AJO-9000

## Luna® Ordering Information

5 µm Microbore and Minibore Columns (mm)								SecurityGuard™ Cartridges (mm)	
Phases	50 x 1.0	150 x 1.0	250 x 1.0	30 x 2.0	50 x 2.0	150 x 2.0	250 x 2.0	4 x 2.0*	
C8(2)	—	00F-4249-A0	—	00A-4249-B0	00B-4249-B0	00F-4249-B0	00G-4249-B0	/10pk AJO-4289 for ID: 2.0-3.0 mm	

5 µm MidBore and Analytical Columns (mm)								SecurityGuard™ Cartridges (mm)	
Phases	30 x 3.0	50 x 3.0	150 x 3.0	250 x 3.0	30 x 4.6	50 x 4.6	75 x 4.6	4 x 2.0*	4 x 3.0*
C8(2)	00A-4249-Y0	00B-4249-Y0	00F-4249-Y0	00G-4249-Y0	00A-4249-E0	00B-4249-E0	00C-4249-E0	/10pk AJO-4289 for ID: 2.0-3.0 mm	/10pk AJO-4290 3.2-8.0 mm

5 µm Analytical and Semi-Prep Columns (mm)					SecurityGuard™ Cartridges (mm)	
Phases	100 x 4.6	150 x 4.6	250 x 4.6	250 x 10	4 x 3.0*	10 x 10 <sup>‡</sup>
C8(2)	00D-4249-E0	00F-4249-E0	00G-4249-E0	00G-4249-N0	/10pk AJO-4290 for ID: 3.2-8.0 mm	/3pk AJO-7222 9-16 mm

\*SecurityGuard™ Analytical Cartridges require holder, Part No.: KJO-4282  
<sup>‡</sup>SemiPrep SecurityGuard Cartridges require holder, Part No.: AJO-9281



If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to a competing product of the same particle size, similar phase and dimensions, return the product with comparative data within 45 days for a FULL REFUND.



# APPLICATION

## Australia

t: +61 (0)2-9428-6444  
f: +61 (0)2-9428-6445  
auiinfo@phenomenex.com

## Austria

t: +43 (0)1-319-1301  
f: +43 (0)1-319-1300  
anfrage@phenomenex.com

## Belgium

t: +32 (0)2 503 4015 (French)  
t: +32 (0)2 511 8666 (Dutch)  
f: +31 (0)30-2383749  
beinfo@phenomenex.com

## Canada

t: +1 (800) 543-3681  
f: +1 (310) 328-7768  
info@phenomenex.com

## China

t: +86 400-606-8099  
f: +86 (0)22 2532-1033  
phen@agela.com

## Denmark

t: +45 4824 8048  
f: +45 4810 6265  
nordicinfo@phenomenex.com

## Finland

t: +358 (0)9 4789 0063  
f: +45 4810 6265  
nordicinfo@phenomenex.com

## France

t: +33 (0)1 30 09 21 10  
f: +33 (0)1 30 09 21 11  
franceinfo@phenomenex.com

## Germany

t: +49 (0)6021-58830-0  
f: +49 (0)6021-58830-11  
anfrage@phenomenex.com

## India

t: +91 (0)40-3012 2400  
f: +91 (0)40-3012 2411  
indiainfo@phenomenex.com

## Ireland

t: +353 (0)1 247 5405  
f: +44 1625-501796  
eireinfo@phenomenex.com

## Italy

t: +39 051 6327511  
f: +39 051 6327555  
italiainfo@phenomenex.com

## www.phenomenex.com

Phenomenex products are available worldwide. For the distributor in your country, contact Phenomenex USA, International Department at [international@phenomenex.com](mailto:international@phenomenex.com)

## Luxembourg

t: +31 (0)30-2418700  
f: +31 (0)30-2383749  
nlinfo@phenomenex.com

## Mexico

t: 01-800-844-5226  
f: 001-310-328-7768  
tecnicomx@phenomenex.com

## The Netherlands

t: +31 (0)30-2418700  
f: +31 (0)30-2383749  
nlinfo@phenomenex.com

## New Zealand

t: +64 (0)9-4780951  
f: +64 (0)9-4780952  
nzinfo@phenomenex.com

## Norway

t: +47 810 02 005  
f: +45 4810 6265  
nordicinfo@phenomenex.com

## Puerto Rico

t: +1 (800) 541-HPLC  
f: +1 (310) 328-7768  
info@phenomenex.com

## Spain

t: +34 91-413-8613  
f: +34 91-413-2290  
espinfo@phenomenex.com

## Sweden

t: +46 (0)8 611 6950  
f: +45 4810 6265  
nordicinfo@phenomenex.com

## United Kingdom

t: +44 (0)1625-501367  
f: +44 (0)1625-501796  
ukinfo@phenomenex.com

## USA

t: +1 (310) 212-0555  
f: +1 (310) 328-7768  
info@phenomenex.com

## All other countries Corporate Office USA

t: +1 (310) 212-0555  
f: +1 (310) 328-7768  
info@phenomenex.com

## Terms and Conditions

Subject to Phenomenex Standard Terms and Conditions which may be viewed at [www.phenomenex.com/TermsAndConditions](http://www.phenomenex.com/TermsAndConditions).

## Trademarks

Kinetex and Luna are registered trademarks, MidBore and SecurityGuard are trademarks of Phenomenex.

© 2017 Phenomenex, Inc. All rights reserved.