



Table 1: F-SPE CARTRIDGES LOADING CAPACITY

Size	Size	Size
2 g, 8 mL tube	801-0027S	100-300 mg
5 g, 10 mL tube	801-0058S	400-600 mg
10 g, 60 mL tube	801-0109S	0.5-1.5 g
20 g, 60 mL tube	801-0209A	1.5-2.5 g

**WHAT'S IN FluoroFlash® CARTRIDGES?** Fluorous solid-phase extraction (F-SPE) cartridges are packed with silica gel containing a perfluorooctylethylsilyl ( $\text{Si}(\text{CH}_2)_2\text{C}_8\text{F}_{17}$ ) bonded phase. Fluorous silica separates compounds based primarily on fluorine content. It selectively retains fluorous molecules while non-fluorous organic compounds, regardless of polarity, are not retained.

**WHAT'S THE UTILITY OF FLUOROUS SPE (F-SPE)?** F-SPE is used for quick separation of reaction mixtures involving fluorous reagents,<sup>1,2</sup> protecting groups,<sup>3</sup> tags<sup>4</sup> and scavengers.<sup>5</sup> In a simple two-step elution, fluorous compounds and non-fluorous compounds are separated into two fractions.

**GENERAL PROCEDURES FOR F-SPE:** Following completion of a reaction involving a fluorous-tagged molecule, the reaction mixture is loaded onto an F-SPE cartridge. Using a fluorophobic wash such as 80:20 MeOH:H<sub>2</sub>O, the non-fluorous organic compounds are washed off the cartridge. The fluorous compounds are then washed off the cartridge using a fluorophilic second wash such as MeOH, acetone or THF. The loading capacity for fluorous SPE is typically between 5-10% by weight of fluorous silica gel. The cartridge can be regenerated by washing thoroughly with acetone or THF and reused multiple times (See FAQ #13).

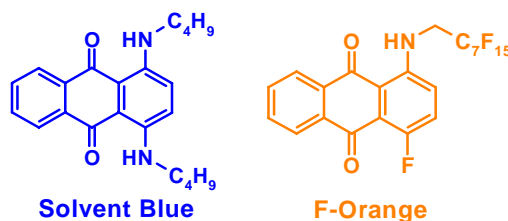
**DEMONSTRATION WITH DYES:** The following dye separation demonstrates how F-SPE works. The non-fluorous compound is Solvent Blue® Dye while the fluorous compound is F-Orange Dye.

Figure 1 shows fluorous cartridges containing the dye mixture in three different stages of elution. The left-hand test-tube illustrates how the F-SPE cartridge appears after loading a mixture of the two dyes and elution with a small amount of 80:20 MeOH:H<sub>2</sub>O. The center tube shows how the non-fluorous components (blue fraction) are washed from the cartridge by using more 80:20 MeOH:H<sub>2</sub>O. The adsorbed fluorous dye is not eluted even with extensive flushing with 80:20 MeOH:H<sub>2</sub>O and remains on the cartridge. Finally, the orange fluorous dye is easily eluted out with 100% MeOH or THF, as shown by the third tube.

Multiple fraction collection and analysis are not required—there is one organic wash and one fluorous wash. Since the separation process is highly reproducible and functional group independent, it can be easily automated or used as plate-to-plate format.



Figure 1. F-SPE with Blue (Organic) and Orange (Fluorous) Dyes



*Left tube:* beginning of fluorophobic wash (80:20 MeOH:H<sub>2</sub>O)

*Center tube:* end of fluorophobic wash

*Right tube:* end of fluorophilic wash (100% MeOH)

**TYPICAL F-SPE PROCEDURE** (For separation of a reaction mixture (100-300 mg) in 0.5 mL of DMF with a 2g SPE cartridge):

- Step 1 - Wash the new cartridge:** Wash a new cartridge with 1 mL of DMF under a vacuum or positive pressure depending on your SPE manifold. This step can be omitted with recycled cartridges.
- Step 2 - Preconditioning:** Pass through 6 mL of 80:20 MeOH:H<sub>2</sub>O to condition the cartridge. Discard the preconditioning eluent.
- Step 3 - Sample loading:** Dissolve sample (100-300 mg) in 0.5 mL of DMF and load onto the cartridge using vacuum or positive pressure to ensure that the sample is completely adsorbed onto the cartridge (see Table 2 for alternative loading solvents).
- Step 4 - Fluorophobic elution:** Wash with 6-8 mL of 80:20 MeOH:H<sub>2</sub>O to obtain the fraction containing the organic compounds.
- Step 5 - Fluorophilic elution:** Wash with 8 mL of MeOH to obtain the fraction containing the fluorous compounds.
- Step 6 - Regenerate the cartridge:** To regenerate the SPE cartridge, wash with 6-10mL of THF or acetone before reuse. Then follow Steps 2-5.

Table 2: Suggested Maximum Loading Solvent Volumes for C<sub>8</sub>F<sub>17</sub> Tagged Substrates

Solvent	Maximum Loading Volume		
	2 g cartridge	5 g cartridge	10 g cartridge
THF	0.2 mL	0.5 mL	1.0 mL
CH <sub>2</sub> Cl <sub>2</sub>	0.2 mL	0.5 mL	1.0 mL
MeOH	0.2 mL	0.5 mL	1.0 mL
DMF	0.8mL	2.0 mL	4.0 mL
DMF/H <sub>2</sub> O (9:1)	2.0mL	5.0mL	10mL
DMSO	2.0mL	5.0mL	10mL

Please contact FTI for information about the use of other solvents with F-SPE

**FREQUENTLY ASKED QUESTIONS FOR F- SPE:**

1. What kind of SPE manifold can be used for F-SPE?  
A: Either a vacuum or positive pressure SPE manifold can be used for F-SPE. We often use a 2 x 12 vacuum manifold such as those commercially available from Supelco, Waters, and United Chemical Technologies, Inc.
2. Can I use F-SPE cartridges without pre-conditioning them?  
A: As with other SPE cartridges, pre-conditioning prior to use is recommended.
3. How much sample can I load onto FluoroFlash® SPE cartridges?  
A: FluoroFlash® silica gel typically has a loading capacity of 5-10% of crude reaction mixture by weight.
4. What solvents are recommended as loading solvents?  
A: The sample can be dissolved in any organic solvent. We like 90:10 DMF:H<sub>2</sub>O, DMF or DMSO, since more solvent can be used. On a 2g F-SPE cartridge, the use of <2mL of solvent is ideal. Other solvents such as CH<sub>2</sub>Cl<sub>2</sub>, THF, MeOH, and acetone can be used although maximum recommended loading volumes are less. See Table 2 for recommended amounts of loading solvent. If a larger amount of solvent is needed for sample loading, then consider using a larger F-SPE cartridge.
5. Is the amount of loading solvent used to dissolve the sample important?  
A: The amount of solvent used to dissolve and load the sample is crucial and should be minimized. Separation of organic and fluorinated compounds can fail if too much loading solvent is used because the loading solvent can elute both fluorinated and non-fluorinated compounds off fluorinated silica gel. This is called breakthrough, and is a common problem seen by first-time users of F-SPE.
6. How can I diagnose and prevent breakthrough?  
A: The usual symptom of breakthrough is that some of the fluorinated compound comes off early in the organic fraction, but the bulk of the fluorinated compound is retained on the column. This happens because the loading solvent elutes the fluorinated compounds, but the elution stops as soon as the fluorophobic solvent elutes the loading solvent from the column. Breakthrough problems can often be solved by using less loading solvent. Other solutions are to use a more fluorophobic loading solvent, use a larger column or lower loading amounts.
7. Do I need to use fluorinated solvents in F-SPE?  
A: No, both the fluorophobic and the fluorophilic wash use common organic solvents.
8. What solvents should be used to elute non-fluorinated compounds while retaining fluorinated compounds?  
A: We often use 80:20 MeOH:H<sub>2</sub>O for the initial wash. Increasing the water content decreases the chance of breakthrough while decreasing the water content increases the chance of breakthrough. 90:10 DMF:H<sub>2</sub>O is also a good solvent. If you prefer H<sub>2</sub>O-free solvent, DMSO is the choice.
9. Do I need to use water in the fluorophobic wash?  
A: Water is the fluorophobic solvent *par excellence*, so a little water goes a long way. The addition of water ensures retention of the fluorinated compounds onto the fluorinated silica gel. If your molecule has 21 fluorines or more, then you can begin to reduce or even eliminate the water from your fluorophobic solvent.
10. What solvent needs to be used to elute the fluorinated compounds?  
A: We recommend using 100% MeOH or MeCN although more fluorophilic solvents such as acetone or THF can be used as well.

11. What kind of scale is suitable for F-SPE?  
A: From mg scale up to 2g scale will fit on an F-SPE. Larger scales may cause clogging of the cartridge. For more than 2g of sample, consider using loose fluorosilica gel in a self-packed filtration column. Please contact FTI for additional larger scale solutions.
12. What is the optimal flow rate when passing solvents through the cartridge?  
A: After the crude mixture has been loaded onto the cartridge, the flow rate of elution can be controlled to finish a single wash of a 2 g cartridge in 1-2 minutes.
13. Can I reuse the F-SPE cartridges?  
A: Yes, if the cartridges are thoroughly washed with 3-5 cartridge volumes of acetone or THF, then they can be reused multiple times, at your discretion. If the fluorosilica compounds are very basic, more THF is needed. Some reactions, such as Pd coupling, which produce particulate matter, may discolor the cartridge.
14. Can I predict if my F-SPE will work in advance?  
A: There are two ways to predict if the F-SPE will work for your application. The easiest method is to evaluate the mixture using the Fluorous TLC Plates (catalog# 803-9510PF). An alternative is to analyze the reaction mixture using Fluorous HPLC columns (catalog# 801-0505C, 803-0510C). For a complete method please contact FTI.
15. What can I do if my fluorosilica compound is not retained well enough?  
A: Several actions can be taken to minimize the chance of breakthrough:  
i. Minimize loading solvent (See Table 2)  
ii. Use a larger F-SPE cartridge  
iii. Modify the loading solvent used or, if possible, add a small amount of water to the loading solvent  
iv. Pre-condition the cartridge with 50:50 MeOH:H<sub>2</sub>O  
v. Please contact us if you still have problems
16. What can I do if I still have questions or problems?  
A: Please feel free to contact us at any time with any questions that you have or problems that you may encounter. We are here to help you succeed and realize the full potential of fluorosilica chemistry. You can reach us by telephone at 412-826-3050 or by e-mail at [contact-fti@fluorous.com](mailto:contact-fti@fluorous.com)

## REFERENCES:

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