

Fast2Flash™ User Guide

The faster and greener way to do all your reaction work-ups and extractions

- Reduce work-up time by 50% or more
- Minimize solvent exposure
- Run parallel samples
- Greener – reduce solvent use by 90% or more
- No emulsion formation
- Easy automation
- Ideal for flash chromatography

Fast2Flash is a hydrophobic and organophilic porous foam that **eliminates the need for time- and solvent-consuming liquid-liquid extractions (LLE) to extract the products from a reaction mixture**. Fast2Flash is conveniently available in sizes for popular loading cartridges for flash chromatography.

Fast2Flash acts as a “foam solvent” for the organic products and solvent in a reaction mixture, which become embedded in the foam. After the organic products and solvents are embedded in Fast2Flash, excess reaction solvent can be evaporated with vacuum or by air or N₂ flushing, often **without rotavaping**. After most of the solvent is evaporated, Fast2Flash can be further washed with aqueous solutions to remove undesirable water-soluble by-products. Fast2Flash loaded with the organic products then becomes a convenient input for flash chromatography.

Fast2Flash absorbs most hydrophobic organic compounds with a molecular weight of less than 1,000 in our testing and should absorb higher molecular weight compounds. Hydrophilic compounds remain in the aqueous phase. Fast2Flash has been tested with many common solvents: EtOH, MeOH, dichloromethane, ethyl acetate, diethyl ether, THF, 1,4-dioxane, hexanes, toluene, DMF, and DMSO.

Below are general procedures for using Fast2Flash based on Faster Chemistry’s experiences. Of course, every reaction is different, and every chemist is creative, so do not hesitate to try variations to get your chemistry done faster than you ever thought possible!

Please read the SDS before use.

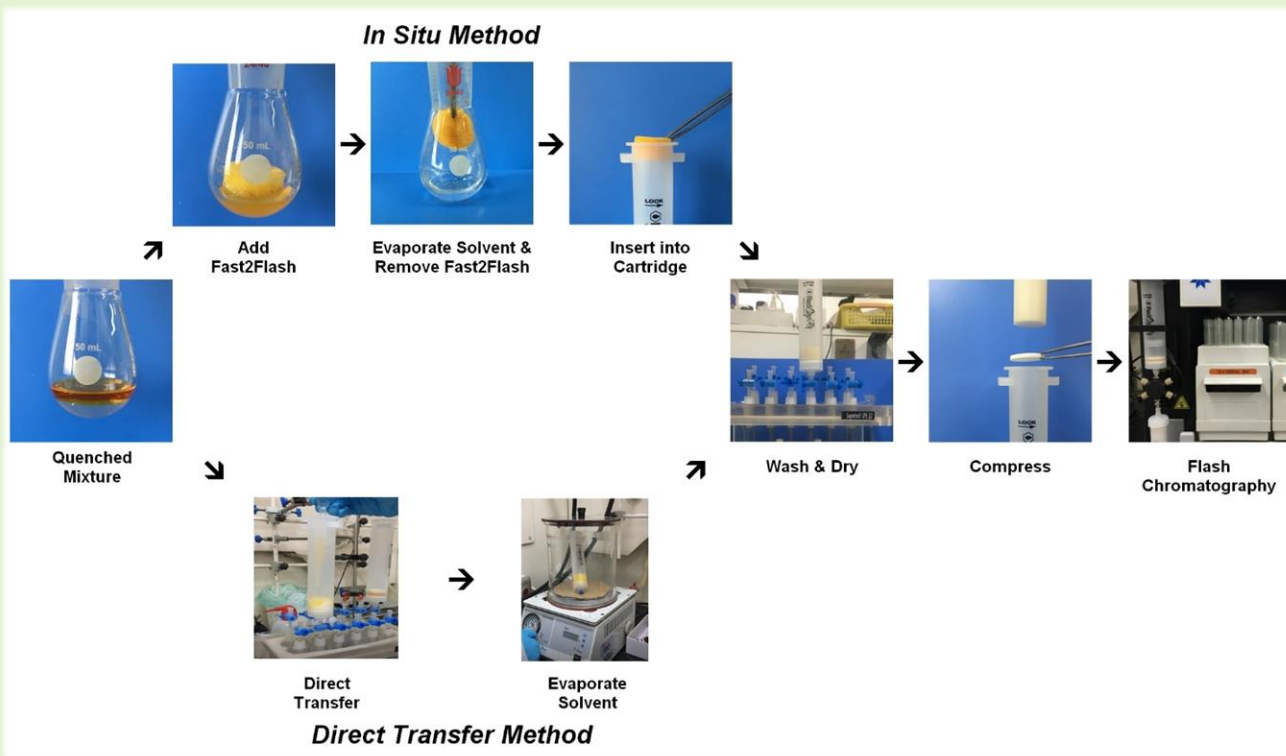
Fast2Flash should not be contacted with strong acids (pH < 1) or bases (pH > 14) or strong oxidizing agents.

If strong acids or bases are present in the reaction mixture, they should be neutralized before contact with Fast2Flash.

General Procedures for Reaction Work-Up with Fast2Flash

General Guidance

Depending on the reaction, there are two methods for using Fast2Flash - the *in situ* method or the **direct transfer method**. Please see the graphic below. With either method, time- and solvent-consuming LLE and emulsion formation are eliminated.



With the *in situ* method, the reaction is conducted and quenched with a suitable aqueous solution in the usual way. Fast2Flash is added to the mixture instead of a large amount of a conventional organic solvent, such as ethyl acetate, for traditional LLE. Then, after evaporating the solvent, Fast2Flash with the organic products embedded in it is separated from the aqueous mixture. The cylindrical Fast2Flash plug is sized to be easily inserted into a dry loading cartridge. It can be washed and dried in place in the cartridge if needed. A top frit is then inserted and the Fast2Flash is compressed and is ready for flash chromatography.

The **direct transfer method** makes work-up even more efficient for small scale reactions. Many reactions can be worked-up without quenching. The reaction is conducted in the usual way and the reaction mixture is directly poured through a loading cartridge preloaded with Fast2Flash. The aqueous phase flows through the Fast2Flash while the organics are absorbed by Fast2Flash. Then, one or multiple cartridges (if doing parallel reactions) are put in a vacuum oven to evaporate most of the organic solvent. Alternatively, the solvent could be evaporated using air or N₂ flow through the cartridge(s). Either drying method can be easily parallelized. As with the *in situ* method, the Fast2Flash in the cartridge(s) can be washed and dried in place if needed. A top frit is then inserted and the Fast2Flash is compressed and is ready for flash chromatography.

In general, the direct transfer method is faster and more convenient to use than *in situ* method. However, if the reaction mixture contains a relatively large amount of solvent, the *in situ* method with rotavaping is recommended.

When water-miscible and high boiling point solvents such as DMF or DMSO are used for a reaction, the reaction mixture can be worked-up using the direct transfer method with the Fast2Flash pre-saturated with water (5 mL). When the reaction mixture contacts the water in the Fast2Flash, the organic product precipitates from the water and is absorbed in the Fast2Flash. The loading cartridge is rinsed with water or brine (20 mL) to remove the water-miscible solvent (e.g., DMF) and is then dried in a vacuum oven for 5 - 10 minutes depending on the vacuum and temperature.

General Step-by-Step Procedures

Step 1: Conduct Your Reaction and Quench – The reaction is conducted in an organic solvent in the usual way. The reaction can be quenched at completion with an appropriate aqueous solution or, if quenching of the reaction is not required, you can go directly to Step 2 of the **direct transfer method** (below). If your products have appreciable water solubility, a saturated solution of a suitable salt such as NaCl or NH₄Cl is recommended for quenching. Also, unlike traditional liquid-liquid extraction, our Fast2Flash methods work well with just a small amount of quench liquid (e.g., 2.0 mL of brine for a 0.5 mmol scale reaction usually works). If the reaction forms a solid or was done in a water-miscible solvent, an appropriate water-immiscible solvent should be added after quenching to dissolve the solids or form an immiscible organic phase that the Fast2Flash can better absorb.

Additionally, instead of using an aqueous solution (e.g., Na₂CO₃ aqueous solution), an organic-based quenching solution can be used to avoid the generation of two phases and shorten the time for drying. The transfer process (from the reactor to the loading cartridge) will be easier and more complete if the quenched reaction mixture is kept as one organic phase. For example, either NEt₃ in DCM or NaOH in MeOH can be used rather than saturated Na₂CO₃ to quench the acids in a reaction mixture. Similarly, HOAc in DCM can be used to quench the bases in a reaction mixture instead of a saturated aqueous HCl solution.

Step 2: Use the *in situ* method or the **direct transfer method** depending on your reaction:

| <i>In situ</i> Method | Direct Transfer Method |
|--|--|
| Use if the reaction mixture contains a large volume of solvent. | Use for small scale reactions without a lot of solvent and that don't need quenching. |
| Add Fast2Flash to the reaction mixture – see the <i>Organic Loading Capacities</i> table below for capacities <i>excluding solvents</i> for the <i>in situ</i> method. Multiple pieces can be used and later stacked in the cartridge for proportionately higher loading but may lead to peak broadening. To minimize peak broadening during chromatography, excess Fast2Flash should not be used. The absorption of more polar/water-soluble compounds can be improved by quenching with a salt solution in Step 1. | Pre-load an empty dry loading cartridge with Fast2Flash. Fast2Flash should be aligned with the bore of the cartridge and fit tightly so all liquids must go through it. See the <i>Organic Loading Capacities</i> table below for capacities <i>including solvents</i> for the direct transfer method. Multiple pieces can be loaded into the cartridge for proportionately higher loading but may lead to peak broadening. To minimize peak broadening during chromatography, excess Fast2Flash should not be used. Pour the reaction mixture through the cartridge. The aqueous phase will pass through the Fast2Flash. |
| By its nature, Fast2Flash is hydrophobic and does not interact readily with an aqueous solution. When possible, vigorously stir or shake for good contacting. | |
| Step 3: Evaporate the solvent using a rotavap. After essentially all the solvent is evaporated, insert the Fast2Flash into a dry loading cartridge. Fast2Flash should be aligned with the bore of the cartridge and fit tightly so all liquids must go through it. | Step 3: Evaporate the solvent in a vacuum oven or by drawing air, N ₂ or other appropriate gas through the cartridge. Multiple cartridges can be dried simultaneously. |

| Fast2Flash Organic Loading Capacities | | |
|--|------------------------------|---|
| Item | For Loading Cartridge | Maximum Organic Loading Capacity |
| Fast2Flash-CF5 | CombiFlash® 5 gram | 180 mg |
| Fast2Flash-CF25 | CombiFlash® 25 gram | 550 mg |

Step 4: Wash the Fast2Flash If Needed – If residual reactants, salts, catalysts and/or by-products are a concern with your reaction, use water or acid or base solutions to wash them from the Fast2Flash in the cartridge. If using acid or base washes, you can finish with water washes to remove any residual acid or base. If a target compound is highly water-soluble, a minimal amount of a saturated inorganic salt solution (like saturated NaCl solution) should be used for the wash step – the use of salt will significantly reduce the solubility of the target during washing.

Step 5: Compress the Fast2Flash in the Cartridge – To reduce Fast2Flash's volume and chromatographic peak widths and to remove the water drops adhering to the wall of the cartridge, a clean frit should be inserted in the top of the loading cartridge, and the Fast2Flash should be compressed to around one-third (1/3) of its
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original volume/height with a suitable tool such as a plastic cylinder or rod. The quality of the separation (e.g., peak width) achieved with compression is similar to the conventional method of dry loading on silica gel.

Step 6: Elute the Target(s) - Elute the target(s) from the Fast2Flash in a flash chromatography instrument with a suitable organic solvent.

Step 7: Reuse and Disposal of Fast2Flash – Fast2Flash can be reused. The practicality of reuse will depend on the application. For small-scale, one-off reactions, little Fast2Flash is used, and recycle is likely impractical. Depending on its last use, Fast2Flash must be solvent-washed or baked-out (can be done at up to 80° C) to avoid cross-contamination.

We believe the reuse of Fast2Flash will be more practical for the larger-scale synthesis of a high-value compound. If you are making the same compound batch after batch in a dedicated system, there are fewer concerns about the residual compounds absorbed in Fast2Flash between batches as they are process-related. Essentially, you are recycling a “foam solvent”.

Fast2Flash is not a hazardous waste if discarded **as supplied**. It is, of course, intended to absorb organic compounds during normal use and, therefore, used Fast2Flash may need to be disposed of as a hazardous waste. A case-by-case determination must be made.

8/21/2023