SIGMA-ALDRICH®

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Technical Bulletin AL-134

Handling Air-Sensitive Reagents

The Aldrich® Sure/Seal™ system

Anhydrous solvents and air-sensitive reagents from Aldrich are packaged in our exclusive Sure/Seal bottles which provide a convenient method for storing and dispensing research quantities of these products. With this bottle, reactive materials can be handled and stored without exposure to atmospheric moisture or oxygen. The reagent comes in contact only with glass and a specially designed resin layer, yet it can be readily transferred using standard syringe techniques.

Fig. 1 Crown cap with hole

The polypropylene cap on a Sure/Seal bottle can be safely removed because the crown cap and liner are already crimped in place. The reagent can then be dispensed using a syringe or double-tipped needle inserted through the hole in the metal cap (**Fig.1**). We recommend only small-gauge needles (no larger than 18-gauge) be used and the polypropylene cap be replaced after each use. After the needle has been withdrawn from the bottle, the new elastomer liner provides outstanding resealing properties to protect the contents within from moisture and oxygen in the atmosphere.

Equipment Overview

Reactions involving our air-sensitive reagents can be carried out in common ground-glass apparatus. Other equipment required are a source of inert gas, a septum inlet, a bubbler, and syringes fitted with suitable needles.

Glassware preparation

Laboratory glassware contains a thin film of adsorbed moisture which can be easily removed by heating in an oven (125 °F/overnight or 140 °F/4 hrs). The hot glassware should be cooled in an inert atmosphere by assembling the glassware while hot and flushing with a stream of dry nitrogen or argon. A thin film of silicone or hydrocarbon grease must be used on all standard-taper joints to prevent seizure upon cooling. Alternatively, the apparatus may be assembled cold and then warmed with a heat gun while flushing with dry nitrogen. The oven-drying procedure is more efficient than using a heat gun because it removes moisture from inner surfaces of condensers and from other intricate parts.

Most of the techniques described in this bulletin were developed for handling various organoborane reagents. However, these methods are applicable to other air-sensitive solvents and reagents on a preparative laboratory scale.

Contents

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Inert gas supply and flushing equipment

Joint clips are required to secure joints during flushing since the nitrogen pressure may open the seals of unsecured standard-taper joints. Only high-purity, dry nitrogen from a cylinder with a pressure regulator (adjusted to 3-5 psi) should be used for flushing. Plastic tubing can be used to connect the nitrogen line to a tube connector adapter (equipped with a stopcock) on the reaction apparatus. Nitrogen may also be introduced through a rubber septum via a hypodermic needle connected to the end of the flexible tubing on the nitrogen line. The needle-tubing connector provides a simple method for attaching the needle to the tubing. When not in use, this nitrogen-flushing needle should be closed by inserting the needle into a solid rubber stopper or septa to prevent diffusion of air into the needle when the nitrogen is turned off (**Fig.2**).

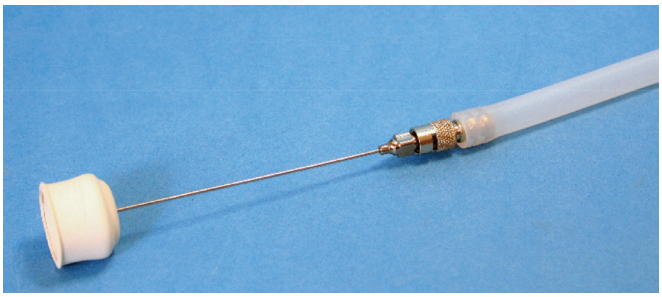

Fig. 2. Nitrogen-flushing needle

Septum inlet glassware

Large rubber septa may be used to cap female joints. However, the use of 6 mm septa and 9 mm o.d./6 mm i.d. medium-wall glass septum inlets is preferred. The small rubber septum provides a more positive reseal after puncture and allows less rubber to be in contact with organic vapors in the reaction vessel. With the recommended medium-wall tubing, the 6 mm septum not only fits the inside diameter of the glass tube but also fits snugly over the outside when the top is folded over (**Fig. 3**). The glass septum inlet can be built into the reaction flask (**Fig. 4**) or placed on an adapter (**Fig. 5**) for use with unmodified glassware. The rubber septum may be secured in place as shown in **Fig. 3**. with a nylon Wrap-it Tie. However, if the 6 mm septum is properly fitted to 9 mm medium-wall tubing, the ties may not be needed unless high pressures (>10 psi) are expected.

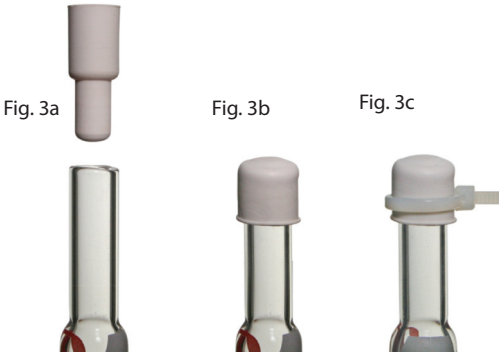

Fig. 3. Use of septum inlet

Bubblers for pressure equalization

To maintain an air-tight system the reaction vessel must be vented through a mercury or mineral oil bubbler. Drying tubes will not prevent oxygen from entering the system. At all times during the reaction, the system should be under a slight positive pressure of nitrogen as visually indicated by the bubbler. **Fig. 6** illustrates a suitable bubbler. A pressure reversal may cause the liquid in the bubbler to be drawn into the reaction vessel. The enlarged head space in the bubbler will minimize this danger. However, if a large pressure reversal occurs, air will be admitted into the reaction vessel. The T-tube bubbler shown can be used to prevent this problem because nitrogen pressure can be introduced intermittently through the septum inlet. The problem can be completely eliminated by a slow and continuous nitrogen flow.

Fig. 4. Flask with septum inlet

Syringe transfer tips

Small quantities (up to 50 mL) of air-sensitive reagents and dry solvents may be transferred with a syringe equipped with a 1-2 ft long needle. These needles are used to avoid having to tip reagent bottles and storage flasks. Tipping often causes the liquid to come in contact with the septum causing swelling and deterioration of the septa, and should therefore be avoided.

Fig. 5 Septum inlet adapter

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A rubber septum provides a positive seal for only a limited number of punctures depending on the needle size. Therefore, always reinsert the needle through the existing hole. It is also advantageous to put a layer of silicone or hydrocarbon grease on a rubber septum to facilitate passage of the needle through the rubber and to minimize the size of the hole in the septum.

Syringe/needle preparation

Ideally, the syringe and needle should be dried in an oven prior to use. Naturally, the syringe body and plunger should not be assembled before being placed in the oven. The syringe should be flushed with nitrogen during the cooling. A syringe may also be flushed 10 or more times with dry nitrogen (**Fig. 7**) to remove the air and most of the water adsorbed on the glass. A dry syringe may be closed to the atmosphere by inserting the tip of the needle into a rubber stopper or septa. (**Fig 2**). The syringe-needle assembly should be tested for leaks prior to use. The syringe is half-filled with nitrogen and the needle tip is inserted in a rubber stopper. It should be possible to compress the gas to half its original volume without any evidence of a leak. A small amount of stopcock grease or a drop of silicone oil placed on the Luer lock tip will help ensure tightness.

Reagent transfer with syringe

The syringe transfer of liquid reagents (up to 100 mL) is readily accomplished by first pressurizing the Sure/Seal™ reagent bottle with dry, high-purity nitrogen followed by filling the syringe (**Fig. 8**).

1. The nitrogen pressure is used to slowly fill the syringe with the desired volume plus a slight excess (to compensate for gas bubbles) of the reagent. Note the nitrogen pressure pushes the plunger back as the reagent enters the syringe. The plunger should not be pulled back since this tends to cause leaks and create gas bubbles.
2. The excess reagent along with any gas bubbles is forced back into the reagent bottle (**Fig. 9**).
3. The accurately measured volume of reagent in the syringe is quickly transferred to the reaction apparatus by puncturing a rubber septum on the reaction flask or addition funnel (**Fig. 10**). **Note:** larger syringes are available but are awkward to handle when completely full.

Reagent transfer with a double-tipped needle

To conveniently transfer 50 mL or more of reagent, the double-tipped needle technique is recommended. **Fig. 11** illustrates liquid-reagent transfer under nitrogen pressure using this technique.

1. To accomplish the double-tipped needle transfer, the needle is first flushed with nitrogen.
2. The Sure/Seal bottle is pressurized with nitrogen using the nitrogen flushing needle.
3. The double-tipped needle is then inserted through the septum on the reagent bottle into the head space above the reagent. Nitrogen immediately passes through the needle. Finally, the

Fig. 6 Bubbler

Fig. 7 Flushing a syringe with nitrogen

Fig. 7a

Fig. 7b

Fig. 8 Filling syringe using nitrogen pressure

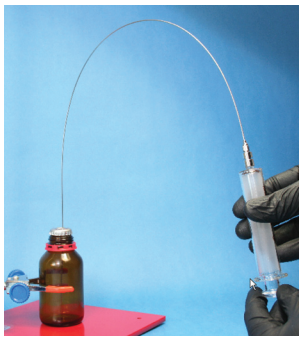

Fig. 9 Removing gas bubbles and returning excess reagent to the Sure/Seal bottle

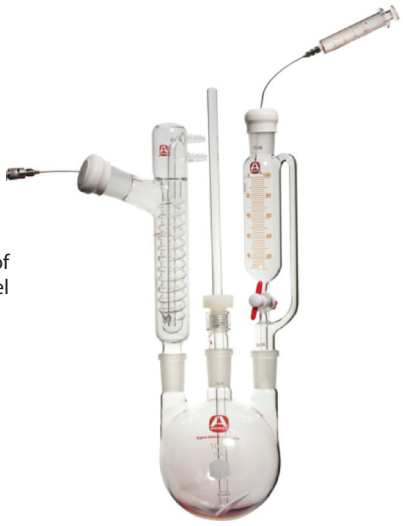

Fig. 10 Syringe transfer of reagent to reaction vessel

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other end of the double-tipped needle is inserted through the septum on the reaction apparatus, and the end of the needle in the reagent bottle is pushed down into the liquid. The volume of liquid reagent transferred is measured by using a calibrated flask or addition funnel. When the desired volume has been transferred, the needle is immediately withdrawn to the head space above the liquid, flushed slightly with nitrogen, and removed. The needle is first removed from the reaction apparatus and then from the reagent bottle.

An alternative method

Transferring measured amounts of reagents (**Fig. 12**).

1. The reagent is first transferred via a double-ended needle from the Sure/Seal bottle to a dry, nitrogen-flushed graduated cylinder (**Fig. 13**) equipped with female joint and a double inlet adapter. Only the desired amount of reagent is transferred to the cylinder.
2. The needle is then removed from the Sure/Seal bottle and inserted through the septum on the reaction apparatus. By applying nitrogen pressure as before, the reagent is added to the reaction apparatus.

If it is necessary to add the reagent slowly, a modified transfer needle is constructed from two long standard needles and a male Luer lock to male Luer lock syringe valve. The valve may be opened slightly allowing only a very slow flow of reagent. Thus, the addition funnel is not needed and many reactions can be carried out in single-necked flasks (**Fig. 13**).

Storage vessels

The 12-gauge stainless steel needles on the Chem-*Flex*™ transfer line provide a rapid means of transferring air-sensitive reagents under nitrogen pressure. However, the needles are so large that once the crown cap liner on the Sure/Seal bottle is punctured, the liner may not self-seal. If only a portion of the contents is to be used, a needle no larger than 16-gauge should be utilized. By using small needles the reagent in a Sure/Seal bottle will not deteriorate even after numerous septum punctures.

However, if the reagent is to be used repeatedly for small scale reactions or if an unused portion is to be stored for an extended length of time, the material should be transferred from the Sure/Seal bottle to a suitable storage vessel.

One type of vessel is the Sure/Stor™ flask for air-sensitive reagents (**Fig. 14**). Alternatively, an appropriate adapter can be used to convert a round-bottomed flask into a storage vessel (**Fig. 15**).

The PTFE valve on the storage vessel keeps solvent vapors away from the septum, thereby minimizing swelling and deterioration of the septum. Furthermore, the valve allows for replacement of the septa. A change of septa is sometimes necessary because they tend to deteriorate on prolonged standing in a laboratory atmosphere.

Fig. 11 Double-tipped needle transfer of liquid reagent

Fig. 12 Double-tipped needle transfer to graduated cylinder

Fig. 13 Double-ended needle transfer with syringe valve

Fig. 14 Aldrich Sure/Stor™ flask

Fig. 15 Aldrich Sure/Stor™ adapter

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Equipment cleanup

Clean-up of equipment that has been used to transfer air-sensitive reagents must not be taken lightly. Since many of these reagents react violently with water, fires are a potential hazard.

Empty Sure/Seal bottles - the crown cap and liner of an empty Sure/Seal bottle should be carefully removed and the open bottle left in the hood to allow the last traces of reactive reagent to be slowly air-hydrolyzed and oxidized. After at least a day, the inorganic residue can be rinsed out with water. Empty storage bottles and storage flasks should be treated similarly. Air-hydrolysis in a hood is appropriate only for the last traces of material that remain after a Sure/Seal bottle has been emptied as completely as possible via syringe or double-ended needle transfer. The Aldrich Catalog/Handbook or material safety data sheets should be consulted for the recommended disposal procedures for larger amounts of reactive chemicals.

Syringes and needles - Immediately clean all syringes and needles that have been used to transfer air-sensitive materials. Also, in general, a syringe should only be used for a single transfer. Failure to follow this practice can result in plugged needles and frozen syringes due to hydrolysis or oxidation of the reagents. The double-tipped needles are flushed free of reagent with nitrogen in the transfer system, and then immediately removed and placed in a clean sink. With water running in the sink and in the complete absence of flammable solvents and vapors, the double-tipped needles or Chem-Flex needle can be rinsed with water. When no activity in the rinse water is observed, acetone from a squeeze bottle can be flushed through the needle. Depending on the reagent transferred, it may be necessary to use dilute acid or base from a squeeze bottle to remove inorganic residue that is not water-soluble.

Following its use, a syringe contains a larger amount of residual reagent. It is advisable to rinse out the reactive reagent by first placing a few milliliters of the same solvent that was used for the reagent in a small Erlenmeyer flask in the hood. Keeping the needle tip under the solvent at all times, no more than half the solvent is then drawn into the syringe. The solvent plus dissolved residual reagent is ejected from the syringe back into the same Erlenmeyer flask. Repeat this rinse treatment at least three times. The wash solution can be safely combined with other waste solvents and the syringe may be further cleaned with water and acetone in the sink. Again, treatment with dilute aqueous acid or base may be necessary.

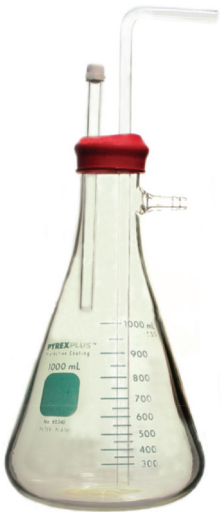

Fig. 16 Needle cleaning and drying technique

Once the syringe needles and double-tipped needles have been rinsed in a sink, they can be further cleaned and dried using a device similar to that shown in **Fig. 16**. Needles are cleaned by inserting them through the septum. Vacuum from a water aspirator is used to pull solvents from squeeze bottles through the needles. After pulling air through the system for a few minutes, the syringe plus needle or double-tipped needle will be dry. The syringe plunger should be replaced in the barrel for storage. If a syringe plunger and barrel are not assembled for storage, dust can settle on the plunger and in the barrel. Upon reassembly, these fine particles will occasionally scratch the barrel or cause seizure of the plunger on the barrel. However, the plunger and barrel must be disassembled before oven drying.

Summary

When handling air-sensitive materials, be prepared for the unexpected. For example, at least one extra set of clean, dry syringes and needles or double-tipped needles should always be available in case the first set of equipment becomes plugged. When working with these air-sensitive reagents keep in mind that these solutions should never be allowed to come in contact with the atmosphere.

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Labware for Handling Air-Sensitive Solvents and Reagents

A wide range of Labware products are available from Sigma-Aldrich for performing the techniques referenced in this technical bulletin. A sampling of these products are listed below. For additional products and ordering information, see the Sigma-Aldrich Labware Catalog or visit our website at sigma-aldrich.com/labware.

BUBBLERS

For safe pressure equalization during material transfers or reactions.

In-line bubbler

Use with oil or mercury, 5-7 mL. For monitoring gas evolution rate or rate of flow, or for closing off a reaction vessel from the atmosphere.
Cat. No. Z101214

In-line bubbler

SYRINGES, FITTINGS, AND NEEDLES

For transferring air-sensitive solvents and reagents.

Micro-Mate™ hypodermic syringes

Made from borosilicate glass with chrome-plated brass metal parts. Interchangeable barrels and plungers. All have needle-lock Luer tips. Additional sizes and tip styles are available.

Cat. No.	Capacity (mL)	Graduated (mL)
Z101052	5	0.2
Z101060	10	0.2
Z101079	20	1.0
Z101087	30	1.0
Z102342	50	2.0

Micro-Mate hypodermic syringes

All polypropylene Luer lock syringes

Non-contaminating, sterile, disposable syringes with safety stop to prevent plunger separation. Individually peel-packed.

Cat. No.	Capacity (mL)	Graduated (mL)
Z248002	3	0.1
Z248010	5	0.2
Z248029	10	0.5
Z248037	20	1.0

Polypropylene Luer lock syringes

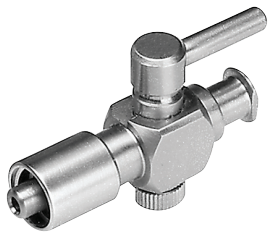
Perfektum® one-way compression-nut stopcock

Additional stopcock types are available.

Female Luer to male Luer lock, not unidirectional.
Cat. No. Z102350

Male Luer lock to male Luer lock, not unidirectional.
Cat. No. Z102377

Perfektum one-way compression-nut stopcock (female to male)



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Syringe needles with noncoring point

304 stainless steel, chrome-plated brass Luer hub, 18 gauge. Additional lengths and gauges are available.

Cat. No.	L (in.)
Z102717	6
Z117102	10
Z101141	12
Z100862	24

Stainless steel
304 syringe needles

Double-tipped transfer needles

304 stainless steel with a noncoring point on both ends. Additional lengths and gauges are available.

Cat. No.	L (in.)	Gauge
Z175595	12	20
Z101095	24	20
Z100889	24	18
Z100897	24	16
Z185221	24	14
Z185213	24	12
Z100900	36	16
Z185205	36	12

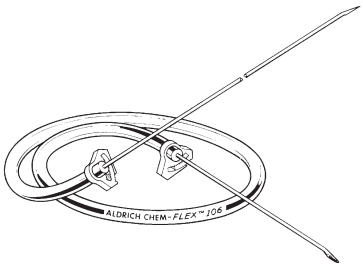
Double-tipped transfer needles

Chem-FLEX™ transfer lines

Two 12 gauge needles (6 and 18 in.) are connected to the Chem-FLEX 106 tubing with clamps. Liquids contact only PTFE and stainless steel during transfers.

Cat. No.	Tubing L (in.)
Z231029	30
Z281751	60
Z281778	120

Chem-FLEX transfer lines



INERT GAS SAFETY REGULATORS

For pressure transfer and purging operations.

The most compact laboratory regulator available. The bonnet is labeled "Inert Gas" to identify use. Outlet needle valve with ¼ inch NPTM connection. CGA 580 inlet.
Cat. No. Z569054

Inert gas regulator

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RUBBER SEPTA

Additional septa sizes and types are available.

Red

Cat. No.	Size
Z565587	8 mm OD tubing
Z565709	9-10 mm OD tubing
Z554073	14/20 joints
Z554103	24/40 joints
Z554111	29/42 joints

White

Cat. No.	Size
Z565695	8 mm OD tubing
Z565717	9-10 mm OD tubing
Z553964	14/20 joints
Z553980	24/40 joints
Z553999	29/42 joints

Rubber septa

SCHLENK TYPE GLASSWARE

Designed specifically for air-sensitive chemical reactions.

Reaction tubes

2 mm glass stopcock with 14/20 joint.

Cat. No.	Capacity (mL)
Z409235	10
Z409243	25
Z409251	50
Z409278	100
Z409286	250

Reaction tube

SEPTUM INLET ADAPTERS AND FLASKS

Small bore inlets for syringe transfers.

Septum-inlet adapters

Additional adapter styles are available.

Cat. No.	Stopcock	Joint
Z107387	Glass	14/20
Z107409	Glass	24/40
Z102288	PTFE	14/20
Z101370	PTFE	24/40

Septum-inlet adapters

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Septum-inlet flasks

Glass stopcock with 14/20 joint. Additional capacities and joint sizes are available.

Cat. No.	Capacity (mL)
Z515868	25
Z515876	50
Z515884	100
Z515914	250

Septum-inlet flasks

STORAGE BOTTLES AND FLASKS

For long-term storage of solvents and reagents.

Sure/Stor™ flasks

Designed for safe, reliable storage and dispensing of air-sensitive and odoriferous chemicals, pyrophorics, alkyl lithiums, Grignards, corrosives, and purified or deuterated solvents. High-vacuum PTFE valve. Additional flasks sizes, amberized, and plastic-coated glass are available.

Cat. No.	Capacity (mL)
Z404977	25
Z404985	50
Z404993	100
Z405000	250

Sure/Stor flasks

Storage bottles

Clear glass with PTFE stopcock and septum inlets.

Cat. No.	Capacity (mL)
Z103284	125
Z103292	250
Z101990	500
Z102482	1,000
Z103306	2,000

Storage bottles