

Safe Handling of Peroxide-Formers (PFs)

Many common laboratory reagents can undergo auto-oxidation under normal storage conditions resulting in the *unwanted* formation of peroxides. This often is only a nuisance, leading to chemical impurities which can adversely affect your research. In some compounds, however, the peroxide formed is stable enough that it can accumulate in the container or vessel. Many of these peroxides are susceptible to violent reaction if shocked or heated. Due to the unpredictability of these materials special care must be taken when handling peroxide-formers (PFs), including specific inventory, handling, storage, and disposal procedures.

What are Peroxidizing-Forming Chemicals?

Organic peroxides have the general structure of R-O-O-R or R-O-O-H, where R is an organic functional group. These are formed when susceptible materials are exposed to atmospheric oxygen – sometimes catalyzed by light. PFs are often segregated into three general categories, described below with common examples shown in Table 1.

Table 1. Common Peroxide Formers

Cat A – High Hazard without Concentration		
Butadiene	Chlorobutadiene (chloroprene)	Divinyl acetylene
Isopropyl ether	Potassium amide	Sodium amide (sodamide)
Tetrafluoroethylene	Vinylidene chloride	
Cat B – Hazard upon Concentration		
Acetal	Cumene (isopropylbenzene)	
Cyclooctene	Cyclohexene	Cyclopentene
Diacetylene	Dicyclopentadiene	Diethylene glycol dimethyl ether (diglyme)
Diethyl ether	1,4-Dioxane	Ethylene glycol dimethyl ether (glyme)
Furan	Isopropanol	Methyl-isobutyl ketone
Tetrahydrofuran	Tetrahydronaphthalene	Vinyl ethers
Cat C - Polymerization Hazard		
Acrylic acid	Butadiene	Chlorotrifluoroethylene
Methyl methacrylate	Styrene	Vinyl acetate
Vinyl chloride	Ethyl acrylate	Vinyl pyridine

Cat A – High Hazard without Concentration. These PFs react with oxygen and generate peroxides which can spontaneously and explosively decompose. Usually these high hazard peroxides form in liquid-state chemicals where the peroxides formed are insoluble in the liquid in which they form. The peroxides can concentrate on the bottom of the container or near the bottle cap threads. A simple impact, friction, or rapid heating can lead to a detonation. Isopropyl ether is a common example.

Cat B – Hazard upon Concentration. Cat B PFs generate peroxides that are just as sensitive and energetic if detonated but will only concentrate if liquid solvent is caused to evaporate away. Distillation, without precautions, can lead to heat induced detonation of the concentrated, less volatile peroxides. These peroxides may accumulate to concentrations high enough to have a noticeably higher viscosity or form a separate liquid phase. Tetrahydrofuran (THF) is a common Cat B PF.

Cat C - Polymerization Hazard. These materials can form peroxides which have the potential to initiate explosive polymerization. Many of these are monomers of common plastics. These have

carbon-carbon double bonds with other substituents such as chlorine, oxygen, carbonyl, phenyl, or another multiple bonds which can stabilize radicals. Inhibitors are usually added to prevent polymerization. Typical examples include vinylidene chloride, methyl acrylate, vinyl ether, styrene or butadiene.

Safe Practices

Preventing Formation of Peroxides

The following practices will help prevent formation of peroxide formers.

- **Store PFs in a cool, dark place.** Light (and heat) can accelerate the peroxide-forming oxidation reactions with the oxygen present in the headspace of opened containers.
Important Note: *Refrigeration of PFs such as diethyl ether has not been shown to slow down peroxide accumulation and can lead to formation of an explosive atmosphere.*
- **Keep containers sealed.** Oxygen is small enough to diffuse through any gaps between the container rim and the cap liner. Loose caps can also lead to deposition of organic peroxides at the rim. Over-tightening lids can lead to uneven contact and greater susceptibility to oxygen exposure.
- **Keep containers free of common contaminants like dust.** Contaminants can contain metals that may facilitate the auto-oxidation process.
- **Purchase only PFs which contain a peroxide formation inhibitor (when possible).** For example, tetrahydrofuran or diethyl ether is commonly sold with a low concentration of butylated hydroxytoluene (BHT). If you purchase PFs without an inhibitor, or if you remove the inhibitor, it is **highly recommended** that the reagents are stored under an inert gas such as nitrogen or argon to decrease peroxide formation. This approach will also help decrease peroxide formation in materials that have added inhibitors. This does not apply to Cat C monomers since the added polymerization inhibitors require oxygen to function.
Important Note: *The inhibitors will slow down – but not stop – peroxide formation and the inhibitor can be overwhelmed. The presence of an inhibitor, while beneficial, should not be relied upon to provide indefinite protection.*
- **Purchase only quantities of PFs that you expect to use within the expiration and disposal timeframes described below.** Long-time storage increases the chances of peroxide formation.

TIP: Besides being a safety hazard, peroxide formation in solvents can interfere with many reactions and generate unwanted side products.

Shelf Life of PFs

Table 2. Recommended Shelf Life of Peroxide Formers

	Cat A	Cat B	Cat C
Date Opened	3 months	12 months	12 months
Date Received	18 months	18 months	18 months

Table 2 shows the recommended shelf life for each category of PFs. When chemicals reach the recommended limit a request for a chemical pick-up should be made. Alternatively, PFs (Cat A and B) can be tested for presence of peroxides on a schedule (see section below) though this approach requires greater diligence. **Important Note:** *Uninhibited List C materials can be a significant hazard. Do not store for longer than 24 hours.*

Labeling PF Containers

All containers of PFs should be labeled with the following information (see below for examples):

- The date received
- The date opened
- The expiration date
- The presence of inhibitor
- The date tested and quantity of peroxide (if applicable)

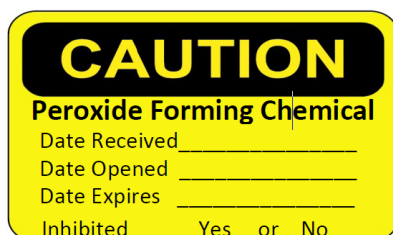


Figure 1: Example Label

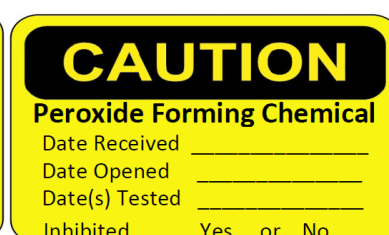


Figure 2: Example Label (for testing)

Labels are available upon request from EH&S Chemical Safety Office. Label templates can also be found on our website.

Before Using PFs

All containers should be carefully examined expiration date and overall condition. Containers that show signs of oxidation (e.g. rusty container or cap) or are stored longer than recommended shelf life should be handled with extreme caution.

Visual indicators of peroxide formation include:

- Whitish crystals around the cap and/or in the bottle
- Visible precipitate or an oily viscous layer present in the material
- Evidence of surface crust or discoloration (in solids)
- Residue after evaporation of a sample

If you encounter materials that show evidence of peroxide formation contact the Environment, Health & Safety department immediately for removal. ***Do not attempt to open the container.***

While chemicals that are still within the shelf life are usually safe for normal operations it is still highly recommended that PFs be tested prior to any procedure that can lead to concentration, such as distillations. For PFs to be retained beyond their normal shelf life these must be tested regularly and prior to every use.

Removing Peroxides

There are a number of ways of removing peroxides from solvents. For example, passing solvents through activated alumina is known to remove peroxides (Grubbs, et al., *Organometallics*, 15 (5), 1518 -1520, 1996). This can also be done by passing through zeolites (Wortel and Bekkum, *Org. Chem.*, 1980, 45 (23), pp 4763–4764). However, these methods are also **likely to remove any inhibitors** that are present which greatly increases the rate of subsequent peroxide formation.

Distilling Peroxide-Formers

Distillation of solvents is often performed in order to remove water, oxygen and residual impurities. Due to the hazards posed by distillation in general – and PFs specifically – this is becoming less common. Column purification systems are replacing stills in many labs. However, if distillation is required, there are methods to increase the safety. When preparing to distill or evaporate compounds listed in the tables, always test for peroxides first, using a method as described below. **Never distill potential PFs to dryness.** At least 20% of solvent should remain at the bottom of the still. The addition of mineral oil, or similar non-volatile organic compound, can dilute the peroxides that may be formed in the distillation pot. Sodium metal is often used during distillation of some solvents (such as diethyl ether and THF). In addition to drying the solvent this will also reduce any peroxides that are formed, though this process has inherent risks since it reacts rapidly with water, generating flammable hydrogen. Add small pieces of sodium metal to the distillation vessel to reduce peroxides that form. Use benzophenone as an indicator for the presence of sodium metal. Benzophenone, in the presence of sodium metal, forms a radical with a deep-blue color. When the blue color disappears, add more sodium metal.

Important Note: The distilled solvents will no longer contain inhibitors.

Testing Peroxide-forming Agents

Testing should be every 3 months for Type A and every 6 months for Type B. [Note: Since the mechanism of the hazards associated with Type C is different testing for peroxides is not meaningful]. Both approaches will allow you to keep peroxide formation from becoming hazardous. You need to know the status of the peroxide-formers in your inventory at all times. **Know which approach you plan on taking with PFs in your chemical inventory.**

When testing for peroxides, we recommend a 100 ppm upper limit for an acceptable level for peroxides in a solvent from a safety perspective. From an application viewpoint, a level of 100 ppm peroxides is often too high and can lead to failed experiments.

By far the easiest method is using simple dip strips such as Quantofix® Peroxide test sticks available through numerous vendors. These are inexpensive color-indicating strips which turn different shaded of blue depending on the concentration. A number of other methods have been used for testing for peroxides. One example is the potassium iodide indicator method.

Add 0.5-1.0 ml of the sample solvent to an equal volume of glacial acetic acid containing about 0.1 g of sodium iodide or potassium iodide crystals. A yellow color indicates iodine formation via iodide oxidation by sample peroxide; a brown color indicates high concentration. A blank determination should be made particularly when color development is faint since iodide/acetic acid mixtures will, over time, turn a yellow - brown color due to air oxidation.

A more sensitive variation of the above method adds one drop of a saturated, aqueous starch solution to the sample solution. Starch and iodine combine to form a bright blue complex that is more easily visualized than the yellow color generated by iodine alone. Dark blue solution color would be indicative of high peroxide concentrations.

Resources and References

Kelly, R. J., "Review of Safety Guidelines for Peroxidizable Organic Chemicals", *Chem. Health Saf.* **1996**, 3(5), 28-36

Jackson, H. L.; McCormack, W. B.; Rondestvedt, C. S.; Smeltz, K. C.; Viele, I. E. *J. Chem. Educ.* **1970**, 47(3), A175-88

Clark, D. E., "Peroxides and Peroxide Forming Compounds", *Chem. Health Saf.* **2001**, 8(5), 12-21

National Safety Council, Recognition and Handling of Peroxidizable Compounds, **1987**, Data Sheet I-655-Rev. 87