FEATURE

Reagent expiration dates: Fact or fiction?

By Russell W. Phifer

Of all the safety information commonly found on a chemical reagent bottle, an expiration date is one of the few items that is likely to change from one container of that chemical to the next. As the only representation of "time" likely to be present, this date could mean the difference between safe storage and an accident waiting to happen. Or could it? How accurate is an expiration date? Who decides the appropriate date, and what information is used to support such a decision? Are these dates guesswork, or are they based on actual stability data? Are they there just to keep us buying more product as frequently as possible? A closer look at expiration dates could leave you more dazed and confused than ever, or it could save your life some day. There are numerous anecdotes about accidents involving old peroxide forming chemicals—from ethers to lithium aluminum hydride to picric acid.

SETTING EXPIRATION DATES

There appear to be at least four factors that go into the establishment of an expiration date for a chemical reagent. First and foremost is the stability of the chemical. Experience with a chemical can certainly give a manufacturer a good idea of how stable it is. How many quality complaints have there been? Does the quality (purity) stand up to analytical testing months later? Years later? Although there is a long-standing suspicion (voiced by numerous chemists who provided background for this article) that expiration dates are simply meant to help the manufacturer sell more chemical, there are regulatory and liability issues that must be considered. As always, there are economic factors, as well. When these considerations are all taken together, the prudent manufacturer would certainly have to acknowledge the value of being as accurate as possible in determining expiration dates. The problem too often, however, is that those who use and/or store reagents ignore the many factors that contribute to degradation of a chemical.

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CONTRIBUTIONS TO LOSS IN QUALITY

Factors that can contribute to quality loss include temperature, humidity, light, presence of contaminants, and exposure to air and/or other substances. All are controlled in one way or another by how inventory is managed—how chemicals are stored. Table 1 provides some examples of chemicals that are dependent on proper storage to maintain their stability and quality.

It could easily be argued that expiration dates are insignificant for many of these chemicals as long as basic storage rules are followed. Nonetheless, it is logical that the longer a chemical is stored, the more likely that it will be forgotten or ignored. This may be the primary use of expiration dates, particularly for facilities that do not date incoming shipments of reagents. Often an expiration date is the only indication of even an approximate age of a chemical, because few manufacturers show a date of manufacture on reagent labels.

SAFETY AND LIABILITY CONSIDERATIONS

How important is liability as a factor in the development of an expiration date? Clearly a manufacturer who has failed to provide a recommended "use by" date for a material such as ethyl ether is more open to liability if there is an explosion due to peroxides that have accumulated. This same issue is a clear incentive for manufacturers and distributors to be as conservative as possible in establishing dates. One area in which this can be a significant issue is in reagent recycling programs at universities. Purdue University, for instance, experienced an explosion in 1998 when a 1L bottle of 1M lithium aluminum hydride in ethyl ether "exploded" as a researcher was wiring a rubber stopple over the sure-seal cap. The container had come from Purdue's chemical

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1074-9098/99/$20.00
PII S1074-9098(99)00030-1

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Published by Elsevier Science Inc.

Table 1. Factors Contributing to Chemical Decomposition/Purity

Chemical Compound	Contributing Factor	Possible Result
Acetic anhydride Aluminum bromide Aluminum chloride Aminohexanol Benzenesulfonyl chloride Boron triiodide Butyl ether Calcium oxalate Cesium fluoride Chlorosilanes Cobalt oxide 1,2 Dichloroethylene Dipropylene glycol Dysprosium 4-(Fluorosulfonyl) benzoic acid Itaconic acid Lithium 2-(Methylthio)phenyl isocyanate 2-Naphthoyl chloride Phenol Phenyl thioproprionate Potassium phosphate Sodium Stearic anhydride Tetramethyl orthocarbonate Tin fluoride Vinylidene chloride	Humidity (moist air)	Solids convert to liquid phase or degrade, some rapidly; liquids degrade to useless hydrated form; some react violently with moist air
Acetyl peroxide Hydrazine Benzoyl peroxide Tris(4-methoxyphenyl)borane-ammonia complex	Heat	Explode, degrade
Butyllithium (and other metal hydrides) Calcium carbide	Moisture	Pyrophoric, degrade
Acrylonitrile 2-Hydroxy-2 methylpropiophenone Indene Vinyl imidazole	Light	Degrade, some violently unless inhibited
1,4 Dioxane Ethyl ether Isopropyl ether 2, 4, 6 Trinitrophenol (picric acid) Tetrahydrofuran	Oxygen (other factors, including impurities)	Form explosive peroxides

waste section's redistribution program; an unopened bottle was stored inside the can from the original shipment. The bottle appeared to be new; however, closer inspection of a cryptic ink-stamp on the paper label of the outer can revealed that it had originally been received by Purdue's Chemistry Stores from the manufacturer ten years earlier! Amazingly enough, there was no fire from the event, but a full liter of 1M lithium aluminum hydride was sprayed all over the laboratory. The researcher fortunately received only lacerations and cuts. There was no expiration date on the bottle.

COST CONSIDERATIONS

Some reagent sellers have discovered that providing expiration dates is a "value added" service that can be extremely beneficial, from several perspectives. The use of expiration dates by manufacturers and distributors can enhance the value of a reagent over time, in that the cost of analyzing and/or tracking the history of a reagent to determine its purity can cost considerably more than the original purchase price; this can be a strong selling point. Expiration dates also increase the frequency of reordering. If there is no shelf-life date, the material is more likely to sit around as inventory for a much longer period of time. In addition, it prevents customers from returning product as off-specification that might simply have degraded due to age.

CAN EXPIRATION DATES BE BELIEVED

As most end users probably know, many reagents are actually manufactured by some company other than the one that placed the label on the bottle.

Laboratory reagents are frequently repackaged from larger stock, meaning that the date of manufacture may have been months or years before the final packaging of the chemical. This additional handling presents risk of contamination of the product; the level of risk depends on the quality-control methods utilized by the company doing the repackaging. Is humidity control provided where necessary? Are the new containers clean and sterile? Are airborne contaminants controlled? There is no way of knowing the impact of handling without running purity checks;

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even then, the quality of the analytical equipment and skill of the operator may result in an inaccurate assessment of quality. All of these factors could result in an expiration date being completely arbitrary. Even if the accuracy of an expiration date is accepted, there are two other dates that should be recorded by the receiving laboratory—the date the material was received and the date the container was first opened. The date of receipt is important for tracking usage, and the date that the container was opened and material removed is important, particularly for chemicals that may degrade rapidly and those that might form explosive peroxides. According to the ACS publication *Safety in Academic Laboratories*, "the principal criteria for assigning time spans to chemicals are the conditions in storage, the rates at which the compounds are oxidized by oxygen, the rates at which the compounds react with moisture and, in some cases, the ways in which they may polymerize.... Chemicals that have been stored for a long period of time, (perhaps five years), should be promptly scheduled for disposal." (ACS Committee on Chemical Safety. *Safety in Academic Laboratories*, 6th ed.; American Chemical Society: Washington, DC, 1995; p 53)

REGULATORY CONSIDERATIONS

Regulatory considerations may be a factor in the development and utilization of expiration dates. For example, FDA regulations require expiration dates in the case of in vitro diagnostic devices. While shelf-life dating solely for package integrity and sterility is not usually required for general medical devices, regulations encourage expiration dating when a particular component of a device, such as a battery or diagnostic reagent, has a finite useful life. Labeling for in vitro diagnostic devices requires an expiration date or some other means by which users may be assured of quality at the time of use. This requirement applies to both sterile and nonsterile in vitro diagnostic devices. Although not required by regulation, most manufacturers of complex devices and sterile devices voluntarily use lot or serial numbers for production control and, if the need arises, to expedite failure investigations, repairs, modifications, or recalls. Lot, batch, or other control numbers are required for:

- implantable and life-sustaining devices [820.65, Traceability];
- some products subject to radiological health standards [1002.30(b)(1), Records to be maintained by manufacturers]; and
- in vitro diagnostic devices [809.10(a)(9), Labeling for in vitro diagnostic products].

The OSHA technical manual specifies specific shelf-lives for sampling media; these time limits were developed by the OSHA Salt Lake Technical Center, primarily for OSHA's own workplace regulatory compliance sampling. Also provided in the technical manual are storage recommendations for some compounds, such as bis(chloromethyl)ether (store in a dark bottle in a refrigerator).

Expiration dates are also referenced in some laboratory accreditation procedures. For example, the American Industrial Hygiene Association (AIHA), in its Laboratory Quality Assurance Program Application, references the use of expiration dates in its Lead Laboratory, Environmental Microbiology Laboratory, and Asbestos Analyst Registry programs. No specific reasoning is provided on why these requirements are included.

Individuals who use "certified" analytical standards may also find expiration dates to be an issue, and *iso* 9000

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implementation has added some interesting twists on this as well. Those familiar with purchasing standards from NIST, or with purchasing environmental reference standards, will typically find an expiration date, perhaps based upon date of shipment from the supplier or the date of "certification." One incident described during research for this article involved an individual who ordered and received several 1L bottles (a supply suitable for a couple of years) of ortho-tolidine for colorimetric determination of residual chlorine in water. This individual was somewhat dismayed to find that the "expiration" date was three weeks from when it was received. Needless to say, the quantity purchased in this instance was exces-

Table 2. Reagent Distributor Policies on Request to Return Chemicals

Distributor	Return Policy
Lancaster Synthesis, Inc.	Within 10 days of receipt
Pfaltz & Bauer, Inc.	Within 30 days of receipt
Fisher Scientific, Inc.	Will not accept reagent bottles that have been opened for return
Sigma-Aldrich	Per terms and conditions on packing slip; all claims must be submitted within one year of receipt
VWR Scientific, Inc.	Within 60 days of receipt
Thomas Scientific, Inc.	Within 30 days of receipt
Fluka Chemie AG	Within 5 days of receipt

sive, particularly when considering the published "expiration" date.

MANUFACTURER POLICIES REGARDING EXPIRATION DATES

A quick review of the policies of major laboratory chemical distributors reveals a wide disparity in how expiration dates are used. A review of the terms and conditions under which chemicals are supplied provides a lesson on why chemicals should be inspected upon receipt—reagents past their expiration dates are not returnable. Failure to inspect the container or evaluate quality immediately can result in the conclusion on the manufacturer's part that any quality problem may have been the result of poor handling by the user. Manufacturers, of course, assume no liability for safety of a material once it has been received. Table 2 shows some representative policies of chemical distributors regarding the return of chemicals according to terms and conditions published in their respective catalogs.

WHAT SHOULD THE PRUDENT FACILITY DO?

The prudent laboratory facility will carefully control each and every chemical reagent from the time it is first received until its ultimate use or disposal. A major part of this inventory control effort should be dating of the label at the time it is first received and on the day it is first opened. If there is an expiration date on the container, this should be reviewed to determine if the chemical is to be used prior to that date. These actions will help considerably, not only in ensuring that high-quality material is available for the end user, but also in determining whether a material should be returned immediately. Assuming that it is not going to be used immediately, any observations regarding the condition of the bottle or the chemical inside should be noted at the time of receipt and appropriate action taken. For example, a cracked cap may be indicative that the integrity of the chemical has been compromised, and the bottle should be returned immediately according to the distributor's terms and conditions. If the product appears to be multi-phased, "dirty," or partially decomposed, the distributor should be notified immediately. This inspection process should ideally be made by an individual with some experience in handling the material.

Expiration dates are becoming a more important part of chemical labeling. Whereas some of the factors that go into determining when a chemical's useful life is past may be beyond the control of the end user, the cost of chemical reagents and the value of a researcher's time dictate that all appropriate measures be taken to assure quality and safety.

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Acknowledgments

The author wishes to thank Guy M. Crawford, University of Texas–El Paso; Dr. Linda Swihart, Purdue University; Dr. Benjamin Greene, Allied Signal; and Mark Yanchisin, University of Florida for their contributions to this article.