Organic Process Research & Development **2003**, *7*, 1029–1033

# *Safety Highlights*

## Safety Notables: Information from the Literature

This is the first of what we hope to be many overviews on safety which are of interest to process chemists and engineers to appear in *Organic Process Research & Development*. This mini-review is broken into two sections. The first section reviews recent articles taken from the literature which address safety issues. This section is not intended to be all-inclusive of the safety literature, nor should the information presented be used to make decisions regarding safety without reading the full text of the article. The section's intent is to give a flavor of the issues facing other chemists and engineers and how they are solving these problems. In the second section several major industrial accidents whose aftermath has impacted public perceptions and influenced the regulatory environment through enhancements to process safety standards are discussed. Through continued reference to case histories and keeping them fresh in the memories of process designers, this information could be used to help prevent similar accidents in the future. A few of the more significant accidents are cited with emphasis on the chemical processes being employed at the time of the incident.

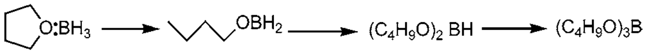
### Some Safety Articles of Interest to Process R&D Chemists and Engineers

**Limits of Flammable and Combustible Liquids.** Mike Schmidt's article on the ignition properties of organic solvents and other fluids (*Chem. Eng.* **2002**, *November*, 58) critically examines the flammability of aqueous mixtures. He states that engineers are often surprised to learn how ignitable aqueous mixtures of flammable liquids really are and that scientists often forget that it is the concentration of flammable or combustible material in the vapor, not the concentration of flammable or combustible material in the liquid that determines how easily it burns. Examples are given of how to estimate the ignitability of aqueous mixtures, using Raoult's law and easily attainable information.

**Detonation of Doubly Lithiated Bis(dimethylamino)methane.** A Safety Letter appeared in *Chem. Eng. News* (June 30, 2003, page 2) describing an explosion of doubly lithiated bis(dimethylamino)methane while drying in vacuo. The compound was prepared according to the literature procedure (*Chem. Ber.* **1996**, *129*, 483) of Karsch.

The authors of the letter (Michael K. Denik, Gurmit Singh, and Nachhattarpal K. Gill) advise that this material and related compounds should be regarded as potentially explosive and treated accordingly.

**Explosion of Borane−THF.** A 400-L cylinder of 2 M borane−THF exploded during storage at Pfizer's Groton, CT, research campus (June 25, 2002), resulting in injuries and property damage. The primary decomposition pathway of borane−THF complexes at ambient temperatures proceeds via THF ring-opening mechanism, ultimately forming tributylborate.



Users of borane−THF should be alerted to new information provided by Callery Chemical (Evans City, PA) in their revised MSDS for 2 M borane−THF, dated December 6, 2002. In it Callery Chemical (www.callery.com) states that the material should be handled as a hazard class 4.1 self-reactive hazardous material with a self-accelerating decomposition temperature (SADT) of 40 °C. Their revised MSDS also stated the following:

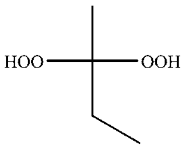
> *Laboratory tests (isothermal adiabatic Dewar and accelerating rate calorimetry tests) indicate that exposure to adiabatic conditions at temperatures over 40 °C may lead to a self-sustaining exothermic reaction that can cause a temperature increase. If the temperature under adiabatic conditions is allowed to reach approximately 60 °C, a violent decomposition reaction may occur (as indicated by further adiabatic laboratory tests (isothermal and dynamic accelerating rate calorimetry, and adiabatic isothermal Dewar tests)). The latter reaction can very rapidly evolve large quantities of heat, flammable hydrogen gas, and flammable and toxic diborane gas, resulting in fire, explosion, or dangerous pressures in sealed containers.*

Pfizer has not had an opportunity to review the data used by Callery to develop their December 6, 2002, material safety data sheet. However, the information is being shared to alert users of 2 M borane−THF of the self-reactive nature of this chemical.

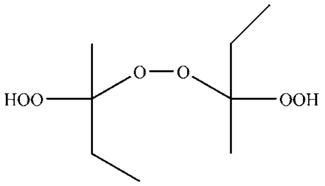
**Thermal Hazard Analysis of Methyl Ethyl Ketone Peroxide.** Over the past four decades, many thermal explosions caused by methyl ethyl ketone peroxide (MEKPO) have occurred in Taiwan and Japan. In a recent article, authors Po-Yin Yeh, Chi-Min Shu, and Yih-Shing Duh have examined the thermal properties of these materials to try and understand its reactivity (*Ind. Eng. Chem. Res.* **2003**, *42*, 1). MEKPO is the common name of peroxides produced by allowing methyl ethyl ketone to react with peroxide. MEKPO is still widely used in industry as a catalyst for initiating and cross-linking polymerization. It is postulated that seven

10.1021/op034143s CCC: $25.00 © 2003 American Chemical Society
Published on Web 10/23/2003

forms of MEKPO may exist, but the two forms used in industry are the monomer and dimer forms shown below.



Monomer



Dimer

Both the monomer and dimer were studied for their decomposition characteristics using both DSC thermal analysis and vent size packing (VSP2) adiabatic calorimetery. The onset temperature for the monomer was determined to be about 40 °C, and the authors note that the monomer is the most hazardous of this class of compounds.

**Causes of Tower Malfunctions.** An in-depth and informative survey into the causes of distillation tower malfunctions has been written by H. Z. Kister (*Trans. Inst. Chem Eng*. **2003**, *81* (Part A), 5). The survey constitutes the review of the case studies of 900 incidents of malfunctioning towers reported over the past 50 years. The author's analysis shows a rapid growth in the number of malfunctions with no sign of decline. The survey looks back over the past five decades to seek out the most common and repeated causes of towers failing to meet their objective. The author hopes that the lessons learned from these past malfunctions can save engineers and operators from falling into the same traps.

**Incidents with NaH or $NaBH_4$ in DMF Solvent Systems.** Deprotonations carried out using alkali metal hydrides are common in organic synthesis. For safety, the choice of solvent should be selected carefully. Incidents including runaway reactions and explosions with DMF have been reported (*Chem. Eng. News* **1979**, *September 24*; *Chem. Eng. News* **1982**, *July 12*; *Chem. Eng. News*, **1982**, *September 13*). DMF is believed to undergo attack by the hydride to form triethylamine and bis(dimethylamino)methane (*J. Org. Chem.* **1993**, *58*, 5005). The use of DMF, DMPU, or DMSO is also not recommended in the presence of alkali metal hydrides. An excellent source of safety information on LiH and NaH and reactivity is available upon request from Chemetall at www.chemetalllithium.com, and the specific technical note is *Lithium Top.* **2000**, *June*.

**Grignard Preparations.** Preparation of Grignard reagents from organic halides and magnesium pose potential safety hazards on both lab and plant scale due to their high exothermic energy which can lead to over pressurization, discharge of contents, or explosion. An incident on industrial scale was described by Yue, Sharkey, Lueng (*J. Loss Prev. Process Ind*. **1994**, *7*, 413) in which an impurity in the feed caused the Grignard formation to stall and later reinitiate, resulting in a release of 30% of the batch through the emergency relief system.

$$R-X + Mg \xrightarrow{THF} R-Mg-X$$

The use of FTIR as an in situ probe to monitor the initiation and subsequent formation of Grignard reagent was recently described (*Org. Process Res. Dev.* **1999**, *3*, 319) as a means toward safer scale-up of these reactions. Grignard reagents, once prepared, (e.g., trifluoromethyl Grignard reagents) can pose their own hazards as highlighted by Trevor Laird in the last issue of *Org. Process Res. Dev.* (**2003**, *7*, 614−623) and by references therein.

**DMSO: Handle With Care.** Urben, P. G. (*Chem. Health Saf.* **1994**, *Oct/Nov*) reports on several explosions with fatalities resulting from incompatibilities with DMSO. In one instance DMSO inadvertently came into contact with small amounts of 70% perchloric acid in an automatic titrator, and there was an explosion. Sodium metal and DMSO used to prepare dimethylsodium resulted in self-heating on dissolution of the sodium resulting in explosion. Many of the reported incidents involving DMSO involved bromides as minor impurities. Bromide-contaminated DMSO is capable of runaway reaction from about 130 °C, according to the paper.

**A New Small-Scale Reaction Calorimeter.** Andreas Zogg, Ulrich Fischer, and Konrad Hungerbühler have developed a new prototype reaction calorimeter with an integrated infrared-attentuated total reflection (IR-ATR) probe that combines the principles of power compensation and heat balance (*Ind. Eng. Chem. Res.* **2003**, *42*, 767). The paper presents a solid background on the state of the current equipment available to generate calorimetric data (for additional information read the review by Regenass: *Chimia* **1997**, *3*, 275). The authors then detail the development of this new calorimeter and demonstrate the system's precision with real chemical examples. The IR-ATR probe provides additional information to what would be obtained from the calorimetric signal alone.

**The Role of Process Chemistry in Fires and Explosions.** A paper authored by M. Sam Mannan, Abdulrehaman A. Aldeeb, and William J. Rogers (*Process Saf. Prog.* **2002**, *21*(4), 323) provided a structural approach to chemical reactivity hazard evaluation using a mixture of computational methods and experimental techniques. This systematic approach is designed to minimize the experimental workload, identify the most important parameters in evaluation of process fire and explosion hazards, and provide a more comprehensive understanding of process chemistry. This systematic approach for reactivity assessment was "put to the test" by examining the thermal decomposition of di-*tert*-butyl peroxide.

**Assessing Exothermic Runaway Risk.** A simplified mathematical and tabular method for assessing the risk of exothermic runaway reactions based on the calculated hazard index was proposed recently by Chen-Shen Kao, Yih-Shing Duh, Thomas J. H. Chen, and S. W Yu (*Process Saf. Prog.* **2002**, *21*(4), 294). The paper reviews the development of a runaway risk index (RRI) that claims to be easy to use and provides a large amount of critical chemical information. Starting with a specific reaction and relevant data regarding the chemical components, the authors walk the reader through reaction hazard analysis. Several case studies are given to demonstrate the usefulness of the system. The authors conclude that the results of this study must be used carefully and that organized systematic thermal hazard reviews of chemical processes are still needed.

**Determining a Safe Operating Envelope.** Linda Tuma's article (*Thermochim. Acta* **2002**, *392−393*, 41) describes the process in which a safe operating envelope for the pilot-plant scale-up of chemical process is determined at Merck. Using a three-tier assessment program and various analytical techniques [differential thermal analysis (DTA), differential scanning calorimetry (DSC), Mettler's RC-1 calorimeter, and FAI's reactive system screening tool (RSST)] Merck identifies both thermal and chemical hazards and evaluates the potential risk of thermal runaway. Tier I testing identifies potential chemical and thermal hazards which may lead to thermal runaway. Tier II evaluates the risk of potential thermal runaway which could arise from the exothermic decompositions, heats of reactions, and other potential heat releases identified in Tier I. Tier III, through several steps, identifies an intrinsically safe process. Once this process is completed, it can be determined if a safe envelope exists or if the process must be modified. Detailed examples are presented along with several useful tables of important safety information.

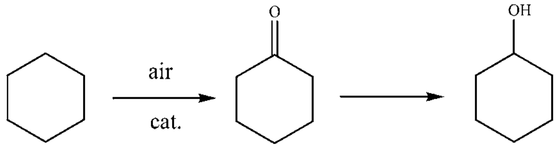
**Evaluation of Reaction Hazards for a Proposed Operating Change.** A production plant within the Dow Chemical Company wished to increase the operating temperature of a wiped-film evaporator (WFE). This proposed operating change set into motion the Dow's Management of Change procedures, which calls for a hazard evaluation to determine if the proposed changes were safe. In an article by Harold Johnson (*Process Saf. Prog.* **2002**, *21*(4), 313), the hazard evaluation of this new process is discussed in detail. Not only are insights given into the safe operation of WFEs, but the logical and critical interpretation of data prior to any operating change is also discussed with an insider's perspective.

**Learn from History or You Are Doomed to Repeat It.** The first step in improving the safety of chemical plants may be to understand and use case histories and general information about accidents that have already happened. A paper by S. G. Balasubramanian and Joesph F. Louvar described in detail the government and private sector sources for information on accidents (*Process Saf. Prog.* **2002**, *21*(3), 237). Through meticulous analysis and case study review, the authors present numerous recommendations for how the documentation and dissemination of accident information could be improved. They also challenge individuals to use the resources already available to avoid repeating history. The article contains the pros and cons of several sources of this information, as well as the web page links to access the data.

## Major Incidents of Interest

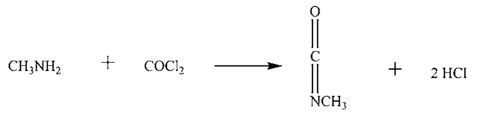
**Conclusions of the Chemical Safety and Hazard Investigation Board.** In the wake of several industrial-scale explosions in recent years attributed to runaway chemical reactions, the Chemical Safety and Hazard Investigation Board (CSB) (www.csb.gov) concluded that reactive incidents are a significant chemical safety problem and recommended in their December 2002 report that the EPA and OSHA broaden their regulations to include reactive chemicals and hazards (Johnson, J. *Chem. Eng. News*, **2003**, *June 30*, 20). In the CSB investigation of incidents available, spanning January 1980 to June 2001, 167 serious incidents involving chemical reactivity were evaluated. The 167 incidents were selected because there was sufficient information and thus represented only a subset of the actual number of incidents. Of those 167 incidents, 108 fatalities were reported from 48 of the incidents (U.S. Chemical Safety and Hazard Investigation Board, Hazard Investigation, Improving Reactive Hazard Management. Report No. 2001-01-H, NTIS No. PB2002-108705, U.S. CSB, Office of Investigations and Safety Programs: Washington, DC, Dec 2002). One of the difficulties in regulating reactive chemicals is that reactivity cannot be managed simply through the use of chemical lists which have been the norm for other regulatory aspects of safety. Thus, no straightforward consensus approach has been reached by regulating agencies or industry to expand the current Process Safety Management (PSM) standard to include reactive chemicals. One of the difficulties is that many of the incidents are a result of incompatibilities resulting from combination of two or more chemicals. The instability rating of a chemical cannot be used to predict a materials reactivity with other materials. Thus, understanding and quantification of the kinetics and thermodynamics of the interaction between two or more materials and the impact of that energy release on the surroundings is necessary (Challenges of Regulating or Implementing Reactive Chemicals Hazard Management Program, Report issued by Mary Kay O'Connor Process Safety Center, September 17, 2002).

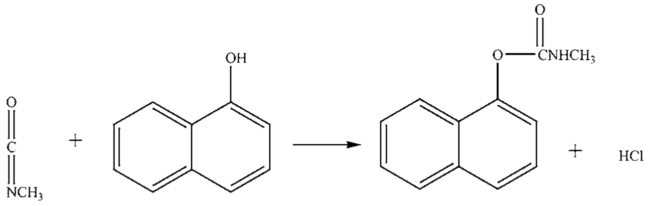
**Flixborough, UK (1974).** The incident involved a caprolactam production plant (Nypro Limited) designed to manufacture 70,000 tons/year. The release occurred in an intermediate process involving an air oxidation of cyclohexane to cylcohexanone, followed by a reduction to cyclohexanol in the presence of a catalyst.



The cause of the incident was a failure of a temporary bypass bellows-style feed pipe connecting reactor 4 to reactor 6 in the oxidation process. The failure, at the process conditions of 155 °C and 7.9 atm, resulted in release of estimated 30 tons of cyclohexane as a vapor cloud that subsequently ignited. The fire and explosion resulted in 28 fatalities and 36 injuries (Crowl, D. A.; Louvar, J. F. *Chemical Process Safety: Fundamentals with Applications*, 2nd ed.; Prentice Hall: Upper Saddle, River, NJ, 2002). The Flixborough incident had a major impact on both chemical engineering emphasis and safety regulations in the UK.

**Bhopal, India (1984).** The Bhopal plant was owned by Union Carbide India Ltd which was 51% owned by the American parent company Union Carbide Co. and the other 49% interest was held by Indian Investors (Lees, F. P. *Loss Prevention in the Process Industries: Hazard Identification,* *Assessment, and Control*, 2nd ed.; Butterworth Heinemann: Boston, 1996). The plant manufactured pesticides. One of the intermediates in the manufacturing process was preparation of methyl isocyanate and subsequent coupling with α-naphthol to make Carbaryl (Crowl, D. A.; Louvar, J. F. *Chemical Process Safety: Fundamentals with Applications*, 2nd ed.; Prentice Hall: Upper Saddle, River, NJ, 2002).

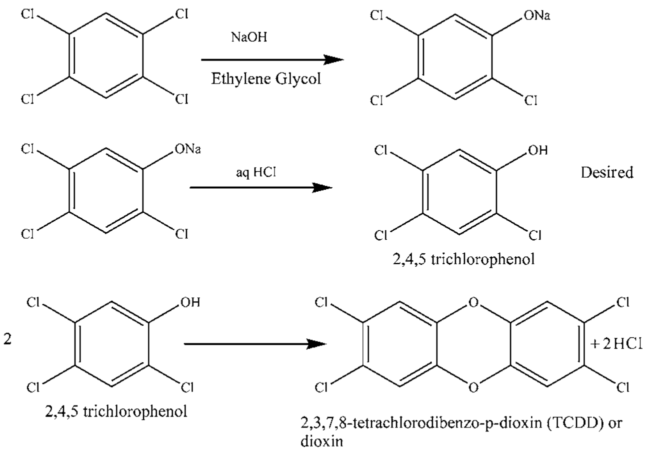




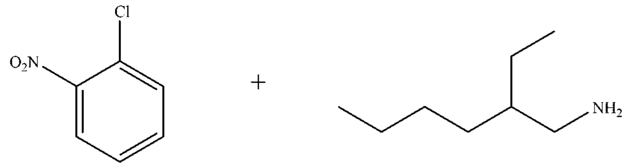
Although the exact cause has not been fully resolved, the accepted theory is that water entered the methyl isocyanate holding tank by careless flushing of some of the process lines (Lepkowski, W. An Interwoven Tale of Bhopal. *Chem. Eng. News* **2002**, *August 26*, book review). Methyl isocyanate reacts exothermically with water; thus, water intrusion into the holding tank would result in an exothermic reaction with a concomitant rise in temperature to the boiling point of methyl isocyanate of 39.1 °C. With the scrubbers and flares not operating properly at the time, an estimated 25 tons of toxic methyl isocyanate was released as a heavier-than-air vapor-cloud to the surrounding area. Estimates range in the thousands for fatalities and injuries. In the aftermath of the Bhopal tragedy, new laws were passed around the world to address emergency response measures for communities in the vicinity of chemical plants. For example, in the United States, OSHA developed and published its Process Safety Management (PSM) Standard (29 CFR 1910.119) and in the European Union, the so-called Seveso directive was further broadened to include storage of dangerous substances.

**Seveso, Italy (1976).** The Seveso incident happened in 1976 at a chemical plant owned by Icmesa Chemical company where they were manufacturing pesticides and herbicides. At the time of the incident, the product being manufactured was 2,4,5-trichlorophenol, a bactericide. (Lees, F. P. *Loss Prevention in the Process Industries: Hazard Identification, Assessment, and Control*, 2nd ed.; Butterworth Heinemann: Boston, 1996).

During normal operation a small amount of the byproduct dioxin was generated and concentrated in distillation residues and subsequently incinerated. After an interruption in the production cycle the reactor was left without agitation and cooling. This resulted in self-heating and runaway reaction. The higher temperatures led to more of the dioxin-forming side reaction, and when the reactor vented, it released an estimated 2 kg to the surrounding area. Dioxin is reported to have a $LD_{50}$ in rat of 22 $\mu$g/kg and is considered one of the most potent toxins known. A leading symptom of TCDD is chloracne, a chemically induced acne-like skin effect. More than 600 people had to be evacuated from their homes, and as many as 2000 were treated for dioxin poisoning. In its aftermath in the EU, legislation was adopted aimed at the prevention and control of such incidents. In particular, the Seveso directive was adopted and is referred to as *Council Directive 82/501/EEC.*



**Paterson, NJ, U.S.A. (1998).** The Paterson plant (Morton International Inc., now Rohm & Haas) manufactures a series of dye products. The explosion and fire occurred during the production of Yellow 96 Dye, which was used to tint petroleum fuel products.



A runaway reaction occurred in a 2000-gallon batch reactor being charged with *o*-nitrochlorobenzene and 2-ethylhexylamine. The runaway led to an explosion, nine injuries, and release of material into the surrounding community. The U.S. Chemical Safety and Hazard Investigation Board (CSB) investigators found that the reactor lacked the cooling capacity to accommodate process-upset conditions. The reactor was not equipped with a quench system or a reactor dump system, to avert the process in the event of a runaway reaction. In addition, the relief vent-size was too small to safely vent the excess pressure during a runaway reaction. (U.S. Chemical Safety and Hazard Investigation Board, Investigation Report, Chemical Manufacturing Incident, Report No. 1998-06-I-NJ, Morton International, Inc, Paterson, NJ, April 8, 1998)

**Allentown, PA, U.S.A. (1999).** An explosion at Concept Sciences, Inc. (CSI) occurred during the distillation of a solution of aqueous hydroxylamine and potassium sulfate, destroying the facility and resulting in five fatalities and 14 injuries. Several buildings in the industrial park were also damaged. On the day of the incident, CSI was in the process of producing its first full-scale batch of 50 wt% hydroxylamine. After the distillation process was shut down, the hydroxylamine contained in one of the process tanks explosively decomposed. The last recorded concentration of the hydroxylamine solution in the tank was 86 wt %. Hydroxylamines have been shown to explosively decompose at high concentrations (i.e., 85 wt %; Koseki and Iwata, 2001). The CSB investigation determined in part that CSI did not adequately evaluate the hazards of hydroxylamine during process development. (U.S. Chemical Safety and Hazard Investigation Board, Case Study, The Explosion at Concept Sciences: Hazards of Hydroxylamine No. 1999-13-C-PA, March, 2002)

A similar incident occurred at Nissin Chemical Company on June 10, 2000, in which hydroxylamine solution was being distilled when the plant exploded—the hydroxylamine concentration immediately prior to the incident was near 85%.

## The Future?

**Green Chemistry and Inherently Safer Design.** The phrase “inherently safer design” coined by Trevor Kletz in the 1970s, is the simple concept that it is better to design processes that eliminate chemical plant hazards at the beginning than to engineer “add-on” technologies later to try and control them. In recent years the concepts on inherently safer design have been adopted into the “new field” of Green Chemistry where the designs for improved safety are imbedded in the “The Twelve Principles of Green Chemistry” (Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998; p 30). The 12 principles are the following:

(1) It is better to prevent waste than to treat or clean up waste after it has formed.

(2) Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

(3) Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

(4) Chemical products should be designed to preserve efficacy of function while reducing toxicity.

(5) The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.

(6) Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

(7) A raw material of feedstock should be renewable rather than depleting wherever technically and economically practicable.

(8) Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided wherever possible.

(9) Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

(10) Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.

(11) Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

(12) Substances and the forms of substances used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Although these are not the typical articles on safety that chemists and engineers usually read, the parallels between “inherently safer design” of chemically processes and “inherently safer design” of chemical plants are striking. Several articles have appeared in the past year discussing the possibility of terrorist attacks on chemical plants and outlining the steps that need to be taken to prevent future catastrophes (Marszal, E. M. *Chem. Eng.* **2003**, *January*, 42, Baybutt, P. *Chem. Eng.* **2003**, *January*, 48, Heylin, M. *Chem. Eng. News* **2003**, *April 14*, 34, Johnson, J. **2003**, *February 3*, 23, and Johnson, J. *Chem. Eng. News* **2003**, *March 17*, 6.)

What the future holds no one can ever be sure but if we keep learning from the past hopefully the future will be a safer one.

David J. am Ende
*Chemical Research & Development,*
*Pfizer, Inc.,*
*Groton, Connecticutt 06340, U.S.A.*
*E-mail: david_j_amende@groton.pfizer.com*

Paul F. Vogt
*Chemical Development,*
*Albany Molecular Research, Inc.,*
*Mount Prospect, Illinois 60056, U.S.A.*
*E-mail: Paul.Vogt@albmolecular.com*

OP034143S