3

Which *chemicals* showed concerns for health risk?

The flexo ink study provides screening-level information about risks to human health and the environment associated with each ink system, and offers a basis for comparison. Chemicals predicted to pose a clear concern for health risk in a screening-level assessment are good candidates for a more rigorous assessment.

Chemicals in flexo inks have the potential to affect workers and the wider community around flexo facilities. The study analyzed potential risks under certain operating conditions, and found concerns for pressroom and prep-room workers in all three ink systems. This indicates the need for flexo professionals to take steps to address worker health concerns as well as the opportunity to make improvements in ink formulations. This chapter identifies the chemicals and chemical categories in the flexo inks that were found to have risk concerns under the conditions of the study. First, however, it explains the aspects of risk that the flexo ink study examined.

Information about human health risk

The health risk concerns posed by ink chemicals can be systemic, developmental, or carcinogenic. *Systemic toxicity* refers to adverse effects on any organ system (such as the lungs or the nervous system). *Developmental toxicity* means adverse effects that may occur to a developing organism any time between conception and sexual maturity. Developmental toxicity can manifest itself in a number of ways, ranging from altered growth or structural (physical) abnormalities to death. *Carcinogenic effects* are malignant tumors caused by cancer.

This study examined systemic and developmental effects, but it was not able to identify cancer risks for the ink chemicals because of insufficient quantitative data. Although some chemicals in the study had some evidence of carcinogenicity (such as tumors in experimental animals), none were known to cause cancer when touched or inhaled.

It is important to realize that risk depends both on the toxicity of a chemical and on the amount of it to which people and the environment are exposed. Thus, risk varies for different ink product lines and formulations. Risk also changes depending upon how inks are handled. As an example, if all workers wear appropriate gloves whenever they handle inks, dermal exposure is largely removed (except for accidental spills on other parts of the body), and so almost all dermal risks will be eliminated. Risk also may vary depending on the quality of pollution control equipment and the pressroom ventilation rate. For all these reasons, *the risk concerns found in the study will not necessarily match those in a particular printing facility.*

The model used for the study showed that there would be little exposure to the general population.

Exposure was "modeled" — that is, it was not based on actual measurements of releases. The study made assumptions about a hypothetical model facility, most of which reflect typical operating conditions. Under a different set of assumptions, the findings might have been different. Some important assumptions follow.

- 30% of VOCs released to air would be uncaptured emissions, and 70% would be stack emissions.
- Solvent-based ink systems would have a catalytic oxidizer with a 95% destruction efficiency.
- Pressroom and prep-room workers would work a 7.5 hour shift, 250 days/year.
- Pressroom and prep-room workers would have routine two-hand contact (no gloves) with ink unless a substance was corrosive.
- Press speed would be 500 feet per minute.

Definitions of risk used in the study

- *Clear concern* for risk indicates that for the chemical in question under the assumed exposure conditions of the study, adverse effects were predicted to occur.
- *Potential concern* for risk indicates that for the chemical in question under the assumed exposure conditions, adverse effects may occur.
- *Low or negligible concern* for risk indicates that for the chemical in question under the assumed exposure conditions, no adverse effects were expected.

The criteria for each level of risk are shown in Table 1.

TABLE 1 Criteria for Risk Levels[2]

Level of Concern for Risk	Hazard Quotient	Margin of Exposure		SAT Hazard Rating*
		NOAEL	LOAEL	
CLEAR	**>10**	**1 to 10**	**1 to 10**	**MODERATE-HIGH**
Potential	1 to 10	>10 to 100	>100 to 1,000	low-moderate
Low or negligible	<1	>100	>1,000	low

* This column presents the level of risk concern if exposure is expected. If exposure is not expected, the level of risk concern is assumed to be low or negligible.

Risk depends both on the toxicity of a chemical and the amount of it to which people and the environment are exposed. Risk varied by the product line, formulation, and how inks were handled. As an example, workers in the study were assumed to not wear gloves. However, if all workers were to wear appropriate gloves whenever they handle inks, dermal exposure would largely be removed (except for accidental spills on other parts of the body), and thus almost all dermal risks would be eliminated. Risk also may vary depending on the quality of pollution control equipment and the pressroom ventilation rate. For all these reasons, *the risk concerns found in the study will not necessarily match those in a particular printing facility.*

[2] Hazard Quotient (HQ) is the ratio of the average daily dose (ADD) to the Reference Dose (RfD) or Reference Concentration (RfC), where RfD and RfC are defined as the lowest daily human exposure that is likely to be without appreciable risk of non-cancer toxic effects during a lifetime. The more the HQ exceeds 1, the greater the level of concern. HQ values below 1 imply that adverse effects are not likely to occur.

Margin of Exposure (MOE) is calculated when a RfD or RfC is not available. MOE is the ratio of the No Observed Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL) of a chemical to the estimated human dose or exposure level. The NOAEL is the level at which no significant adverse effects are observed. The LOAEL is the lowest concentration at which adverse effects are observed. The MOE indicates the magnitude by which the NOAEL or LOAEL exceeds the estimated human dose or exposure level. High MOE values (e.g., greater than 100 for a NOAEL-based MOE or greater than 1,000 for a LOAEL-based MOE) imply a low level of risk. As the MOE decreases, the level of risk increases.

Information for some chemicals was incomplete. In these cases, systemic toxicity concerns were ranked by EPA's Structure Activity Team (SAT) according to the following criteria: high concern — evidence of adverse effects in humans, or conclusive evidence of severe effects in animal studies; moderate concern — suggestive evidence of toxic effects in animals; or close structural, functional, and/or mechanistic analogy to chemicals with known toxicity; low concern — chemicals not meeting the above criteria.

Every ink product line in the study contained chemicals that showed *clear* risk concerns for workers in the pressroom and prep-room.

Findings about chemical risk

Under the conditions of the study, certain chemicals in each ink system were predicted to pose a clear occupational risk to workers. Table 2 lists the chemical categories and chemicals showing clear risk concern for workers, as well as exposure routes and toxicological endpoints for each chemical.

Alcohols contained the most chemicals of clear concern for risk in the solvent-based and water-based ink formulations.

Systemic and developmental effects that have been reported in the medical literature (from animal or human studies) in association with use of a chemical are known as *toxic endpoints*. Neurotoxic effects, eye irritation, lung effects, decreased growth, and increased mortality are just a few examples of possible toxic endpoints. Toxic endpoints provide an idea of the kinds of adverse effects on body organ systems that may occur from exposure to a chemical.

Although some chemicals in the study had some evidence of carcinogenicity (such as tumors in experimental animals), the study was not able to identify cancer risks for these chemicals because of insufficient quantitative data.

All chemical categories except olifin polymers included one or more chemicals that were predicted to pose a risk concern for flexo workers. Ten solvents presented clear risk concerns for workers. This was the largest number of chemicals serving any one ink function. Thus, the solvents in solvent-based and water-based inks deserve scrutiny to determine whether they may present risks to the workers in flexo facilities. Several amides or nitrogenous compounds in water-based formulations presented a clear concern for systemic risks to workers. The acrylated polyols contained four chemicals posing a clear concern for risk in the UV-cured formulations.

Substantial use of some press-side additives may contribute to potential worker health concerns.

The use of press-side additions, such as solvents and additives, increased the worker risk concern for many of the solvent- and water-based ink formulations. In particular, propanol and propylene glycol methyl ether in solvent-based systems, as well as ammonia, propanol, isobutanol, and ethyl carbitol in water-based systems, presented potential or clear worker risk concerns when used in the volumes observed during the performance demonstrations.

TABLE 2 Flexo Ink Chemicals Showing Clear Risk Concerns for Flexo Workers (under conditions of the CTSA)

Chemical	Function in Ink	Exposure Route*	Toxic Endpoints**
Acrylated polymers (found in UV system)			
Glycerol propoxylate triacrylate	UV reactive compound	derm	tissue necrosis, decreased body weight, neurotoxic and respiratory effects
Acrylated polyols (found in UV system)			
Dipropylene glycol diacrylate	UV reactive compound	inhal, derm	SAT: genotoxicity, neurotoxicity, oncogenicity; developmental and reproductive effects; derm and respiratory sensitization; skin and eye irritation
1,6-Hexanediol diacrylate	UV reactive compound	inhal, derm	developmental effects
Hydroxypropyl acrylate	UV reactive compound	inhal, derm	respiratory effects
Trimethylolpropane triacrylate	UV reactive compound	derm	decreased body weight; skin and neurotoxic effects; changes in clinical chemistry; altered organ weights; respiratory effects
Alcohols (found in all systems)			
Ethanol	Solvent	inhal, derm	blood, liver, neurotoxic, and reproductive effects, decreased cellularity of the spleen, thymus, and bone marrow; dev: fetal malformations
Isobutanol	Solvent	inhal	blood and neurotoxic effects, changes in enzyme levels; dev: cardiac septal defects
Isopropanol	Solvent	inhal, derm	blood and skin effects, tissue necrosis; kidney, liver, neurotoxic, reproductive, spleen, and respiratory effects; changes in enzyme levels and clinical and urine chemistry; dev: fetal death, musculoskeletal abnormalities, fetotoxicity
Alkyl acetates (found in all systems)			
Butyl acetate	Solvent	inhal, derm	changes in serum chemistry, fluctuations in blood pressure; dev: fetotoxicity, musculoskeletal abnormalities
Ethyl acetate	Solvent	inhal	blood, cardiovascular, gastrointestinal, kidney, liver, neurotoxic, and respiratory effects; decreased spleen and liver weight; increased adrenal, lung, and kidney weight
Amides or nitrogenous compounds (found in all systems)			
Ammonia	Multiple	inhal, derm	skin and eye irritation; corneal, liver, spleen, and respiratory effects
Ammonium hydroxide	Multiple	inhal, derm	eye effects, nasal irritation, respiratory effects
Ethanolamine	Multiple	inhal, derm	respiratory irritation; kidney, liver, neurotoxic, and respiratory effects
Hydroxylamine derivative	Multiple	inhal, derm	SAT: genotoxicity, dermal sensitization, developmental toxicity

TABLE 2 Flexo Ink Chemicals Showing Clear Risk Concerns for Flexo Workers

Chemical	Function in Ink	Exposure Route*	Toxic Endpoints**
Ethylene glycol ethers (found in water system)			
Alcohols, C11-15-secondary, ethoxylated	Solvent	derm	Overall concern; severe skin irritation, eye irritation, lung effects
Butyl carbitol	Solvent	inhal, derm	blood and skin effects, liver effects
Ethyl carbitol	Solvent	inhal, derm	decreased food consumption, bladder, blood, kidney, liver, neurotoxic, reproductive, and spleen effects; dev: sperm, liver, brain, and birth weight in offspring***
Hydrocarbons — low molecular weight (found in solvent and water systems)			
n-Heptane	Multiple	inhal	auditory and neurotoxic effects, altered serum chemistry
Inorganics (solvent and water systems)			
Barium	Solvent	derm	decreased body weight, increased arterial blood pressure, reproductive and respiratory effects; dev: reduced survival, decreased weight gain, blood effects
Organic acids or salts (found in solvent and water systems)			
Dioctyl sulfosuccinate, sodium salt	Additive	derm	death, gastrointestinal and neurotoxic effects; dev: body weight effects; (SAT) derm sensitizer to humans***
Organophosphorous compounds (found in solvent and UV systems)			
Phosphine oxide, bis(2,6-dimethoxybenzoyl) (2,4,4-trimethylpentyl)-	Multiple	derm	neurotoxic, food consumption and body weight, adrenal, blood, skin, and liver effects***
Organotitanium compounds (found in solvent system)			
Isopropoxyethoxy-titanium bis (acetylacetonate)	Additive	derm	SAT: neurotoxicity, genotoxicity, oncotoxicity, and developmental/ reproductive toxicity. Skin, eye, mucous membrane irritant
Titanium diisopropoxide bis(2,4-pentanedionate)	Additive	derm	SAT: irritation of the eyes, skin, and mucous membranes. Moderate concern based on release of hydrolysis products: 2,4 pentanedione, inorganic titanium, and isopropanol. 2,4 pentanedione: concern for neurotoxicity, mutagenicity, oncogenicity, and developmental/reproductive toxicity. Inorganic titanium: concern for mutagenicity and oncogenicity. Isopropanol: concern for liver, neurotoxic, reproductive, respiratory, and spleen effects; changes in enzyme levels and clinical and urine chemistry; fetal death, musculoskeletal abnormalities, fetotoxicity, blood and skin effects, tissue necrosis at application site, increased kidney and liver weight.

Chemical	Function in Ink	Exposure Route*	Toxic Endpoints**
Titanium isopropoxide	Additive	derm	irritation of the eyes, skin, and mucous membranes. Moderate concern based on release of the hydrolysis products, inorganic titanium and isopropanol. Inorganic titanium: concern for mutagenicity and oncogenicity. Isopropanol: concern for liver, neurotoxic, reproductive, respiratory, and spleen effects; changes in enzyme levels and clinical and urine chemistry; fetal death, musculoskeletal abnormalities, fetotoxicity, blood and skin effects, tissue necrosis at application site, increased kidney and liver weight.
Pigments — organic (found in all systems)			
C.I. Pigment Red 23	Colorant	derm	blood, kidney, and stomach effects***
Pigments — organometallic (found in all systems)			
D&C Red No. 7	Colorant	derm	thymus and reproductive effects, changes in clinical chemistry, kidney effects, decreased thymus weight***
Propylene glycol ethers (found in solvent and water systems)			
Propylene glycol methyl ether	Solvent	inhal, derm	increased mortality; blood, developmental, liver, neurotoxic, reproductive, respiratory, and skin effects; altered organ weights; and decreased growth

These chemicals were predicted to pose risk concerns under the specific conditions of this study; they might be associated with different risks, or with no risk at all, under different conditions.

Abbreviations: dev = developmental effects. All endpoints not specifically indicated as developmental are systemic.

SAT = Structure Activity Team and acute data reports.

*Only pressroom workers were assumed to have exposure via inhalation (inhal). Both prep-room and pressroom workers were assumed to have dermal exposure (derm).

**Toxicological endpoints are the potential effects on organ systems (e.g., cardiac, respiratory) that have been reported in the medical literature and other reports in association with use of a chemical. A reported association does not mean that the effect is necessarily caused by the chemical.

***Reported effects may have been observed from a different exposure route.

Aspects of inks to learn more about

Press-side additions

Cleaning products

Air emissions (VOCs and HAPs)

Safety hazards (e.g., flammability, ignitability, reactivity, corrosivity)

Environmental hazards

Health risks to workers

Health risks to community

Energy consumption and opportunities for conservation

Solid wastes

Unregulated chemicals

Untested chemicals

The databases and resources listed at the back of this booklet identify chemical substances by specific chemical name. It is important to obtain the correct chemical identification information, which includes Chemical Abstract Service (CAS) names and numbers when doing research on chemical formulations.

Ways to reduce health risks of flexo inks

Inhalation risks to flexo workers can be managed to a great extent by ensuring good ventilation in the pressroom and prep-rooms, and by creating and enforcing clear policies for use of masks and respirators. Dermal risks can be managed by making sure that all workers wear the right gloves whenever they are handling inks, press-side additions, or cleaners.

Many of the substances analyzed in the study were found in multiple ink formulations and are likely to be found in other inks as well. Risks posed by ink chemicals can continue to exist as long as toxic chemicals are present and being used. Therefore, whether choosing among the ink systems or choosing an ink formulation, it is important to consider the EH&S impacts of the chemical substances that make up a formulated product. The flexo ink study can serve as a first step in bringing a more positive environmental profile into the printing shop.

Health considerations are as basic to good printing as are performance and cost. Identifying chemicals that have lower toxicities provides important opportunities to remove these chemicals from formulations before they can enter the workplace and the environment. In addition, moving to chemicals with reduced impacts will increase environmental and health benefits. Possible benefits of switching to a cleaner ink formulation may include

- reduced health and safety risk concerns for workers and the community,
- fewer regulatory requirements,
- greater customer satisfaction,
- increased efficiency,
- a move to innovative technologies, and
- lower operating costs while maintaining high quality standards.

Flexo professionals play an important role in minimizing the impacts of ink chemicals. This responsibility extends beyond the walls of facilities to the greater community and the environment. Ensuring that workers wear appropriate protective gear is just the starting point. Only a very small percentage of the perhaps 80,000 chemicals available for commercial use today have been adequately tested for health and environmental hazards. More than half of the chemicals in the flexo ink study had no little or no published toxicological data available at the time of the study. Many chemicals that are not regulated by any U.S. government organization were predicted to present a clear or possible risk concern to workers under the conditions of the study.

The inadequacy of much chemical data points to the importance of learning more about the categories and specific chemicals in flexo inks and related products. It is important to support research on untested and inadequately tested flexo ink chemicals, especially those with clear or potential risk concerns and those produced in high quantities. Very little basic toxicity information is publicly available on most of the commercial chemicals made and used in the United States. Without this basic hazard information, it is hard to make sound judgments about what risks these chemicals could present to people and the environment.

Flexo professionals can and should work to identify and use formulations that will help protect workers and the environment. The DfE Program encourages printers, ink manufacturers, and distributors to actively engage in a dialog on *"getting the right mix"* in flexo facilities. Printers and suppliers need to work together to evaluate inks, identify possible alternatives, and compare current and alternative ink products. This may yield benefits for printers and formulators, as well as providing benefits for workers and the environment.

The Material Data Safety Sheet (MSDS) and the product label are excellent places to start in understanding the potential impacts of a chemical. However, the MSDS or label may not provide enough information to make a better choice. Often, chemicals are generically described by chemical class or by trade name. Structural and other differences in chemicals of the same general class and makeup may not be apparent from product literature or labels, especially for imported substances. Descriptions in distributor or supplier literature and catalogs may define a chemical type, but not detail an actual chemical structure (e.g., whether a carbon chain is branched or linear — a key distinction from an environmental standpoint since linear chains biodegrade more rapidly than branched). Also, sales materials may only list trade names, often an imprecise descriptor, since a name might remain the same while the actual product composition may change.

Table 3 lists some ways that flexo professionals can reduce risks and improve environmental responsibility related to ink chemicals.

Because any given printing facility may use different inks and have different operating conditions than those of the Flexo CTSA, these chemicals may not pose a clear concern at that facility. However, a facility that does work with chemicals studied by the CTSA should carefully assess their use and potential worker exposure, and manage appropriately.

There are approximately 2,800 high-production-volume (HPV) chemicals for which little data are available. HPV chemicals are those manufactured in, or imported into, the US in amounts equal to or exceeding 1 million pounds per year. To provide important data, EPA challenged industry to provide testing or further information about these chemicals. In response, many of the HPV chemicals have been ponsored by industry, and EPA hopes to have all HPV testing completed by 2004.

TABLE 3
Ways to Reduce Environmental, Health, and Safety Concerns of Ink Chemicals

- Ensure that all workers who handle inks wear appropriate personal protective gear (e.g., butyl or nitrile gloves and respirators as needed) to minimize exposure to chemicals. More information on which gloves to choose for working with specific chemicals can be found at the National Toxicology Program website: http://ntp-server.niehs.nih.gov
- Maximize good ventilation, particularly in ink prep-rooms and pressrooms.
- Develop other safety policies and practices for inks, and ensure that workers follow them.
- Make environmental and health information about ink chemicals more accessible and understandable (e.g., expand MSDSs, provide best practice tips, include chemical information in sales materials).
- Become familiar with environmental and health impacts of chemicals in inks.
- Select the cleanest inks that make business sense.
- Minimize use of hazardous inks as well as press-side additions.
- Ensure that all pollution control devices are maintained properly and work correctly at all times.
- Look at all steps in the printing process throughout the facility to identify ways to improve operations and environmental performance. If not already in process, start developing an **environmental management system**.
- Support further research on ink chemicals.

The DfE Program has developed an *Integrated Environmental Management System (IEMS) Implementation Guide* that helps businesses plan, set up, and maintain an IEMS. You may download it from the DfE website (www.epa.gov/dfe), or contact EPA's National Service Center for Environmental Publications. The publication number is EPA 744-R-00-011.

4

How did the three ink *systems* compare?

The three ink systems were analyzed in terms of health risk concerns for flexo workers and the surrounding population, performance characteristics, environmental impacts (including emissions and material and energy use), and costs.

Health risk concerns

The flexo ink study assessed possible risks for both dermal and inhalation exposure to chemicals. Each ink system was found to contain chemicals that, under presumed conditions, showed clear health risk concerns for workers who handle inks in the prep-room or pressroom.

General population

No chemicals in the study presented a *clear concern* for risk to the general population (people living near a printing facility), and most chemicals presented a negligible concern. Each ink system, however, had one category with chemicals that posed a *potential concern* for the general population: alcohols (functioning as solvents) in one solvent-based and two water-based formulations, and acrylated polyols in one UV-cured ink formulation (serving as reactive diluents). Based on reports by EPA's Structure Activity Team[3] (SAT), some propylene glycol ethers in one solvent-based ink, amides or nitrogenous compounds in two UV-cured inks, and acrylated polyols in one UV-cured ink may pose a potential risk concern to the general population.

Pressroom and prep-room workers

Every ink product line in the study contained chemicals that, under presumed conditions, showed *clear* risk concerns for workers in the pressroom and prep-room.

One way to compare the relative risk of the three ink systems is to rank formulations by the number or percent of chemicals predicted to pose a clear concern for worker risk. As shown in Table 4, the solvent- and water-based product lines[4] each included an average of 16 chemicals with clear risk concern. The total number of chemicals in an ink product line was determined by adding the numbers of base chemical ingredients and press-side solvents and additives for each formulation within a product line, and then summing the totals for all five formulations. Using this method, a chemical

Every ink product line in the study contained chemicals that showed *clear* risk concerns for workers in the pressroom and prep-room.

Risk depends both on the toxicity of a chemical and the amount of it to which people and the environment are exposed. Risk varied by the product line, formulation, and how inks were handled. As an example, to help identify cleaner formulations, workers in the study were assumed to not wear gloves. However, if all workers were to wear appropriate gloves whenever they handle inks, dermal exposure would largely be removed (except for accidental spills on other parts of the body), and thus almost all dermal risks would be eliminated. Risk also may vary depending on the quality of pollution control equipment and the pressroom ventilation rate. For all these reasons, *the risk concerns found in the study will not necessarily*

[3] Information for some chemicals was incomplete. In these cases, systemic toxicity concerns were ranked by EPA's Structure Activity Team (SAT).

[4] A product line is a group of inks that is made by one manufacturer, shares certain printing characteristics, includes multiple colors, and is intended to be used with one ink system. For the flexo ink study, each product line contained five colors—blue, white, cyan, magenta, and green.