classic chronic toxicity and tumorigenesis until the mechanisms for both are completely understood for a specific chemical substance. The scientific literature is replete with demonstration of tumor induction in animals exposed by one or more of several routes to a large variety of chemical substances. Although even one such finding should immediately alert industry and governmental agencies alike to a possible problem, certainly in-depth review and critical evaluation is necessary prior to establishment of mandatory control standards by such agencies. Such in-depth review requires that all available information and data bearing on the problem be considered and evaluated on their merits.

Certainly degrees of carcinogenicity do exist, and it is entirely possible that thresholds for tumor induction may exist. Until such time as this hypothesis is proved, however, only the most stringent of control measures will suffice to assure that employees are adequately protected from chemical substances considered to be potential human carcinogens. The assessment of carcinogenic potential for a specific chemical substance must include the consideration of published information, monitoring and control data from affected industries, and the in-depth, epidemiologic experience of affected employees. Negative experience in industry regarding the incidence of cases of human cancer must be considered in proper perspective, not only in terms of pure versus mixed exposures and adequacy of statistical data, but also in the light of the proven experience in the dyestuffs industry that the average latency period for development of bladder cancer is approximately 20 or more years.

With these considerations in mind, it is necessary to reflect that the final decision in promulgating an occupational exposure control regulation must be that standard ". . . which most adequately assures, to the extent feasible, on the basis of the *best available evidence*, that no employee will suffer impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life." (Occupational Safety and Health Act of 1970.)

CASE STUDY 4: INORGA
LEVEL APPROACH
OCCUPATIONAL CANC

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INTRO

Arsenic, known and used since
which is truly ubiquitous from both
estimate is that in the U.S.A. alone
are potentially exposed to inorganic

HISTORICA

In 1820, 45 years after Percival
J. A. Paris ascribed the first associ
occupational. While practicing in Cor
that ". . . a cancerous disease in
chimney sweeps . . ." occasionally
fumes of a local copper smelting wor
and Paris' original specific observation
a subject of dispute and controversy
clinically that occupational contact wi
cancer—particularly among sheep-dip
sodium arsenite, a veterinary pestici
medical or environmental arsenical exp
well established by 1930.[8]

Medical reports had postulated
cancer among sheep-dip workers
senicals.[9,10] The first strong implica
tional exposure to these arsenicals
when four fatal cases of lung cance
sheep-dip workers.[11]

EPIDEMIO

The above evidence prompted
tional group exposed to inorgani
ported on a study of the mortali
arsenite sheep-dip, a topical vete
(1975), ten epidemiological studi

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#212

CASE STUDY 3: VINYL CHLORIDE— BEST AVAILABLE TECHNOLOGY

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Because one person out of every four in the United States dies of cancer, it is of great concern that most estimates of the proportion of cancer induced by environmental factors are in excess of 50%. Boyland, in the United Kingdom has further estimated that 90% of all human tumors result from the action of chemicals of environmental or endogenous origin, with the remaining 10% induced by viruses and ionizing radiation.

The significance of these estimates for the occupational environment, as well as similar estimates made here, is quite clear: long-term exposure of employees to carcinogenic chemicals must certainly increase risk of cancer. Yet, in only a handful of instances has this general conclusion been amply demonstrated. Explosive revelations such as those which characterized the finding that vinyl chloride induced angiosarcoma of the liver in exposed workers are very rare, at least for the present. Few would dispute the conclusion, however, that if those employees who contracted this fatal liver tumor had not been exposed to vinyl chloride, the probability of their contracting this rare disease would have been infinitesimally small. Absolute prevention of this particular tumor could have been assured if substantial exposure to vinyl chloride had not occurred.

The increase in incidence of urinary bladder cancer among aromatic amine dyestuffs workers has been well documented. The greatly increased incidence of mesothelioma among asbestos workers and of "oat cell" carcinoma of the lung among chloromethylation workers represent still other instances of occurrence of rare cancers in much greater frequency among exposed workers than among the general population or unexposed cohorts.

The truly alarming common feature in each of these instances has been retrospective recognition of cause and effect some twenty or more years following initiation of exposure. During these periods of latency, many more tumors undoubtedly have been initiated and now only await clinical verification. Unfortunately, such experiences have been necessitated in the past to demonstrate clearly the need for exposure controls. We must not, however, permit the "body count" mentality of the Viet Nam era to find new acceptance in our nation's workplaces.

The situation is not so simplistic, however, as to suggest the immediate, total elimination of all chemicals tainted with suspicion of carcinogenic potential in order to assure an exposure-free working environment.

Socioeconomic benefits to be derived from large-scale chemical production activities for the individual employed in this industry as well as his employer and the nation must be considered. Such considerations, however, are valid, from the standpoint of occupational health, only to the extent that they may affect

decisions concerning substitution or elimination of substa[illegible] demonstrated to be only weakly tumorigenic. In instances where carcinoge[illegible]azard to man of a chemical is established, the overriding consideration of the employer will be whether he can remain competitive in a situation in which costly engineering controls must be instituted as required by stringent regulations designed to control exposure, and which will assure minimum employee risk of cancer.

Differences between situations involving absence of controls, minimum controls, or stringent controls depend principally on substantiality of scientific evidence available to support regulatory decisions. Where such evidence is equivocal, regulatory controls must reflect the current state-of-the-art in concern for the following principles of carcinogenicity:

1) realization of a period of latency, possibly of 20–30 years, or longer in duration;
2) possibility of extremely low threshold of species or individual response;
3) possibility of metabolic modification of parent chemical substance to unidentified proximate or ultimate carcinogenic metabolite(s);
4) additive or synergistic effects of concomitant workplace exposures to other agents or factors, including cigarette smoke.

In the preamble to the rule promulgated on October 4 by the Occupational Safety and Health Administration (OSHA) regulating occupational exposure to vinyl chloride, four important policy determinations appear that will set the stage for future regulations involving occupational carcinogens:

1) ". . . the demonstration of cancer induction in humans at a particular level is not a prerequisite to a determination that a substance represents a cancer hazard for humans at that level.
2) "It would be imprudent to assume man to be less sensitive to vinyl chloride exposure than experimental animals in the absence of contrary positive evidence.
3) ". . . the precise level of exposure which poses a hazard and the question of whether a 'safe' exposure level exists, cannot be definitively answered. . . . Nor is it clear to what extent exposures can be feasibly reduced. We cannot wait until indisputable answers to these questions are available, because lives of employees are at stake. Therefore, we have had to exercise our best judgment on the basis of the best available evidence. These judgments have required a balancing process in which the overriding consideration has been the protection of employees and those who may have regular exposures to VC throughout their working lives.
4) ". . . [the exposure limit of 1 ppm] is based on evaluation of the best available evidence and on a judgment that the health and safety of employees must be protected to the fullest extent feasible."

Mechanisms of carcinogenesis are far from being completely comprehended and fully understood, and the many variables surrounding occupational carcinogenesis serve to cloud the situation further, even when a specific agent is suspect. A more important aspect concerning occupational cancer must be recognition of cause and effect, at least from the standpoint of control measures. Hazards associated with occupational exposure to a specific chemical substance must be considered not only from aspects of acute and subacute toxicity, but also from the potential to induce tumors. A clear distinction cannot be drawn betw