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To: NIOSH Docket Office (CDC)
Subject: Docket number NIOSH-240

In response to Request for Information: Announcement of Carcinogen and Recommended Exposure Limit (REL) Policy Assessment, I submit the following:

As a hospital pharmacist with responsibility to support cancer treatment with intravenous antineoplastic drugs, I am very concerned with the limitations of current NIOSH policies on occupational exposure to carcinogens as well as reproductive hazards and neurotoxins.

The antineoplastic drugs represent the largest category of known, probable and possible human carcinogens as classified by the International Agency for Research on Cancer (IARC). This is understandable as these are therapeutic chemicals robustly used in human patients to treat malignancies. We have known since the early 1970s that these drugs actually represent a risk of secondary malignancies to treated patients. While the benefits of using these drugs outweigh the risks to patients, those of us exposed to these drugs during their compounding and administration have only the risk. In addition to being carcinogenic, these drugs are reproductive hazards, neurotoxins and are toxic to other organ systems.

Pharmacy and nursing staffs handling these drugs are exposed to a number of them throughout the workday resulting in exposures to complex mixtures, sometimes of tremendous doses, as in the treatment of neoplastic disease with ablative doses of antineoplastics followed by a rescue protocol.

In the 2004 NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings [DHHS (NIOSH) Publication Number 2004-165], NIOSH estimates the number of exposed workers to exceed 5.5 million, excluding the manufacturing sector. The adverse effects of occupational exposure to these drugs have been anticipated since the 1970s. Safe handling recommendations have been advocated since the 1980s. Then, as now, it has been the position of OSHA and NIOSH, that the workers protect themselves with a complex set of work practices within the framework of engineering controls adopted from other industries and supplemented with personal protective equipment. As much of the exposure takes place at the patient bedside, few "engineering controls" are possible. The expensive burden of this questionable protection falls solely to the health care providers with no chance of offsetting this cost as there are no regulations to require protection and no exposure limits to identify a reasonable goal of successful mitigation.

Numerous studies have been done showing the extent of health care worker exposure to these drugs. Many of the studies have documented that the outside of drug vials and surrounding packaging are contaminated with measurable quantities of drug residue thus increasing the number of exposed workers and presenting complicated challenges to safe handling practices. NIOSH, OSHA and especially, FDA, have turned a blind eye to this issue allowing drug manufacturers to continue this practice of failing to control toxic substances and passing them along to mainly unsuspecting "middle men". Manufacturers of antineoplastic drugs have taken little to no responsibility in the

exposure of countless health care workers to these potent and toxic drugs. Better packaging is available and should be required by regulation as it clearly will not be instituted without it. The cost of protection should be at least partially borne by the manufacturer.

With regard to the specific questions that NIOSH proposes:

1. NIOSH should implement a **boarder** policy that will identify and classify carcinogens, reproductive hazards and neurotoxic agents to encompass a larger protective grid.

2. IARC already has criteria, nomenclature and categorizations that form the basis for determining carcinogenic potential in humans. It would seem reasonable to adopt this and harmonize the approach to classification. Similar classification (i.e. known, probably, possibly) could be used for other hazards, such as adverse reproductive events. While these negative health events are more easily determined than carcinogenicity, chemicals with similar structures, such as with many of the antineoplastic drugs, could be reasonably anticipated to produce similar negative health effects and should be categorized earlier in the release process.

3. While an REL of 1 in 1,000 working lifetime risk (for persons occupationally exposed) is a reasonable target level for ONE antineoplastic drug, the actual exposure is a multiple of that as rarely is a health care worker (unlike an employee of a drug manufacturer) exposed to only ONE antineoplastic drug during a workday. Consideration should be given to targets that express the actual exposure and are calculated for total exposure to complex mixtures.

4. In health care we routinely use *ALARA - As Low As Reasonably Achievable* for exposure to ionizing radiation. As "safe" exposure levels to antineoplastic drugs have not been established and there is no way of measuring them, achieving exposure limits "to the extent feasible" is difficult to interpret and apply. The "extent feasible" should not be determined to be what is not too expensive or not too much work, however.

5. In the European community, exposure to hazardous drugs (antineoplastic and other drugs that produce negative effects in health care workers) are measured by using surface wipe sampling of "marker" drugs in the health care work environment. Drugs that may be assayed in nanogram and picogram quantities are sampled from surfaces and "action levels" are set for surface contamination. Surface contamination of one drug has been calculated to correlate to urine levels in exposed workers which were then compared to patient and animal data and calculated to represent a specific cancer risk – for the ONE drug.

Of concern is that multiple studies, even those by NIOSH, have failed to demonstrate a reliable correlation of surface contamination to urine levels. This is partly due to the limited sampling that has been reported.

This, again, becomes problematic when dealing with multiple exposures to multiple drugs as in worker exposure to complex mixtures. Hazard banding of antineoplastics with similar structures, basis of effect and toxicities may be one way to reduce the large number of drugs into categories (bands) and allow for an estimated REL for each band, and calculated REL for more exposure to multiple bands.

For exposure to antineoplastic and other hazardous drugs, much more research is needed to determine an REL, to find a way to measure exposure at least in the workplace if not in the worker, and to establish reasonable methods of reducing exposure. NIOSH should endeavor to find a method to measure exposure.

Establishing limits to the amount of drug residue that can be on the outside of drug vials before shipping should be a major priority. This one measure would significantly reduce health care worker exposure. Packaging vials in shrouds or plastic shields has been shown to reduce the drug residue on the outside of the packing.

Additional effort must be made to provide mechanisms to pay for the protective measures needed to at least reduce the exposure and allocate the costs to include the responsibility of the drug manufacturers.

Additional consideration should be given to the fact that a number of the 5.5 million workers will develop cancer, regardless of their occupational exposure, and require drug therapy as patients. With no method to calculate occupational exposure, therapeutic limits on drug doses for drugs with a specific risk level of cancer, such as cyclophosphamide, or life-time dose toxicity, such as the anthracyclines, are impossible to estimate. The risk is definitely increased and any help to determine its significance would be an accomplishment.

Thank you for allowing me to comment on this important subject.

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