The NIOSH Retrospective Pesticide Reference Database

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ABSTRACT. *For the National Institute for Occupational Safety and Health (NIOSH) case-control study of glioma among non-metropolitan residents, pesticide information was considered critical. Responses to open-ended questions about pesticide exposures had to be grouped for analysis. Our aim was to classify pesticide responses in biologically relevant categories. We built the NIOSH Retrospective Pesticide Reference Database (NIOSH-RPRD) on over 1000 pesticide products and chemicals, particularly those likely to be used in the upper Midwest, using multiple sources. We obtained first and last years of product registration and product pesticide ingredients and their relative weights from the U.S. Environmental Protection Agency's Pesticide Product Information System. We added fields for pesticide class (organophosphate, etc.), carcinogenicity ratings, and evidence regarding endocrine-disrupting activity. Participant data were merged with the database, allowing each product recalled by a respondent to be linked to one or more chemicals, as appropriate. Respondents named 1,347 different pesticides (or pesticide-targeted species) used on the farm, at non-farm jobs, or at home. Database usefulness was assessed by comparing numbers of responses naming actual chemicals to total responses linked to those chemicals. Sixty percent of farm pesticide, 59% of non-farm occupational, and 65% of house and garden responses named products, not chemicals. Among farm pesticide users, 182 (46%) reported using a total of 440 pesticides 1 to 40 years (mean 8.5 years) before those pesticides actually were marketed. The NIOSH-RPRD, now available to other investigators, has been a useful tool for us and other researchers to evaluate, group, and correct pesticide responses.*

Keywords. *Agricultural workers, Agriculture, Agrochemicals, Pesticides Classification, Research design, Risk assessment.*

Submitted for review in May 2008 as manuscript number JASH 7492; approved for publication by the Journal of Agricultural Safety and Health of ASABE in January 2009.

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The Upper Midwest Health Study (UMHS), a case-control study of glioma among non-metropolitan residents conducted by the National Institute for Occupational Safety and Health (NIOSH), focused on farmers, so pesticide information was considered critical. The UMHS questionnaire, like those of other case-control studies, included open-ended questions about occupational and environmental exposures. Respondents were asked about pesticides used on the farm, at non-farm jobs, or in their homes and gardens. For our analyses, our aim was to classify pesticide responses in biologically relevant categories.

Various pesticide databases, or chemical databases incorporating a number of pesticides, are available in print or on the internet. Materials focusing on exposure to applicators include data on pesticide poisonings (CDC, 2007), applicator exposure levels (Hamey, 2001; van Hemmen, 1992; van Hemmen and van der Jagt, 2001; Leighton and Neilsen, 1995; Carmichael, 1989), quantities of pesticides used (NCFAP, 2008), and possible long-term effects of exposure (Reprotox, 2007; Gold et al., 1987). Other reference materials focus on environmental exposures, especially ingestion of pesticide-contaminated foods (Troiano et al., 2001; Hamey, 2000; Dornseiffen and van Eck, 2000; Cook et al., 1999; Chan, 1998; FDA, 2004; FAO and WHO, 2006).

For the analysis of UMHS pesticide data, our primary tasks were to confirm that all the substances named by study respondents as pesticides actually were pesticides, to determine the active ingredient(s) in each substance, to obtain information about the potential toxicity and carcinogenicity of each chemical, and to find an appropriate scheme for grouping the chemicals. This article describes the methods we used to achieve these objectives and the results of some pesticide analyses.

Methods

UMHS eligible cases were adults ages 18 to 80 at diagnosis (January 1995 to January 1997) residing in non-metropolitan counties of Iowa, Michigan, Minnesota, and Wisconsin. Possible controls were randomly selected within age and gender strata from state license bureaus (ages 18 to 64) and the Health Care Financing Administration database (ages 65 to 80). Consenting participants (or their proxies) were interviewed at a time and place of their choosing (usually at home) (Carpenter et al., 2008).

Pesticide data were solicited in four questionnaire sections: farm and agricultural chemical work history, non-farm work history, house and garden pesticide use, and medical history. That is, respondents (study participants or their proxies) could report participant exposure from using pesticides on a farm, living on a farm where pesticides were used, using pesticides in non-farm jobs (such as exterminators, janitors, U.S. Army personnel in Vietnam, etc.), house and garden pesticide use, or applying pesticides to the body (anti-lice treatments). The questionnaire is available at www.cdc.gov/niosh/topics/agriculture/UMHS.html or from the first author. Key questions included:

- "Were insecticides ever used on livestock, farm crops, farm buildings, or lots? Insecticides are chemicals used for killing insects, for example, on livestock, farm crops, buildings, or lots."
- "Were herbicides ever used? Herbicides are chemicals used to kill plants or retard plant growth, especially weeds."
- "Were fungicides ever used? Fungicides are chemicals used to kill organisms that cause molds, mildews, rots, and smuts."

- "Were fumigants or miticides ever used? Fumigants are gaseous substances or mixtures of substances that are used to kill insects, bacteria, or rodents. Miticides are substances used to control mites."
- "Did you handle pesticides on any non-farming job that (you/he/she) held for a year or longer?"
- "Did you ever work with pesticides around (your/his/her) home, garden, lawn, or yard?"
- "Did you ever use a prescription shampoo, cream, or lotion to treat lice or scabies such as Kwell?"

A handout listing 429 product names and 113 pesticide chemicals, years of general use, and some crops and crop pests was sent to respondents approximately two weeks before the interview (available at www.cdc.gov/niosh/topics/agriculture/UMHS.html or from the first author). The listed pesticides were selected on the basis of: (1) volume of use in the four study states (Iowa, Michigan, Minnesota, and Wisconsin) through 1985 (to allow at least ten years latency between exposure and possible effect, since cases were diagnosed starting in 1995); and (2) evidence of their toxicity (Sanderson et al., 1997). For many pesticides, the handout included the range of years the pesticide was on the market as well as a list of crops the pesticide was used on.

We created the NIOSH Retrospective Pesticide Reference Database (NIOSH-RPRD) starting with the products and pesticide chemicals in the handout. All other unique products and chemical pesticides named by respondents were added to the database. We then began searches of on-line databases and print references to obtain information on these pesticides (Tomlin, 2003; Krieger, 2001). We added fields for class of pesticide (organophosphate, etc.), carcinogenicity ratings from the International Agency for Research on Cancer, evidence as to whether a pesticide had endocrine-disrupting activity, and other measures of possible toxicity. Table 1 shows the fields included in the database and explains each field.

Many pesticide components are actually the salts or esters of common pesticide chemicals, such as 2,4-D. To link each chemical with the active moiety, we created a variable, BASE_CHEM. For example, the pesticide chemicals 2,4-D butoxyethyl ester, 2,4-D diethanolamine salt, 2,4-D dimethylamine salt, etc., all link to 2,4-D as BASE_CHEM.

The database includes ratings of pesticides for carcinogenicity and toxicity by a number of U.S. and international agencies. We incorporated these ratings so that we could, for example, compare participants who did and did not use pesticides classified by the International Agency for Research on Cancer (IARC) as definite or probable human carcinogens.

The pesticide registration files we downloaded from the Environmental Protection Agency's Pesticide Product Information System (EPA, 2006) were linked in a Microsoft Access database, and a set of queries was developed to extract the information needed for the database. The master database is maintained as an Excel spreadsheet.

The database was merged with study files to compare numbers of questionnaire responses naming a pesticide chemical to total responses linked to that pesticide chemical, to determine how many IARC-designated carcinogens were named by case and control participants, to compare reported dates of first use with official registration dates, and to compare how participants classified pesticides with how the database classified them. All analyses used SAS (SAS, 2006).

Table 1. Variables in the NIOSH Retrospective Pesticide Reference Database.

Variable Name	Explanation
TRADENAME	Commercial tradename, product name. All generic chemical names should be entered as tradenames as well (since study participants interchangeably refer to tradenames and chemical names).
UMHS_ERA	Was this product on the market 1992 or earlier? (N if not, blank if Y or unknown).
SYNONYM	Is this "product name" a known synonym for a generic chemical (e.g., Roundup for glyphosate)? (Y if yes, blank if N or unknown).
EPA_ON	Year this product was registered by EPA. For a generic chemical or its EPA synonym, the earliest year a product containing this chemical was on the market.
EPA_OFF	Year this product's registration was cancelled. For a generic chemical or its EPA synonym, the latest year a product containing this chemical was on the market. EPA_OFF = 3000 if the product/chemical is still on the market.
EPA_REGNAME	For a product, name as it appears in EPA registration database (if not = TRADENAME). For a chemical or its EPA synonym, the number of products in the EPA database containing this chemical.
MFGR	Manufacturer of the product.
MIX	Y if tradenamed product has >1 active ingredients.
EPA_PCT_GNRC	For a product, percentage of this generic as listed in the EPA database. For a chemical or its EPA synonym, the range of percentages among all products containing the chemical.
GENERIC	Name of the chemical/pesticide. In two circumstances, this field will be coded "unknown," "unknown herbicide," etc., depending on whether we know how the tradenamed product was used: 1. We have been unable to locate any information about the tradename or 2. We cannot tell to which of two or more products with the same tradename, but different generic ingredients, the respondent referred.
PCTGNRC	Percentage of this generic among all active ingredients in this product. For example, if active ingredients total 2.5% of total product and this generic is 1% of the total product, then PCTGNRC for this generic would be 0.40 (1/2.5).[a]
BASE_CHEM	If generic is a salt or an ester, the chemical parent. This field was added so that we can code the exact chemicals in a product but yet consolidate for analysis. For example, salts of 2,4-D are widely used. In this database, 2,4-D butoxyethyl ester, 2,4-D diethanolamine salt, 2,4-D dimethylamine salt, etc., all link to 2,4-D as BASE_CHEM.
CAS_1ST	The first part of the CAS number (added so a sort on CAS number, done as a sort on CAS_1ST and then CAS_NUM, results in the CAS numbers being in the correct order (all with 2-digit part first, etc.). For chemicals with authentic CAS numbers, this has 2 to 6 digits. O is used when no CAS number exists; -1 is used when there are multiple CAS numbers (e.g., organophosphates, arsenates).
CAS_NUM	The Chemical Abstract Service number. Blank if CAS_1ST = 0, "many" if CAS_1ST = -1.
CHEMNAME	CAS name, if different from generic name. Very long names (>256 characters) are in a supplement to this codebook.
GENERIC_CMNT	Source of information on the generic. Data in the EPA_ fields should be assumed to be from the EPA database.[b]
TRADE_CMNT	Source of information on the tradename. If coded as synonym and not in the EPA database, then source should be given here.[b]
ACTIVITY	Alkyl, Aryl, Benzimid azone-alkyl, Cyclodiene, Cycloparaffin, Formamidine, Halogen, Halogenated aromatic, O-alkyl phosphorothioate, Phosphate, Phosphonate, Phosphoramidate, Phosphorothioamidate, Phosphorothioate, Organophosphate, or Thiocarbamate.
METAL1	Does this generic contain a heavy metal?[b] If so, which one?
METAL2	Second heavy metal[b] in this generic compound.
SUPERGRP	Grouping of BASE-CHEMs by chemical classes using any of the categorizations. The goal is to have as few groups as possible so that each group will be of sufficient size for analysis.

Table 1 (cont'd). Variables in the NIOSH Retrospective Pesticide Reference Database.

Variable Name	Explanation
TOMLIN_GRP	Grouping of BASE_CHEMs by chemical classes as used in *The Pesticide Manual: A World Compendium* (Tomlin, 2003).
TOMLIN_BIOCHEM	BASE_CHEM biochemistry per *The Pesticide Manual: A World Compendium* (Tomlin, 2003).
TOMLIN_MOA	BASE_CHEM method of action per *The Pesticide Manual: A World Compendium* (Tomlin, 2003).
NCI_CA_STD	National Cancer Institute carcinogen standard.
HCLRSS_GRPS	Grouping of BASE_CHEMs by chemical classes as used in the Compendium of Pesticide Common Names (www.alanwood.net/pesticides/index.html) (Wood, 2007).
GA_PEST_MGT	Grouping of BASE_CHEMs by chemical class, using the Georgia pest management categories (Guillebeau, 2003).
ONTARIO	Grouping of BASE-CHEMs by function, using the Ontario pesticides guidelines (Ontario Pesticides Advisory Committee, 1999, 2006).
NEUROTOX	NE = not evaluated NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers.
NEUTOX_SRC	Citation for neurotoxicity
USE1 USE2 USE3	ac = acaricide (acarids = mites and ticks) al = algacide av = avicide ba = bactericide b-r = bird repellent cs = chemosterilant fg = fungicide fl = fertilizer[c] hb = herbicide no = no pesticide use[c] ns = insecticide ns-a = insect attractant ns-r = insect repellent mc = microbiocide ml-r = mammal repellent md = mating disrupter ml = molluscicide nm = nematicide ps = pesticide synergist p-a = plant activator (defends plant) pgr = plant growth regulator (us. herbicide) rd = rodenticide uk = unknown[d] vr = vermicide vs = virucide wp = wood preservative
MUTAGENICITY	NE = not evaluated NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers.
TERATOGENICITY	NE = not evaluated NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers.

Table 1 (cont'd). Variables in the NIOSH Retrospective Pesticide Reference Database.

Variable Name	Explanation
IARC_HUM	The International Agency for Research on Cancer rating for this BASE_CHEM for human carcinogenicity (online as of March 2004). Choices include: 1 = definitely carcinogenic 2A = probably carcinogenic 2B = possibly carcinogenic 3 = insufficient information to determine NE = not evaluated by IARC NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers.
IARC_ANIM	The IARC rating for this BASE_CHEM for animal carcinogenicity (online as of March 2004). Choices include: ES = evidence suggesting lack of carcinogenicity I = inadequate evidence of carcinogenicity (encompasses "no adequate data") L = limited evidence of carcinogenicity NE = (not evaluated by IARC. Note that some chemicals have a human carcinogenicity rating but no animal carcinogenicity evaluation was provided) NA = (not applicable; used for broad groups of chemicals) NO = (used for "no pesticide use" and fertilizers) S = sufficient evidence of carcinogenicity.
NTP_10ROC	Ratings from the National Toxicology Program Tenth Report on Carcinogens (online as of March 2004). Choices include: K = known human carcinogen NE = not evaluated by NTP R = reasonably anticipated to be human carcinogen.
WHO_TOX	The World Health Organization recommended classification of pesticides by hazard (immediate toxicity) for this BASE_CHEM. Choices include: IA = extremely hazardous, LD50 < 5 mg/kg IB = highly hazardous, LD50 = 5 to 50 mg/kg II = moderately hazardous, LD50 = 50 to 500 mg/kg III = slightly hazardous, LD50 > 500 mg/kg U = unlikely to be hazardous O = obsolete, chemical no longer in use NE = not evaluated by WHO NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers.
SARA	Is this BASE_CHEM on the EPA Title III list of chemicals subject to the emergency planning and community right-to-know act and section 112(r) of the clean air act, as amended? NE = not evaluated by EPA NA = not applicable; used for broad groups of chemicals NO = used for "no pesticide use" and fertilizers Y = yes.

Table 1 (cont'd). Variables in the NIOSH Retrospective Pesticide Reference Database.

Variable Name	Explanation
EPA_OPP	Is this BASE_CHEM on the EPA Office of Pesticide Programs list of chemicals evaluated for carcinogenic potential? ND = chemical is in EPA IRIS database; not evaluated for carcinogenicity. Chemicals classified using 1986 criteria: A = human carcinogen B = probable human carcinogen B1 = limited evidence from epidemiologic studies B2 = inadequate evidence from epidemiologic studies C = possible human carcinogen D = not classifiable as to human carcinogenicity E = evidence of non-carcinogenicity for humans. Chemicals classified using 1996 criteria: K = known to be carcinogenic in humans L = likely to be carcinogenic in humans Q = carcinogenic potential of this chemical cannot be determined N = not likely to be carcinogenic in humans. Chemicals classified using 1999 criteria: H = carcinogenic to humans LC = likely to be carcinogenic to humans S = suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential D = data are inadequate for an assessment of human carcinogenic potential NC = not likely to be carcinogenic to humans q = a potency factor was determined for the chemical CV = EPA interagency Carcinogenic Risk Assessment Verification Endeavor (CRAVE) workgroup assessed the chemical; q and CV data are on file.
EPCRA_CA	Is this BASE_CHEM considered to be hazardous under the Emergency Protection/Community Right to Know Regulations? (EPA, 2008).
ED_Y_N	Is this BASE_CHEM considered to be an endocrine disrupter? Y = yes (all sources agree), Q = perhaps (sources disagree), N = no (all sources agree), blank = not discussed by any sources.
ED_Cooper	Endocrine disruptor? R = reproductive effects, blank = not discussed (Cooper et al., 2007).
ED_Crisp	Endocrine disruptor? D = developmental effects, R = reproductive effects, T = thyroid effects, blank = not discussed (Crisp et al., 1998).
ED_EDSP	Endocrine disruptor? T = chemical to be tested, TI = "inert" ingredient to be tested (EPA, 2007).
ED_NRC	Endocrine disruptor? A+ = androgenic, A- = anti-androgenic, E+ = estrogenic, E- = anti-estrogenic, D = developmental effects, R = reproductive effects, T = thyroid effects, Y = yes (not specified), blank = not discussed (NRC, 2000).
ED_Pocar	Endocrine disruptor? Y = yes, blank = not discussed (Pocar et al., 2003).
ED_Safe	Endocrine disruptor? Y = yes, blank = not discussed (Safe et al., 2000).
ED_Schantz	Endocrine disruptor? A+ = androgenic, A- = anti-androgenic, C = cognitive function effects, E+ = estrogenic, E- = anti-estrogenic, T = thyroid effects, blank = not discussed (Schantz and Widholm, 2001).
ED_Soto	Endocrine disruptor? E = estrogenic (xenobiotic), N = non-estrogenic, blank = not discussed (Soto et al., 1995).
ED_Van Ton	Endocrine disruptor? Y = yes (Van Tongeren et al., 2002).
ED_Notes	Notes about the evidence for endocrine disruption, including misc. references from: Hayes et al., 2006; Vandelac and Bacon, 1999; Ghisari and Bonefeld-Jorgensen, 2005.

Table 1 (cont'd). Variables in the NIOSH Retrospective Pesticide Reference Database.

Variable Name	Explanation
WS_G	Y if chemical name was on list sent before interview to UMHS respondents.
WS_T	Y if tradename was on list sent before interview to UMHS respondents.
GNRC_ONMKT	The year the generic went on the market in the U.S.; blank = not yet known to us.
GNRC_OFF	The year the generic went off the market in the U.S.; blank = not yet known to us (possibly still on market).
TDNM_ONMKT	The year the tradenamed product went on the market in the U.S.; blank = not yet known to us.
TDNM_OFF	The year the tradenamed product went off the market in the U.S.; blank = not yet known to us (possibly still on market). Note: Products known to be still on the market are currently coded "3000" in this field.

[a] Ideally, one would have the total composition of each product and thus could enter the true percentage. However, this would mean knowing, for the "single-ingredient" products as well as the mixes, the names and amounts of any and all "inert substances," solvents, fillers, propellants, etc.

[b] Using the OSHA definition: "generally interpreted to include those metals from periodic table groups IIA through VIA. The semi-metallic elements boron, arsenic, selenium, and tellurium are often included in this classification."

[c] Fertilizer and "no pesticide use" are presumably pesticide free.

[d] Could be known chemical with unknown use or unknown chemical.

Results

The NIOSH-RPRD currently includes over 1000 product and pesticide chemical names. The database also currently includes 413 known pesticide chemicals definitively identified by CAS Registry Number and 14 categories each encompassing two or more CAS chemicals (aliphatic petroleum hydrocarbons, inorganic and organic arsenic compounds, copper compounds, cube extracts, dichloropropane or dichloropropene, organophosphates, phenoxys, phosphorothioates, pyrethroids, rodenticides, sodium methanarsonates, and thiocarbamates).

The 1,347 different pesticide names provided by Upper Midwest Health Study respondents were resolved down to 624 product and pesticide chemical names by AMR and MAB, mostly by correcting spelling and other errors (e.g., "Sara's son" instead of cerusan, "Dual paraquat" instead of separate entries for Dual and paraquat).

Over 85% of the responses given by respondents have been resolved into their pesticide chemical components. However, 35 product names could be linked only to general categories (fungicide, herbicide, insecticide, or pesticide). Examples include "Scotts herbicide" and "Ortho insecticide" (each company manufactures multiple herbicides and insecticides). Seventeen "mystery" products (14C-Carboxy-SD 84811, Alert, Bancide, Bovona oil, Coppies, Delpar, EM-7217, Goban, HDH, Kar, Laxor, Melnor, Methelon, Picizimen, Post, Rotomet, Toxidrew) could not be linked to pesticide chemicals because a reference that provided the chemical ingredients, or even just identified the product as a pesticide, could not be found. Thirty responses such as "unknown insecticide" were linked to one of 13 general categories (algacide, avicide, "fertilizer with pesticide," fumigant, fumigant insecticide, fumigant rodenticide, fungicide, herbicide, insecticide, miticide, acaricide, pesticide, rodenticide, and unknown). In practical terms, the 82 "products" (6.1% of total "products") described above can be included only in the most general analyses of pesticide use. Most were given in response to the section of the UMHS questionnaire devoted to house and garden, not farm or occupational, pesticide use.

Database usefulness in improving our analyses was assessed by comparing numbers of questionnaire responses naming a pesticide chemical to total responses (chemical names and product names) linked to that pesticide chemical; determining how many IARC-designated definite, probable, and possible carcinogens were named by case and control participants; comparing reported dates of first use with registration dates; and comparing how participants classified the pesticides they used with how the database classified them.

Responses by Product Name or Chemical Name

We compared the numbers of questionnaire responses naming a pesticide chemical to total responses (product names and chemical names) linked to that pesticide chemical by using the database. Because the types of pesticides used on the farm, in non-farm occupational settings, and in house and garden differ, as do the users' familiarities with chemicals, we conducted separate analyses for farm, non-farm occupational, and house and garden use, excluding chemicals with fewer than ten total responses.

The only pesticide chemical always identified as such was DDT, with 257, 29, and 90 responses, respectively, for farm, non-farm occupational, and house and garden use. By contrast, over 90% of farm users of alachlor, glyphosate, dicamba, cyanazine, trifluralin, chloramben, metolachlor, chlorpyrifos, bentazon, phorate, imazethapyr, carbofuran, and metribuzin used product-name identifications. Overall, 60% of farm responses were product names rather than pesticide chemicals (results not shown). Over 90% of non-farm occupational users of glyphosate, MCPP, and chlorpyrifos used product-name identifications, as did 90% of house and garden users of carbaryl, glyphosate, MCPP, dicamba, phenoxy, and borax. Overall, 59% of non-farm occupational responses and 65% of house and garden responses were product names rather than pesticide chemicals (results not shown).

"Use" Before Pesticide on Market

We compared the reported start and end years for pesticide use with the years that pesticides went on and off the market. Among 398 farm pesticide users, 182 (46%) reported using a total of 440 pesticides 1 to 40 years (mean 8.5 years) before those pesticides were on the market, and 17 reported using a total of 26 pesticides 1 to 9 years (mean 2.6 years) after those pesticides were no longer marketed. Among 189 participants who stated that they used pesticides on their non-farm jobs, 29 (15%) reported using a total of 93 pesticides 1 to 34 years (mean 10.2 years) before those pesticides were on the market, and 12 reported using a total of 18 pesticides 1 to 9 years (mean 3.3 years) after those pesticides were no longer marketed. Among 1062 participants who stated that they used pesticides in their homes or gardens, 57 (0.5%) reported using a total of 69 pesticides 1 to 39 years (mean 8.4 years) before those pesticides were on the market, and 26 reported using a total of 27 pesticides 1 to 4 years (mean 2.8 years) after those pesticides were no longer marketed.

Definite, Probable, and Possible Carcinogens

We analyzed responses by IARC carcinogenicity ratings. Among 4917 farm responses, 4025 (82%) were resolvable to individual pesticide chemicals (the others named categories such as herbicides or "unknown"). Among resolvable responses, 37 case and 75 control responses linked to nine pesticides that the IARC classifies as group 1 human carcinogens; 276 case and 590 control responses linked to 27 pesticides that the IARC classifies as group 2A and 2B probable and possible human car-

cinogens; and 368 case and 661 control responses linked to 40 pesticides that the IARC classifies as group 3 chemicals; while 762 case and 1256 control responses linked to 106 chemicals not yet evaluated by the IARC. Control responses were more likely than case responses to link to IARC-evaluated chemicals ($\chi^2 = 6.42$, $p < 0.02$), but not more likely to link to IARC group 1 vs. groups 2A-3 chemicals.

Among 647 non-farm occupational responses, 465 (72%) were resolvable to individual pesticide chemicals. Among resolvable responses, one case and ten control responses linked to four pesticides that the IARC classifies as group 1 human carcinogens; 46 case and 109 control responses linked to 18 pesticides that the IARC classifies as group 2B possible human carcinogens; and 23 case and 75 control responses linked to 20 pesticides that the IARC classifies as group 3 chemicals; while 17 case and 184 control responses linked to 66 chemicals not yet evaluated by the IARC. Case responses were more likely than control responses to link to IARC-evaluated chemicals ($\chi^2 = 24.29$, $p < 0.00001$), but not more likely to link to IARC group 1 vs. groups 2A-3 chemicals..

Among 3286 house and garden responses, 1232 (37%) were resolvable to individual pesticide chemicals (unresolvable responses included many over-the-counter pesticides). Among resolvable responses, six case and 17 control responses linked to five pesticides that the IARC classifies as group 1 human carcinogens; 137 case and 281 control responses linked to nine pesticides that the IARC classifies as group 2B possible human carcinogens; and 116 case and 237 control responses linked to 21 pesticides that the IARC classifies as group 3 chemicals; while 153 case and 285 control responses linked to 31 chemicals not yet evaluated by the IARC. Control responses were neither more likely than case responses to link to IARC-evaluated chemicals nor more likely to link to group 1 vs. groups 2A-3 chemicals.

Questionnaire Section vs. Database Classification

Over 99% of the 2279 farm herbicide section responses mapped to "herbicide," 98% of the 1785 farm insecticide section responses mapped to "insecticide," and 89% of the 103 farm fungicide section responses mapped to "fungicide." Only 48% of the 91 farm fumigant section responses mapped to "fumigant"; 31% mapped to "insecticide" and 12% mapped to "rodenticide."

Discussion

We have made extensive use of the NIOSH-RPRD in previous reports on farm pesticide exposure, including applicators and non-users (Carreón et al., 2005; Ruder et al., 2004). The database facilitated analysis by chemical components rather than product names and the grouping together of chemicals of the same class, chemicals having the same activity or structure, or chemicals with the same IARC carcinogenicity rating. NIOSH-RPRD data make it possible to perform analyses focusing on specific elements in compounds, such as heavy metals, arsenic, or halogens.

The pesticide reference data also have quality control applications, permitting quantitative answers to such questions as: Are reported dates of use compatible with when a pesticide was on the market? Is reported mode of use (insecticide, etc.) compatible with intended use? Was personal protective equipment used as suggested in pesticide documentation? These will be relevant in our forthcoming analyses of pesticide applicators, for whom detailed information, such as years of use, was collected.

Our analysis showed that farm pesticide users reported a total of 3731 years, non-farm occupational users a total of 949 years, and home pesticide users a total of 579.5 years of pesticide use before those pesticides became available. (Far fewer years of post-marketing use were reported and could be explained as participants using up pesticides purchased before those pesticides went off the market.) Were we to use the reported dates in our analyses, we would overestimate pesticide exposure for these individuals, biasing the results.

The concordance of farm section responses with database use categories was very good for herbicides, insecticides, and fungicides. The farm fumigant section responses were divided among the use categories fumigant, insecticide, and rodenticide. This indicates that asking about use of a fumigant, a procedure rather than a category of pesticides, may not have been the best way to elicit use of rodenticides. It probably would have been better to ask participants what pesticides they used to kill rodents and other non-insect pests.

One limitation of the database is the problem of product ingredients not itemized in pesticide formulations. "Proprietary chemicals" and ingredients presumed to be inert are not included in formulation listings on labels or material safety data sheets. The definition of inert is "not damaging the crop plant or animal"; these chemicals are not necessarily inert with regard to possible human health effects (New York State, 1996; EPA, 1988).

Only 37% of house and garden pesticide responses were resolvable to individual chemicals, versus 82% of farm and 72% of non-farm occupational responses. The major reason was that companies market a number of formulas with the same or similar tradenames; respondents remembered only the approximate tradenames, so we could not resolve the ingredients. Interviewers of participants in future cross-sectional studies of current house and garden pesticide use could ask to see the pesticide containers; retrospective studies such as ours will have to analyze results by groupings such as herbicides and insecticides rather than chemical groups such as organochlorines and pyrethroids.

Our comparison of pesticide chemicals named in questionnaire responses with pesticide chemicals identified by linkage with the database demonstrates the value of using a database such as the NIOSH-RPRD even for analyses of a single pesticide chemical. When participants, even professional pesticide applicators, are more likely to name a product rather than the corresponding pesticide chemical(s), a comprehensive product-name to pesticide chemical conversion database enhances analyses by increasing numbers of responses linked to each pesticide chemical.

The NIOSH-RPRD is an ongoing project. For some product names reported by study participants, we continue trying to obtain a complete list of components and their relative proportions; for some, we have not yet obtained the range of years during which they were marketed; and for some pesticide chemicals, we have not yet verified the years during which they were available. Once we complete the pesticide analyses for our case-control study, we do not anticipate continuing to update the database. As it stands, however, for retrospective studies covering the period from 1920 to 1993, it is probably fairly comprehensive for the Upper Midwest; for other eras or geographic regions, it would need to be augmented. For studies of immediate health effects, rather than cancer or reproductive effects, data on symptoms of toxicity, as well as the classifications of toxicity already in the database, would be a useful addition to the database.

The NIOSH-RPRD contains information that permits investigators to evaluate pesticide responses provided by participants in a variety of studies. In addition, it provides information to check the validity of the respondent's replies as well as evaluate mechanistic hypotheses.

The NIOSH-RPRD has already been a useful tool for NIOSH and extramural epidemiologists and other environmental and occupational health professionals conducting pesticide exposure assessment on human populations. The most current version of the database will be accessible through the study website (www.cdc.gov/niosh/topics/agriculture/UMHS.html) or from the first author.

Acknowledgements

Our thanks to Richard Dain for searching for some of the product names and entering corresponding pesticide chemicals. The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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