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NWRC Chemical Effects Database – What's Old is New Again

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Abstract: The United States Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services (USDA APHIS WS), National Wildlife Research Center (NWRC) "Chemical Effects Database" is an internet-accessible and searchable database that contains bioassay data records for chemicals evaluated for repellency, toxicity, reproductive inhibition, and immobilization of higher vertebrates, and phytotoxicity. These data are of value for environmental risk assessment, conduct of toxicology studies, and the development of safe, effective, and responsible tools to manage vertebrate pest species that cause damage. Chemical screening studies were conducted from 1943 to 1987 by predecessors of the NWRC, and by the U.S. Geological Survey Patuxent Wildlife Research Center (PWRC), formerly the Patuxent Research Refuge (PRR) and part of the U.S. Fish and Wildlife Service. The screening activities were broadly divided into 2 phases. Data collected primarily at the PRR prior to 1960 are published in DeWitt et al. (1953) and Bowles et al. (1974). Research after 1960 was conducted at the Denver Wildlife Research Center (DWRC). Much of these data are also published and now accessible by searching the online "Chemical Effects Database" located on the NWRC website (http://www.aphis.usda.gov/wildlife_damage/nwrc/information_services/chemical_effects.shtml). The database search capabilities provide easy access to approximately 11,000 bioassay data records for nearly 2,000 chemicals.

Key Words: chemical, Chemical Effects Database, National Wildlife Research Center, pesticide, repellent, toxicant, risk assessment, USDA, wildlife

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INTRODUCTION

Two federal laboratories conducted an intense chemical screening program from 1942 to 1987. The program goals were to discover new chemicals for eventual development as toxicants, repellents, immobilizing agents, and reproductive inhibitors for use in management and control of vertebrate species; and to evaluate the potential hazards of many of these chemicals on non-target species. To that end, these laboratories conducted bioassays on several mammal, bird, amphibian (specifically bullfrogs), and plant species to screen over 10,000 chemicals in all (Schafer and Bowles 2004). Research was conducted at two principal facilities, 1) the U.S. Fish and Wildlife Service Patuxent Research Refuge, Laurel, MD (PRR), renamed the Patuxent Wildlife Research Center (PWRC) around 1956, and currently a U.S. Geological Survey facility; and 2) the U.S. Fish and Wildlife Service Wildlife Research Laboratory (WRL), renamed the Denver Wildlife Research Center (DWRC) in 1959, transferred to the U.S. Department of Agriculture in 1985, and currently the National Wildlife Research Center, Fort Collins, CO (NWRC).

Although the initial screening assays were conducted nearly 70 years ago, these data may represent the only available toxicity, repellency, reproductive inhibition, immobilization, and phytotoxicity data available for many of these chemicals, and represent millions of dollars of research that would likely never be repeated today. Consequently, these data are a potentially rich source of information useful for environmental and human health risk assessments, conduct of toxicity studies, and even as a potential source for new products.

We describe the new internet-accessible and searchable NWRC Chemical Effects Database containing nearly 11,000 bioassay records and data for more than 2,000 chemicals. The online database comprises published information from 21 sources (Table 1). Additional unpublished data are also available in the NWRC Toxicity Database, which is accessible to NWRC staff and available to the public upon request. Copies of the raw data paper records may also be obtained by contacting NWRC.

DATA DEVELOPMENT

In 1942, according to the Boston City Health Department, it was estimated that rats were responsible for $200 million of damage annually in the U.S. (Society for Science and the Public 1942, Keiner 2005). The impetus for the chemical screening program grew out of a shortage of pesticide products, primarily for rodent control, that were a direct result of World War II. Prior to the war, arsenic compounds, barium carbonate, cyanides, red squill, strychnine, thallium sulfate, and zinc phosphide were all available to control rodents (Ward 1946). An example of wartime disruption was the unavailability of red squill. This product, plant-derived from the Mediterranean area, became unavailable due to global shipping disruptions, including the forced

Table 1. Complete chemical testing citation listing of publications to date, containing approximately 11,000 bioassay results for nearly 2,000 chemicals from the DWRC (approximately 1960-1987) and cataloged under the DRC system. Note that 2 important primary publications containing bioassay data from the PRR and the WRL prior to approximately 1960 are DeWitt et al. (1953) and Bowles et al. (1974).

Publications Reporting Chemical Test Results Cataloged Under the DRC System (1960 - 1987)
DeCino, T. J., D. J. Cunningham, and E. W. Schafer, Jr. 1966. Toxicity of DRC-1339 to starlings. J. Wildl. Manage. 30(2):249-253.
Frank, F. R., E. W. Schafer, Jr., and J. L. Guarino. 1970. Laboratory and field studies with an avian repellent for sprouting seeds. Proc. Bird Control Seminar 5:86-89.
Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Resource Publication No. 153, U.S. Fish and Wildlife Service. 90 pp.
Kverno, N. B., G. A. Hood, and W. E. Dodge. 1967. Development of chemicals to control forest wildlife damage. Pp. 222-226 *in*: Proc. Soc. Am. Foresters (Sept. 12-15, 1966, Seattle, WA).
Schafer, E. W. 1972. The acute oral toxicity of 369 pesticidal, pharmaceutical and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21:315-330.
Schafer, E. W., Jr., and W. A. Bowles Jr. 1985. Acute oral toxicity and repellency of 933 chemicals to house and deer mice. Arch. Environ. Contam. Toxicol. 14:111-129.
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Schafer, E. W., Jr., and R. B. Brunton. 1971. Chemicals as bird repellents: Two promising agents. J. Wildl. Manage. 23(3):569-572.
Schafer, E. W., Jr., and R. B. Brunton. 1979. Indicator bird species for toxicity determinations: Is the technique usable for test method development? Pp. 157-168 *in*: J. R. Beck (Ed.), Vertebrate Pest Control and Management Materials. Special Technical Publ. No. 680, American Society of Testing and Materials, Philadelphia, PA.
Schafer, E. W., Jr., R. B. Brunton, and D. J. Cunningham. 1973. A summary of the acute toxicity of 4-aminopyridine to birds and mammals. Toxicol. Appl. Pharmacol. 26:532-538.
Schafer, E. W., Jr., R. B. Brunton and N. F. Lockyer. 1976. Evaluation of 45 chemical as chemosterilants in adult male quail. J. Reprod. Fertil. 48:371-375.
Schafer, E. W., Jr., R. B. Brunton, E. C. Schafer, and G. Chavez. 1982. Effects of 77 chemicals on reproduction in male and female coturnix quail. Ecotoxicol. Environ. Safety 6:149-156.
Schafer, E. W., Jr., and D. J. Cunningham. 1972. An evaluation of 148 compounds as avian immobilizing agents. Special Scientific Report-Wildlife No.150, U.S. Fish and Wildlife Service. 30 pp.
Schafer, E. W., Jr., J. L. Guarino, and R. B. Brunton. 1977. Use of male coturnix quail in the laboratory development of avian chemosterilants. Pp. 225-236 *in*: W. B. Jackson and R. E. Marsh (Eds.), Test Methods for Vertebrate Pest Controls and Management Materials. Special Technical Publ. No. 625, American Society of Testing and Materials, Philadelphia, PA.
Schafer, E. W., R. I. Starr, D. J. Cunningham, and T. J. DeCino. 1967. Substituted phenyl N-methyl carbamates as temporary immobilizing agents for birds. J. Agric. Food Chem. 15(2):287-289.
Schafer, E. W., R. I. Starr, D. J. Cunningham and T. J. DeCino. 1973. Comparative toxicity of seventeen pesticides to the Quelea, house sparrow and red-winged blackbird. Toxicol. Appl. Pharmacol. 26:154-157.
Schafer, E. W., R. R. West, and D. J. Cunningham. 1969. New starling toxicant: DRC-1347. Pest Control 37(9):22,24,30.
Shefte, N., R. L. Bruggers, and E. W. Schafer, Jr. 1982. Repellency and toxicity of three bird control chemicals to four species of African grain-eating birds. J. Wildl. Manage. 46:453-457.
Shumake, S. A., S. E. Gaddis, and W. E. Schafer, Jr. 1976. Behavioral responses of quelea to methiocarb. Proc. Bird Control Seminar 7:250-254.
Tucker, R. K., and D. G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. Resource Publication No. 84, U.S. Fish and Wildlife Service. 131 pp.

closure of North African ports. Thallium sulfate, another affected rodenticide, was placed under allocation of the War Protection Board during the Pacific Campaigns, and diverted from domestic use to Pacific locations where bubonic plague was prevalent. In addition, the military forces encountered tsutsugamushi disease (Ward 1945, 1946; Keiner 2005). This rickettsial disease is transmitted to humans via a bite from a parasitic mite found on rats.

In response to these rodenticide shortages, the U.S. Government Office of Scientific Research and Development (OSRD) funded initial rodenticide research to identify potential new products (Ward 1945, Keiner 2005). Toxicity and repellency bioassay screening of chemicals on rodents began at the PRR and at the WRL. A timeline of significant research activities is shown in Table 2. While we could not determine the duration of the funding for this program, the OSRD was disbanded on December 31, 1947. Some contracts were transferred to the U.S. Army Quartermaster Corps, Natick Laboratories (Stewart 1948).

Chemicals for testing were solicited or accepted by the PRR from chemical, pesticide, and drug companies, or contributed by other government entities or individuals for testing (Keiner 2005). Between 1946 and 1954, 4,585 chemicals were screened at PRR (Kverno 1954). The most promising chemicals were sent to the WRL for further testing. By 1955, the WRL had received 335 chemicals from the PRR and also had accepted some chemicals for screening from other cooperators (Spencer and Kverno 1955). This work continued through 1959. Data from this period are reported in 2 primary

publications: DeWitt et al. (1953) and Bowles et al. (1974). The records for many of these tests, including some unpublished data, were transferred to the DWRC and currently reside in the NWRC Archives and the National Archives at Denver, CO.

In 1959, when the U.S. Fish and Wildlife Service WRL was renamed the Denver Wildlife Research Center (DWRC), the PRR had also been renamed (in 1956) to the PWRC. The role of the PWRC in this chemical screening program essentially ended, and research emphasis shifted to the study of environmental contaminants (Perry 2004). Congress also mandated the DWRC to establish a program for the study impacts of pesticides on wildlife (NWRC website, accessed July 20, 2012). The DWRC program ended in 1976 when the USFWS environmental contaminant research activities were consolidated at the PWRC. The data from this program are published in Tucker and Crabtree (1970) and Hudson et al. (1984). Building on the existing screening program for rodent toxicants and repellents, a new phase of testing at the DWRC was initiated to include bioassays to identify potential markers, emetics, antiemetics, immobilizing agents, tranquilizers, and chemosterilants on a variety of wild and domestic birds and mammals, and potential phytotoxic effects of some chemicals on plants.

Over the years, emphasis on specific agricultural concerns resulted in the conduct of several projects. Toxicity, repellency, and phytotoxicity studies were conducted beginning in 1960 with the goal of protecting reforestation and range re-vegetation areas from bird and mammal damage (Kverno and Hood 1963). Approximately 800 chemicals were screened per year for 2 years. For the next several years, fewer chemicals were screened, but studies were more targeted, and included laboratory, enclosure, and field studies (Kverno et al. 1967). After 1964, there was an emphasis on the development and application of chemicals and chemical classes having known repellent activities that were uncovered in the initial testing (Bowles et al. 1974).

The impact of bird damage to agricultural crops ushered in testing of chemicals as potential avian immobilizing agents, toxicants, and repellents, beginning in 1961 (Starr et al. 1964). Schafer and Cunningham (1972) reported bioassay results for 148 immobilizing agents. Potential acute avian toxicant bioassay results of 369 chemicals are reported in Schafer (1972). Schafer and Brunton (1971) reported 724 chemicals were screened for avian repellency since 1961. A program to research potential avian chemosterilents was conducted from 1972 to 1978 on 51 chemicals (Schafer et al. 1982). The data for 45 of these chemicals was published in Schafer et al. (1976). The DWRC cooperated with the USDA Agricultural Environmental Quality Institute in 1979 to evaluate 55 naturally occurring and related compounds for avian repellency (Schafer and Jacobson 1983).

Some chemicals submitted for screening were provided as blind samples until 1967, when all were required to be identified before testing. As a result, cataloging systems were developed for tracking purposes: one at the PRR, and one at the DWRC. Dr. J. B. DeWitt, a researcher at the PRR, developed a catalog of approximately 7,000 chemicals tested at the PWRC and the WRL from 1942 through 1959, using "DR" numbers, which refers to "DeWitt Research". The data developed at the DWRC was compiled under the "DRC (Denver Wildlife Research Center) Chemical Tracking System." Approximately 6,800 DRC numbers were assigned. Schafer and Bowles (2004) estimated that over 10,000 unique chemicals were screened during the entire 45-year chemical screening period by both laboratories, although the exact number may never be known.

DATA RETRIEVAL

There are 3 options for retrieving the chemical screening bioassay data cataloged in the "DRC Chemical Tracking System". First, the original records residing in the NWRC Archives and the National Archives may be accessed by NWRC personnel upon request. Second, in 1981, the U.S. Environmental Protection Agency (EPA) provided funding to begin a process of archiving and compiling these data, with the goal of facilitating EPA activities related to hazard evaluation (Schafer, June 6, 1983, United States Government Memorandum to Director, Wildlife Research Center, Denver). As a result, a subset of these data has been compiled into the "Toxicity Database," also accessible by NWRC personnel upon request. This subset of data consists of approximately 14,000 bioassay results that have been verified for chemicals cataloged using the DRC identification system, which includes data from research conducted at the DWRC from 1959 to 1987. Third, a subset of the 14,000 bioassay results have been published in 21 publications, reporting on nearly 11,000 bioassay results for over 2,000 chemicals. These published data have been compiled into the new publicly accessible on-line NWRC Chemical Effects Database.

It is important to note that data prior to 1959 from the PRR and the WRL are cataloged using the "DR Chemical Tracking System" and are not included in the internet-accessible database. However, the 2 primary publications from this period (DeWitt et al. 1953 and Bowles et al. 1974) contain a significant number of bioassay results. These 2 works are somewhat obscure but are available as PDF documents on the NWRC website.

NWRC Chemical Effects Database

The "NWRC Chemical Effects Database" is accessible on the NWRC website at http://www.aphis.usda.gov/wildlife_damage/nwrc/information_services/chemical_effects.shtml. The site provides a browse option including several chemical and species parameters, and a search option that allows the user to create a query with bioassay test, chemical, and species parameters. When searching for chemical data, it is recommended to search using the Chemical Abstract System (CAS) number. The results output may be a table that can by copied into a spreadsheet, or as a Comma Separated Values (CSV) file.

Three other pages on the site contain important metadata and other information for users of these data:

1) The "About the Date" page contains back-

ground information about the chemical screening program, hotlinks to pertinent citations, and NWRC contact information for anyone wanting to request a search of the NWRC Toxicity Database or access the NWRC Archives.

2) The "Published Bioassay Data Citations" page contains all 21 citations of the published data, also shown in Table 1, with hotlinks to PDFs of each publication.

3) The "Testing Methodology and Glossary of Terms" page provides definitions of the various test methods that were used in the studies, and where possible, hotlinks to references describing the methodologies. This information is especially important, as test methodologies have changed over time.

Table 2. Timeline of selected chemical screening activities (1942 - 1987).

Activity	1942-1945	1946-1950	1951-1955	1956-1960	1961-1965	1966-1970	1971-1975	1976-1980	1981-1985	86-87
Chemical screening funded by US Office of Scientific Research and Development [a b]										
Patuxent Research Refuge (PRR) chemical screening program [c]										
Rodent repellent & toxicity testing for US Army Quartermaster Corps conducted by PRR & WRL [d e]										
PRR screened 4,585 chemicals [f]										
WRL tests 335 promising chemicals identified by PRR [g]										
DWRC conducts Pesticide-Wildlife Ecology Program [h]										
DWRC conducts avian & mammal repellent and toxicity testing & phytotoxicity testing to protect reforestation & range revegetation [i]										
DWRC conducts testing of 148 chemicals as potential avian immobilizing agents [j]										
DWRC conducts testing of 369 chemicals as potential avian toxicants [k]										
DWRC conducts testing of > 700 chemicals as potential avian repellents to protect seed and agricultural crops [l]										
DWRC conducts screening of 51 potential avian chemosterilants [m]										
DWRC with the USDA Ag. Environ. Qual. Institute begins testing of naturally occurring chemicals (and related chemicals) as potential avian repellents & toxicants [n]										
DWRC screened >2000 chemicals for avian toxicity, repellency & hazard potential [o]										

[a] Ward 1946
[b] Stewart 1948
[c] Kverno et al. 1967
[d] Tigner 1966
[e] Keiner 2005
[f] Kverno 1954
[g] Spencer and Kverno 1955
[h] NWRC website accessed July 20, 2012, Tucker and Crabtree 1970, Hudson et al. 1984
[i] Kverno and Hood 1963
[j] Schafer and Cunningham 1972
[k] Schafer 1972
[l] Schafer and Brunton 1971
[m] Schafer et al. 1982
[n] Schafer and Jacobson 1983
[o] Schafer et al. 1983

DATA APPLICATIONS

These data include a large and unique archive of chemical bioassay data in danger of becoming largely forgotten outside of limited circles within the Federal agencies and others who were involved with the projects. Such a loss could result in needless repetition of animal studies, or hinder risk assessment efforts because of belief that no data exists to inform the process. There may also be potential vertebrate control products for development that were dismissed at the time, but may have value today due to advances in technology and application techniques. While testing methodologies have evolved over time and sample sizes may have been small, especially during initial screening assays, the data may provide a starting point for risk assessors and research scientists designing studies or investigating new pesticide products. In fact, NWRC encourages users of these data to contact the NWRC Archives for access to the original data sheets to evaluate the appropriateness for any given application. The availability of the internet-accessible NWCR Chemical Effects Database is intended to provide easy access to the published data from the 45 years of chemical screening research, and to also remind potential users of the additional data available by contacting the NWRC.

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Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Resource Publication No. 153, U.S. Fish and Wildlife Service. 90 pp.

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Perry, M. C. 2004. The evolution of Patuxent as a research refuge and a wildlife research center. USGS Patuxent Wildlife Research Center, Laurel, MD. 20 pp.

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