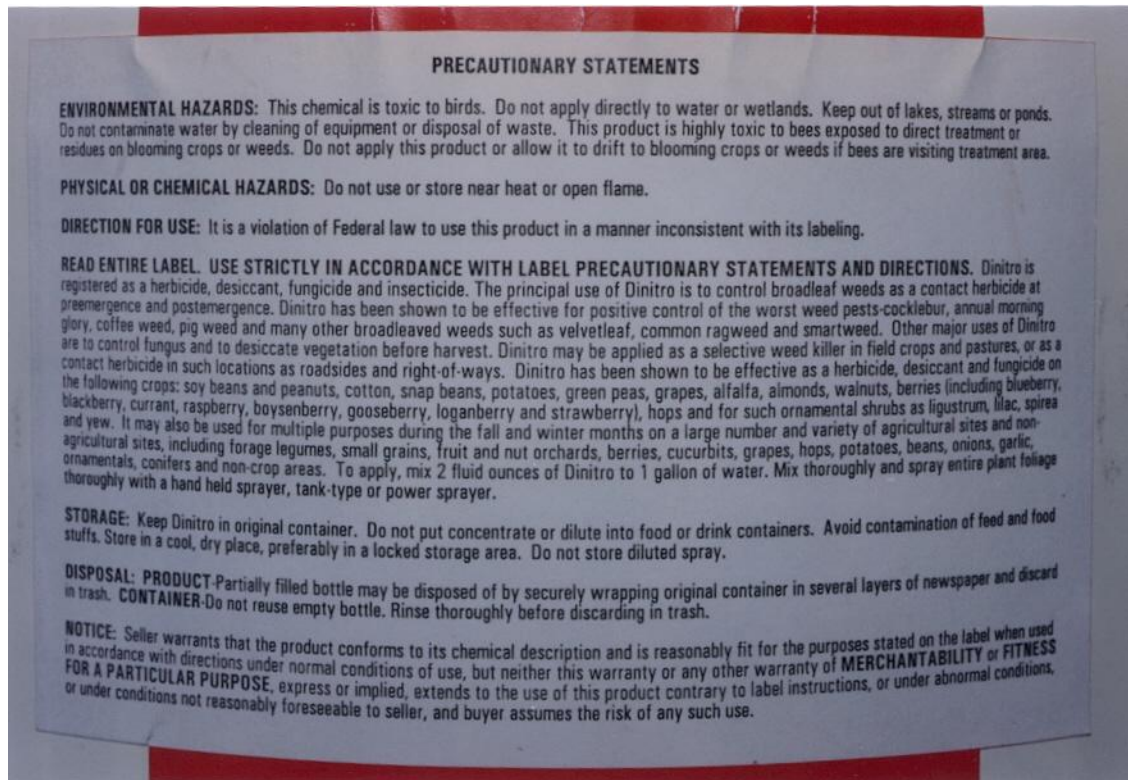
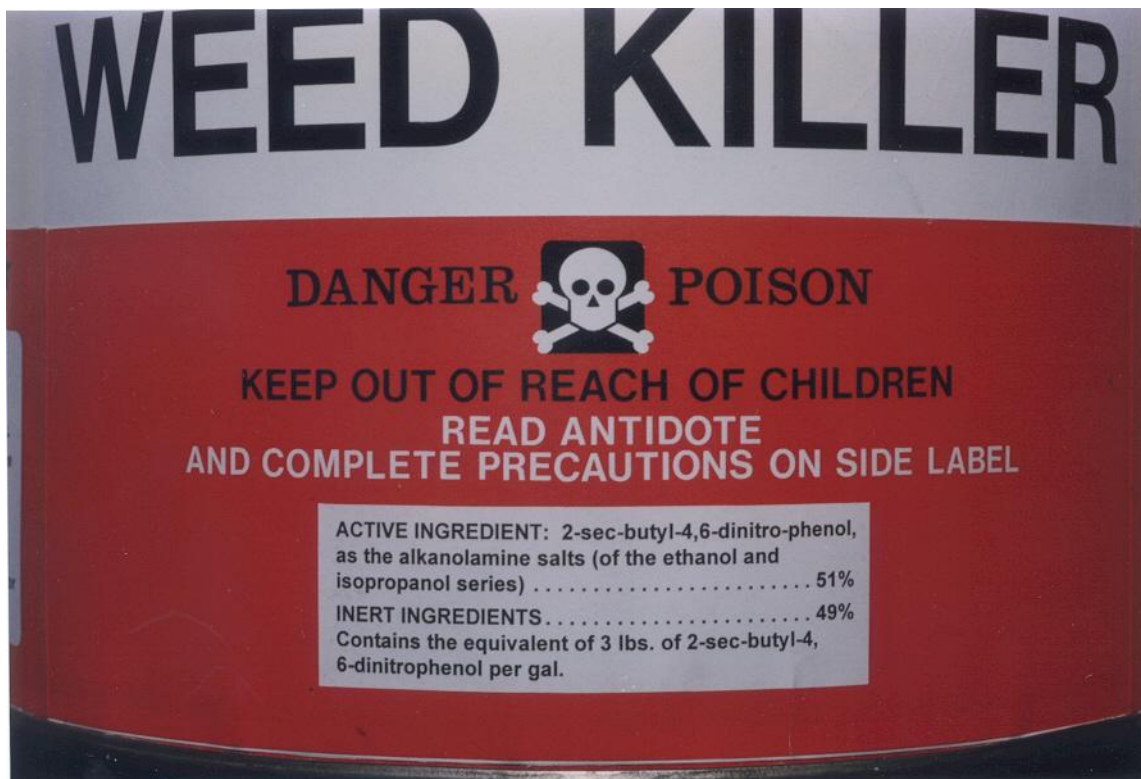


Labeling on can sold to Wilson





Tax and Credits**Standard Deduction for Most People**

Single: \$4,300
 Head of household: \$6,350
 Married filing jointly or Qualifying widow(er): \$7,200
 Married filing separately: \$3,600

34	Amount from line 33 (adjusted gross income)	34	30,000
35a	Check if: <input type="checkbox"/> You were 65 or older, <input type="checkbox"/> Blind; <input type="checkbox"/> Spouse was 65 or older, <input type="checkbox"/> Blind. Add the number of boxes checked above and enter the total here. 35a		
b	If you are married filing separately and your spouse itemizes deductions or you were a dual-status alien, see page 30 and check here. 35b		
36	Enter your itemized deductions from Schedule A, line 28, OR standard deduction shown on the left. But see page 30 to find your standard deduction if you checked any box on line 35a or 35b or if someone can claim you as a dependent	36	7,200
37	Subtract line 36 from line 34	37	22,800
38	If line 34 is \$94,975 or less, multiply \$2,750 by the total number of exemptions claimed on line 6d. If line 34 is over \$94,975, see the worksheet on page 31 for the amount to enter	38	5,500
39	Taxable income. Subtract line 38 from line 37. If line 38 is more than line 37, enter -0-	39	17,300
40	Tax (see page 31). Check if any tax is from a <input type="checkbox"/> Form(s) 8814 b <input type="checkbox"/> Form 4972	40	2,599
41	Credit for child and dependent care expenses. Attach Form 2441	41	
42	Credit for the elderly or the disabled. Attach Schedule R	42	
43	Child tax credit (see page 33)	43	
44	Education credits. Attach Form 8863	44	
45	Adoption credit. Attach Form 8839	45	
46	Foreign tax credit. Attach Form 1116 if required	46	
47	Other. Check if from a <input type="checkbox"/> Form 3800 b <input type="checkbox"/> Form 8396 c <input type="checkbox"/> Form 8801 d <input type="checkbox"/> Form (specify)	47	
48	Add lines 41 through 47. These are your total credits	48	
49	Subtract line 48 from line 40. If line 48 is more than line 40, enter -0-	49	2,599

Other Taxes

50	Self-employment tax. Attach Schedule SE	50	
51	Alternative minimum tax. Attach Form 6251	51	
52	Social security and Medicare tax on tip income not reported to employer. Attach Form 4137	52	
53	Tax on IRAs, other retirement plans, and MSAs. Attach Form 5329 if required	53	
54	Advance earned income credit payments from Form(s) W-2	54	
55	Household employment taxes. Attach Schedule H	55	
56	Add lines 49 through 55. This is your total tax	56	2,599

Payments

57	Federal income tax withheld from Forms W-2 and 1099	57	2,400
58	1999 estimated tax payments and amount applied from 1998 return	58	
59a	Earned income credit. Attach Sch. EIC if you have a qualifying child		
b	Nontaxable earned income; amount and type	59a	
60	Additional child tax credit. Attach Form 8812	60	
61	Amount paid with request for extension to file (see page 48)	61	
62	Excess social security and RRTA tax withheld (see page 48)	62	
63	Other payments. Check if from a <input type="checkbox"/> Form 2439 b <input type="checkbox"/> Form 4136	63	
64	Add lines 57, 58, 59a, and 60 through 63. These are your total payments	64	2,400

Refund

Have it directly deposited! See page 48 and fill in 66b, 66c, and 66d.

65	If line 64 is more than line 56, subtract line 56 from line 64. This is the amount you OVERPAID	65	
66a	Amount of line 65 you want REFUNDED TO YOU	66a	
b	Routing number	c	Type: <input type="checkbox"/> Checking <input type="checkbox"/> Savings
d	Account number		
67	Amount of line 65 you want APPLIED TO YOUR 2000 ESTIMATED TAX	67	

Amount You Owe

68	If line 56 is more than line 64, subtract line 64 from line 56. This is the AMOUNT YOU OWE . For details on how to pay, see page 49	68	199
69	Estimated tax penalty. Also include on line 68	69	

Sign Here

Joint return? See page 18. Keep a copy for your records.

Under penalties of perjury, I declare that I have examined this return and accompanying schedules and statements, and to the best of my knowledge and belief, they are true, correct, and complete. Declaration of preparer (other than taxpayer) is based on all information of which preparer has any knowledge.

Your signature	Date	Your occupation	Daytime telephone number (optional)
Spouse's signature. If a joint return, BOTH must sign.	Date	Spouse's occupation	

Paid Preparer's Use Only

Preparer's signature	Date	Check if self-employed <input type="checkbox"/>	Preparer's SSN or PTIN
Firm's name (or yours if self-employed) and address	EIN		ZIP code

REPORT OF ARTHUR STEELE

Arthur Steele
123 Broadway
Denver, Colorado

November 6, YR-5

Scientific Examination and Evaluation of Chemical Accident in Franklin, Roosevelt, August 4, YR-5

Introduction

Scientific examination and evaluation were requested of a chemical container to determine the cause of an accident during which a user of the container splashed chemical onto his person. Mr. David Wilson was pouring from a 5-gallon container of Dinitro herbicide into a 1-gallon pail. As Mr. Wilson was tipping the can to pour the chemical, the bottom of the can slipped and chemical splashed onto various parts of his body. The 5-gallon can had a flexible spout on the top of the can. There was no reported leaking around the spout.

Examination and Evaluation

Examination of the involved components conclusively establishes that the splashing of the chemical onto Mr. Wilson was a result of the design of the spout. The use of the flexible spout on a 5-gallon container of hazardous liquid chemicals renders the container unreasonably dangerous to reasonably foreseeable slippage of the container during pouring.

The environment of use of a product must be considered before design of the product is completed. Foreseeable hazards should be designed out of the product, if possible. If hazards cannot be designed out, they should be guarded against. If guards are not feasible, then adequate warnings and instructions should be used.

It was to be expected that the herbicide would be used by farmers in the field and foreseeable that portions of the liquid herbicide would have to be transferred from the container in which it was sold to other containers for transfer to spraying equipment. There are potential hazards associated with spilling or splashing the liquid chemical on one's person.

To design out these hazards associated with transferring the chemical, the shape of the container could be designed differently to broaden the base, thereby creating a more stable surface and alleviating the risk of accidental tipping of the container during transfer of the chemical. Another design change that would have alleviated the risk of injury would be to use a rubber bulb siphon. An appropriately designed siphon and tube would have eliminated the need to tip

the container at all. Finally, yet another alternative means would be to place a spigot near the bottom of the can.

Considering the environment of use of the chemical container, the reasonably foreseeable hazards associated with spilling and splashing the chemical during transfer operations, and the ready availability of alternative designs known in the art to eliminate the hazards, the design of the container was unreasonably dangerous to the normal and foreseeable use to which it was being put at the time of Mr. Wilson's accident. The appropriate design hierarchy is first to design hazards out of the product, second, to design additional safety features to guard against hazards, and third, to warn and instruct. The use of warnings or instructions in place of designing out the hazard or designing in additional safety features is in my opinion negligence and renders the design defective.

A handwritten signature in black ink, appearing to read 'Arthur Steele', written over a horizontal line.

Arthur Steele

REPORT OF HAROLD WHITEHOUSE

December 5, YR-5

Comments about Scientific Examination and Evaluation of Arthur Steele

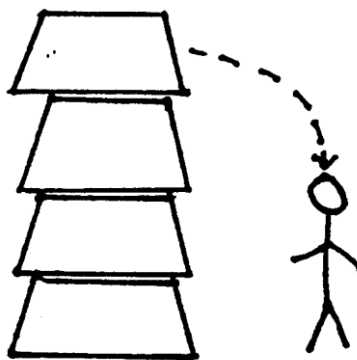
Introduction

The report of Mr. Arthur Steele, dated November 6, YR-5 and entitled "Scientific Examination and Evaluation of Chemical Accident in Franklin, Roosevelt, August 4, YR-5" has been reviewed. Mr. Steele is of the opinion that the use of a flexible spout rendered the 5-gallon liquid chemical container unreasonably dangerous to reasonably foreseeable slippage of the container during pouring of the chemical. He recommends three alternatives: (1) use a different container shape to alleviate tipping hazards; (2) use a spigot; or (3) use a siphon bulb. Each of these alternatives creates hazards and other problems as discussed below.

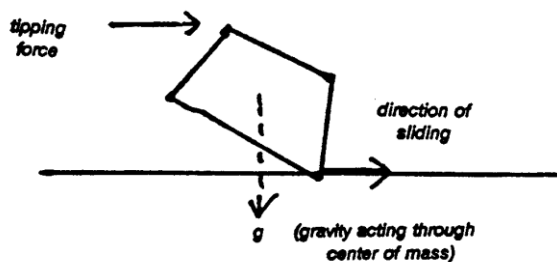
1. Alternative shape of the container.

To alleviate a tipping problem, the container must be configured so that the center of gravity (center of mass) does not extend past the base of the container during pouring of the chemical. If this is to be accomplished by increasing the area of the base, then falling hazards and sliding hazards may be created as follows:

A. Falling Hazard:



B. Sliding Hazard:



A falling hazard would be present whenever the containers are stacked. A sliding hazard is created by the tendency of the container to try to right itself. On a low friction surface, the edge of the container can slip or slide along the surface, thereby exacerbating the risk of splashing the chemical.

There is also the problem created by changing the design and therefore the performance characteristics of a container that consumers have become accustomed to using. Consumer expectations and behavior are difficult to change even with specific instructions and warnings.

Finally, the cost of designing and manufacturing a new container would probably outweigh the risks associated with accidental splashing or spilling.

2. Use of a Spigot

The use of a spigot (or stop-cock) increases the risk of leakage because spigots protrude from a container and can be damaged by impacts. In particular, a spigot located near the bottom of a container makes leakage a virtual certainty if the spigot is damaged. A spigot located near the top of a container would still require that the container be tipped or tilted to dispense the chemical.

3. Use of a Siphon Bulb

The use of a siphon bulb would require a detached, additional component. This component can be lost. Its absence would require that the container be tipped or tilted. Without a flexible spout, loss of the siphon bulb increases the risk of splashing or spilling.

Use of a siphon would require additional instructions that illiterate users could not understand.

Finally, users who are instructed to use a siphon to dispense the chemical may prime the siphon hose by mouth if the siphon bulb is lost or damaged. This could lead to ingestion of the chemical.


HAROLD WHITEHOUSE

**IN THE CIRCUIT COURT OF FARRAH COUNTY
STATE OF ROOSEVELT**

**DAVID OTIS WILSON and
DEBRA B. WILSON,**

Plaintiffs,

v.

**THE ROE CHEMICAL COMPANY,
INC.,**

Defendant.

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Civil No. YR-4-1001

JURY INSTRUCTIONS

(In addition to the customary charges given in any civil action involving issues of tort liability such as weight of evidence, burden of proof, etc., the following specific charges have been approved by the court and will be read in full.)

1. It is the law that the manufacturer, supplier, or seller who markets a product which is in a condition unreasonably dangerous to the ultimate user or consumer when placed on the market and which remains in substantially the same condition until used by the ultimate user is liable to one who may be reasonably expected to use or be affected by such product when used for its intended use and who is injured as a proximate consequence of the unreasonably dangerous product.
2. The plaintiff charges (1) that he suffered injury or damages to himself proximately caused (2) by one who sold a product in a (3) defective condition or which was unreasonably dangerous (4) to him as the ultimate user or consumer and (5) that the seller was engaged in the business of selling such a product and that (6) the product was expected to, and did, reach the user and consumer without substantial change in the condition in which it was sold.
3. The plaintiff charges that the weed killer and its container were defective in manufacturing and design and were used as they were intended or were reasonably foreseeable to be used. Defective means unreasonably dangerous.
4. A defect is that which makes the product unreasonably dangerous. Unreasonably dangerous means the product sold must be dangerous to an extent beyond that which would be contemplated by the ordinary consumer who buys it.
5. An act or omission is a proximate cause of an injury if it was a substantial factor in bringing about the injury; that is, if it had such an effect in producing the injury that reasonable men would regard it as a cause of the injury.

6. The plaintiff also charges that such product and the container in which it was sold was defective in its warning and instructions. When a seller or manufacturer has reason to anticipate that damage may result from a particular use, he may be required to give adequate warning of the danger, and a product sold without such warning is in a defective condition.
7. Where a product contains ingredients to which a substantial number of the population are allergic and ingredients are those whose danger is not generally known, or if known is one which consumers would reasonably not expect to find in a product, the seller is required to give warning against it if he has knowledge of the danger.
8. The seller and manufacturer of a product whose use could result in foreseeable harm has a duty to give a warning which adequately advises the user of the attendant risks and which provides specific directions for safe use.
9. The warning must adequately indicate the scope of the danger and must reasonably communicate the extent or seriousness of harm that could result.
10. Failure to give adequate warnings renders the product unreasonably dangerous.
11. The manufacturer must also provide sufficient instructions with the product to permit it to be used with reasonable safety. Supplying even adequate instructions will not satisfy the manufacturer's duty to warn if the user is not hereby alerted to the hidden dangers in the product.
12. A manufacturer or other defendant whose product is accompanied by warnings or instructions, is entitled to assume that appropriately worded warnings or instructions will be heeded by those who receive them.
13. It is a question of fact for the jury whether particular warnings or instructions are appropriately worded
14. The law places the burden on the plaintiff to reasonably satisfy you of the truthfulness of each of the material elements of his claim. If you are not reasonably satisfied that the plaintiff has met this burden, then you will find that the defendant is not liable. If, however, you are reasonably satisfied that the plaintiff has met the burden of proving the material elements of his claim, then you will consider the following affirmative defense asserted by the defendant.
15. The defendant contends that the plaintiff was comparatively at fault. Comparative fault is negligence on the part of the plaintiff which combining with a defect in a product contributes as a proximate cause in bringing about the injury.
16. Comparative fault, if any, on the part of the plaintiff does not bar recovery by plaintiff against the defendant, but the total amount of damages to which plaintiff would otherwise

be entitled shall be reduced by the percentage that the plaintiff's comparative fault contributed as a proximate cause of his injury.

17. If the plaintiff is more than 50% at fault, he is barred from recovery.
18. The negligence of the plaintiff, David Wilson, does not reduce or bar Debra Wilson's recovery, if you find the defendant at least 1% at fault and that she suffered damages.
19. Negligence is the doing of something which a reasonably prudent person would not do, or the failure to do something which a reasonably prudent person would do, under circumstances similar to those shown by the evidence. It is the failure to use ordinary or reasonable care.
20. It is the law that mere compliance with federal statutes, regulations, or agencies is not a complete defense to a manufacturer or seller.

If after a consideration of all the evidence in this case, you are not reasonably satisfied of the truthfulness of the plaintiffs' claim, your verdict should be for the defendant. This would end your deliberations. On the other hand, if after a consideration of all the evidence in the case you are reasonably satisfied of the truthfulness of the plaintiffs' claim, your verdict should be for the plaintiffs with said award to be reduced by the plaintiffs' comparative fault, if any. If you so find, it will be necessary for you to arrive at an amount to be awarded in the verdict from which I will read to you and describe later in my charge.

I now give you the following rules of law to assist you in your deliberations in arriving at an amount in the event you find for the plaintiffs.

21. The plaintiffs seek compensatory damages. Under our law, the parties are not entitled to recover so-called punitive damages in this action. The purpose of awarding compensatory damages is to fairly and reasonably compensate the injured party for the loss or injury sustained. Compensatory damages are intended as money compensation to the party wronged, to compensate him for his injury and other damages which have been inflicted upon him as a proximate result of the wrong complained of.
22. The measure of damages for medical expenses is all the reasonable expenses necessarily incurred for doctors' and medical bills which the plaintiff has paid or become obligated to pay and the amount of the reasonable expenses of medical care, treatment, and services reasonably certain to be required in the future. The reasonableness of, and the necessity for, such expenses are matters for your determination from the evidence.
23. In determining the amount of damages for loss of earnings, you should consider any evidence of the plaintiff's earning capacity, his earnings, the manner in which he ordinarily occupied his time before the injury, and his inability to pursue his occupation,

and determine what he was reasonably certain to have earned during the time so lost, had he not been disabled.

24. It is for you to determine from the evidence the nature, extent and duration of the injuries of the plaintiff, David Otis Wilson. If you are reasonably satisfied from the evidence that the plaintiff David Otis Wilson has suffered permanent injuries and that such injuries proximately resulted from the wrongs complained of, then you should include in your verdict such sum as you determine to be reasonable compensation for such injuries.
25. The law has no fixed monetary standard to compensate for physical pain and mental anguish. This element of damage is left to your good sound judgment and discretion as to what amount would reasonably and fairly compensate the plaintiff David Otis Wilson for such physical pain and mental anguish as you find from the evidence the plaintiff did suffer. If you are reasonably satisfied that the evidence that the plaintiff David Otis Wilson has undergone, or will undergo, pain and suffering or mental anguish as a proximate result of the injury in question, you should award a sum which will reasonably and fairly compensate him for such pain, suffering, or mental anguish already suffered by him and for any pain, suffering, or mental anguish which you are reasonably satisfied from the evidence that he is reasonably certain to suffer in the future.
26. Debra B. Wilson has also brought this suit. She claims loss of consortium. If you find for the plaintiff, Debra Wilson, you may also determine the amount of money that will reasonably compensate her for any damages sustained by loss of her husband's company, fellowship, cooperation, and assistance in the marital relationship as a partner in the family unit. Loss of consortium includes the impaired ability of her husband to perform his usual services in the care of the home (and in the education and rearing of the children), as well as her loss of his society, companionship, and comfort, taking into account the length of time of such loss and the reasonably certain duration of any future loss of consortium.
27. Mrs. Wilson has also made a claim for loss of future earning capacity. In determining a claim for loss of future earning capacity you must consider the reasonableness of the plaintiff's claim and the likelihood that the plaintiff would have completed her educational requirements and would have competed in the job market.

ECONOMIST REPORT

APPRAISAL OF ECONOMIC LOSS TO DAVID WILSON

**J. Smith
SMITH ECONOMICS, INC.
1234 Orchard Drive, Suite 200
Palo Alto, California 94301
(650) 123-4567**

SUMMARY

The total net present value of economic loss as a result of the injury to Mr. Wilson amounts to \$727,000. The components of this loss figure include earnings, home services, and medical care expenses. No dollar amounts for pain and suffering, loss of enjoyment of life, etc. have been included in this analysis. Also, unless specifically stated, this evaluation makes no offset for any monies received prior to the issuance of this report.

All future losses are adjusted for probable earnings growth, price increases, and probable interest returns. Because this loss is discounted to net present value, it is the probable fund required today to compensate for probable losses from the date of the incident in August, YR-5 to the trial and to replace the future lost stream of earnings and other future needs. The assumptions and data described in the following sections are the basis for this loss analysis.

CASE BACKGROUND

Mr. David Wilson sustained severe injury to the nerves, muscles, and tissues of his body when he was exposed to a weed killer on August 4, YR-5. Among the problems he continues to experience are weakness, nervousness, and severe headaches. Mr. Wilson's physicians do not anticipate any significant improvement in the future or that he will be able to return to his former employment. It is understood that Mr. Wilson should be able to handle most of the responsibilities associated with his small farm.

Mr. Wilson had been farming for approximately 30 years prior to his injury and had been employed as the manager/supervisor at Consolidated Farming ("Consolidated") for the past 15 years. His condition has precluded him from returning to Consolidated, and he has found that it will be necessary to hire additional help on his small, personal farm. Mr. Wilson has also not been able to continue repairing equipment during the past winter months, but anticipates he will soon be able to return to this work.

Mr. Wilson's condition has also impacted his wife, Debra. Prior to the accident, she had been pursuing her accounting degree but delayed her education as a direct result of the need for her to provide additional assistance at home and on the farm as well as additional care for her husband. Also, it was financially necessary for her to return to part-time employment following the incident. At a minimum, Ms. Wilson has lost approximately one and a half years in the labor market.

RELEVANT DATES AND TIME PERIODS

DATE OF BIRTH:	November 18, YR-55
DATE OF INJURY:	August 4, YR-5
DATE OF TRIAL:	July 30, YR-0
AGE AT INJURY:	49 years; 9 months.
LOSS PERIODS:	
PAST:	5.0 years
FUTURE:	6.7 years of remaining worklife (<i>Worklife Expectancies</i>) 23.3 years of life expectancy (<i>U.S. Vital Statistics</i>)
FAMILY DATA:	Married; one grown son from a previous marriage
EDUCATION:	High school degree
WORK HISTORY:	Farming for over 30 years; employed with Consolidated Farming for over 15 of those years

ECONOMIC FOUNDATION

In analyzing this particular case, the following documents have been reviewed:

- Income tax returns and/or W – 2 forms for the years YR-11 through YR-1;
- Interrogatories answered by Mr. and Ms. Wilson;
- Deposition of David Wilson and Statement of Debra Wilson;
- Pay stubs and benefit information from Consolidated Farming;
- Statement from Mr. George Wilson;
- Correspondence from Mr. Wilson to Mr. Weeks dated Sept. 24, YR-5;
- Depositions and medical reports from Drs. Jason, Donald, McGee, Gordon, Ogle and Towe; and
- Attorney correspondence.

In addition, specific inquiries and/or research related to this case were also performed by our office, including, a personal interview with Mr. and Ms. Wilson regarding their work histories, the operation of the farm, the changes in their lifestyle since the incident, etc.

A wealth of general economic data exists which is typically relied upon in any economic evaluation. This information includes:

- current and historical relationships between interest rates, inflation, and wage growth indices in addition to private and government agency forecast data for these economic indicators;
- state and federal labor department information regarding labor force participation rates, employment probabilities, geographic differentials, etc.;
- information on disabled workers including labor force participation, earnings, employment opportunities, unemployment rates, severity of limitations, etc.;
- age-earnings profiles and occupational mobility data;
- materials regarding employee benefit levels;
- retirement and pension information; and
- numerous documents regarding time contributions for household activities.

Academic and government citations for these data sources are located in the Appendix to this report.

TIME FRAME DEFINITIONS

The past loss time period reflects the losses incurred from the time of the incident to the time of the trial in July YR-0 (5.0 years). The amount of past net pecuniary loss is not adjusted for any probable interest earnings. No offset has been made for any monies which may have been received from other sources.

The probable future time frame commences at the time of the trial and continues through the remainder of Mr. Wilson's expected worklife or life expectancy from the time of the accident (6.7 and 23.3 years respectively), depending on the component being evaluated.

Annual loss amounts are set forth in today's dollars, but the stream of future loss amounts is discounted to reflect the probable net level of interest earnings relative to inflation and/or wage growth. In this particular evaluation of probable future loss, the discount rate used for the net present value analysis assumes that probable future average annual wage growth will be less than the probable annual interest returns on a lump-sum payment. The discount rate used for the net present value analysis of future medical care assumes that the probable future annual inflation of medical costs will be less than the relevant interest earnings on a lump-sum payment for this type of loss. See the Appendix for a more detailed explanation of discounting to net present value.

In the economic loss calculations, the following areas are analyzed:

- Earnings
- Home Services
- Medical Care Expenses

LOSS EVALUATION

EARNINGS – David O. Wilson

Mr. Wilson's average annual pre-injury wages were \$30,000. Since the accident, Mr. Wilson's wages would have grown in the past period with average growth rates in earnings. His expected wages in the past period are as follows:

YR-5	\$31,140
YR-4	\$32,323
YR-3	\$33,261
YR-2	\$34,225
YR-1	\$34,944
YR-0	\$35,679

His future wages are based on his YR-0 expected wages of \$35,679 per year. His anticipated average annual wages commencing in the future period are based on wages at Consolidated Farming or a comparable position consistent with Bureau of Census data regarding earnings of similarly situated males in YR-0 dollars.

Mr. Wilson's benefits from employment at Consolidated Farming were 20% of wages. This incorporates the value of legally required benefits, medical coverage and a pension/retirement plan or other typical benefits. In addition, the value of a company car that was available to Mr. Wilson while employed at Consolidated Farming was \$250-\$350 per month.

FARMING WAGES

The average annual loss associated with Mr. Wilson's decreased contribution to his farm, which recognizes the value of an extra farm laborer now needed based on \$5.50 per hour for seasonal assistance of some 500 hours per year during the past period, is \$2,750 per year. In the future period, the average annual loss is expected to be \$2,875 based on \$5.75 for some 500 hours per year, associated with hiring additional farm help in YR-0 dollars.

Included in the expenses for farming operations is the value of legally required benefits, which are 10% of money wages paid to the farm employee that Mr. Wilson must hire for the additional farm help in the past and future periods.

EQUIPMENT REPAIR WAGES

Mr. Wilson has lost \$2,500 each year since the accident because Mr. Wilson was unable to do this work during the winter months as he had prior to the accident. There is no loss in the future period as Mr. Wilson is expected to be able to do this work in the future.

DISCOUNT RATE

With respect to Mr. Wilson's lost earnings at Consolidated Farming and from equipment repairs and the cost he incurs from additional farm help, the net discount rate is 2.5% in the future period.

EARNINGS – Debra Wilson

Ms. Wilson's probable delay in graduation and, therefore, delay in typical entry level wages of a college graduate will be a loss in wages of \$18,400 per year over a 1.5 year period commencing at Ms. Wilson's expected pre-incident college graduation. These are the anticipated lost accounting wages which reflect the occupational opportunities available to Ms. Wilson in a rural community. This amount will be offset by monies Ms. Wilson will earn until she can return to school in YR-0 dollars.

Ms. Wilson's expected benefits associated with accounting wages are 15-20% of wages, the value of post-graduation employee benefits for full-time work within the field of accounting. This percentage incorporates the value of legally required benefits, medical coverage and/or a pension/retirement plan. Included in the offset is 10% of wages for the value of employee benefits for the waitress positions Ms. Wilson will likely have during the delay period, which incorporates the value of legally required benefits only and recognizes the part-time nature of Ms. Wilson's employment opportunities.

DISCOUNT RATE

With respect to Ms. Wilson's lost earnings due to the delay in college graduation, the net discount rate is 3.0% in the future period. This analysis does not consider any ongoing, incremental loss of earnings from the delay.

HOME SERVICES – Mr. Wilson

Mr. Wilson contributed 5 to 10 hours each week to household activities. This includes such chores as home maintenance, car maintenance, yard work, etc. per information from an interview with Mr. and Ms. Wilson and tracked to labor market studies.

Lost home services total \$2,730 per year using a rate of \$5 to \$9 per hour, the market replacement wage over past and future periods. This rate is based on area wage rates for variety of household activities and responsibilities, adjusted for geographical location.

DISCOUNT RATE

With respect to lost home services from Mr. Wilson, the net discount rate is 1.0% in the future period. The past loss reflects the value of time, not out of-pocket expenses, while in the future period a fund of money is provided to meet these needs.

MEDICAL CARE EXPENSES – David Wilson

As of December YR-1, Mr. Wilson's past medical care expenses totaled \$15,000 per year. This amount may need to be adjusted at the time of trial. His anticipated cost for lab tests and additional physician visits in the future period is \$250 per year.

DISCOUNT RATE

With respect to medical care expenses for Mr. Wilson, the net discount rate is 0.5% in the future time period.

CONCLUSION

The following chart summarizes the past and future time periods with their associated loss elements as previously discussed. Based upon the analysis presented here, an aggregate fund of \$727,000 will compensate Mr. and Ms. Wilson for the probable past losses and also replace probable future losses.

- Drawn upon each year in the future, this fund will serve as a substitute for the probable economic losses each year.
- Thus, at the end of the probable future loss period, the fund balance would be \$0. (That is, the actual purchasing power of losses replaced year by year at levels enumerated herein will be maintained.)
- To ignore the cost of living or earnings growth factor would understate the losses sustained while a failure to incorporate interest earned from funds on hand today would overstate the probable losses.
- By simultaneously considering these two magnitudes (earnings and interest factors), this economic evaluation appropriately reflects the net present values in real terms.

**SUMMARY OF ECONOMIC LOSS AMOUNTS
MR. DAVID WILSON**

<u>PAST LOSSES</u>	
EARNINGS – Mr. Wilson	\$248,100
HOME SERVICES	\$13,700
MEDICAL CARE EXPENSES	\$75,000
TOTAL PAST LOSS	\$336,800
<u>FUTURE LOSSES</u>	
EARNINGS – Mr. Wilson	\$306,000
EARNINGS - Ms. Wilson	\$22,700
HOME SERVICES	\$56,800
MEDICAL CARE EXPENSES	\$4,700
TOTAL NET PRESENT VALUE OF FUTURE LOSS	\$390,200
<u>TOTAL VALUE OF LOSS</u>	\$727,000

APPENDIX

Notes on the Determination of Probable Net Present Value

Selected Tables of Economic Indicators

Bibliography of General Economic Sources

JULY YR-0 UPDATE

NOTES ON THE DETERMINATION OF PROBABLE NET PRESENT VALUE

The derivation of the net present value in an appraisal of economic loss must take into account both expected inflationary earnings growth and probable interest returns. When future expenditures for products, equipment, medical care, etc. are considered, the relevant comparison is future price inflation relative to interest returns. When wage losses are considered, the relevant comparison is growth in earnings (both macroeconomic and individual) relative to interest returns. The following discussion focuses on the relationship of earnings growth versus interest returns to establish net present value. The same analysis is valid for the inflation versus interest returns relationship.

EARNINGS GROWTH

The reality of wage increases (earnings growth) is a future probability. Although earnings growth may fluctuate from year to year, the trend over the long-term is more predictable. The significance of such economic circumstances is that a continuation of the general historical pattern is, with some variation, probable into the future. By incorporating economic trends into an appraisal one is able to identify the appropriate real earnings loss to be compensated in the future. Identifying the real earnings loss is critical because economic losses involve a loss of living standards into the future, and it is this lifestyle that is sought as recovery, not an endlessly diminishing monetary value.

Notably, part of the increase in earnings growth is inflationary in nature while further growth is a result of technological advances in our economy, which improve overall (macroeconomic) productivity. A third component in earnings growth recognizes the increased productivity that accrues over the work years as an individual acquires specific experience and training.

For example, inflation growth or cost of living increases over time can be found on Table II of this Appendix. Table II indicates that, although price level increases have slowed in recent years, over the last thirty-three years the YR-2 price level is greater than four and one-half times the YR-35 level. That is, one currently needs \$4.74 to purchase each dollar (\$1.00) of goods and services consumed thirty-three years ago (i.e., divide the YR-2 index of 184.0 by the YR-35 index of 38.8). Thus, to maintain the same standard of living or the same basic purchasing power in YR-2 as one had in YR-35, earnings must also have a similar 4.74 fold increase.

For a variety of market reasons, hourly wage earners just barely “kept up” with inflationary increases over this same thirty-three year period. As noted on Table I-A for YR-2 vis-à-vis the base year in YR-35 produced a 4.69 fold increase (i.e. 196.6 divided by 41.9). However, over the same time frame the wages of salaried workers (indicated in Table I-B) improved by a multiple of 7.09 compared to the 4.74 inflation multiple. This information indicates that a typical thirty year old male *hourly* wage earner in YR-2 has simply maintained his standard of living in relation to inflation since YR-35 while a thirty year old male *salaried* worker in YR-2 has a substantially better standard of living than his YR-35 counterpart. Of note (and also good news) is that over the past decade, while the overall increase in inflation was approximately twenty-seven percent, the increase in the average aggregate earnings for hourly wage earners was up thirty-nine percent, resulting in a recent increase in the standard of living for these workers. Detail by year for the aggregate average hourly wage earners, salaried workers, and the inflation phenomena can be found in Tables I-A, I-B, and II, respectively.

However, the aggregate average earnings discussed above are not the only wage increases either hourly or salaried workers can expect to receive over their work years. As earlier noted, in addition to wage increases due to inflation and/or technological advances (macroeconomic factors), individual workers receive earnings increases due to their own experience, skill, and training. It is relatively common knowledge that wages tend to increase substantially faster in the early years of an individual's worklife and as the training and experience accrues, wages continue to increase but at slower rates in the latter work years. Also, conventional wisdom suggests and various government and academic data confirm that increased levels of education and training will, on average, produce not only better wage increases, but also prolonged opportunity for these wages to continue at accelerated rates. This well recognized phenomena is best captured in the "age-earnings profiles" compiled by the *Bureau of Census* and also replicated on Chart I in this Appendix.

As described above, wage increases consider numerous factors including, but not limited to, general economic conditions, industry specifics, and the special characteristics of the worker such as age, education, occupation, etc. These factors and special characteristics are important but do not invalidate the universality of inflationary earnings growth in the U.S. economy, either historically or in the future.

INTEREST EARNINGS

In addition to probable earnings growth considerations, interest earnings from a lump sum payment must be incorporated into the analysis. A sum of money available today as compensation for probable future losses has the capacity and expectation to earn additional monies. Since it is necessary that all probable future losses be summarized *in toto* today, the interest earnings available from a lump-sum payment in the present must be taken into account. (The concept of interest earnings is more precisely labeled "net" interest earnings since the yield, net of investment expenses, is the relevant measure.)

Not surprisingly, if one is required to replace \$10,000 ten years from today, less than \$10,000 can be set aside for this future obligation. How much less depends upon the probable net interest rate. At a five percent net interest, only 61 cents is needed now to replace each dollar (\$1.00) in ten years; that is, the "present value" of \$10,000 is \$5,139, the remaining amount being accumulated through ten years of compound interest.

The data in Tables III and IV depict interest returns on U.S. Treasury bills and bonds. These government securities are regarded as appropriate rates to use (especially in determining monies needed in regular intervals for wages, medical needs, etc.) when discounting to present value for several reasons:

- (1) They are relatively stable and reasonably prudent investments as these types of government securities reflect a predictable and reliable stream of income;
- (2) They are characterized by high liquidity, being easily transformed into money needed for day-to-day living; and

- (3) Management costs and the degree of difficulty in managing such an investment are minimal in comparison to investments that are more risky, less liquid, and more likely to have a volatile value.

Taxable government bonds of varying time frames or tax-free municipal bonds have appropriate applications, depending upon the nature of the economic loss.

NET PRESENT VALUE

Whereas earnings growth factors will cause probable future earnings loss values to rise in magnitude over time, the adjustment of probable future dollar quantities for interest earnings will have the opposite effect.

One approach in the determination of the probable net present value is to project the loss of an expected earnings stream by adjusting the current annual dollar loss by a projected wage growth factor and then discounting this value by an anticipated interest rate. This procedure incorporates explicit assumptions about the level of probable earnings growth as well as interest rates. As these magnitudes are tied to general economic conditions and to the fiscal and monetary policies of our federal government, they can be expected to vary, within a reasonable range, over time and across administrations. Nonetheless, using a variety of interest rates (in combination with wage and/or inflation rates) within a reasonable range will result in similar present value amounts.

The second method of analysis determines the probable differential between earnings growth and interest yields. This approach recognizes both the statistical relationship among inflation, wage increases, and interest rates plus the dynamic nature of our economy. That is, if inflation is high, wage increases tend to be larger than “average”; however, interest rates (with some lead or lag) also tend to be higher than “average.”

Indeed, as anticipated from basic economic principles, an extremely high correlation between aggregate earnings growth and investment yields exists over time. Also, the percentage spread between these two economic magnitudes is relatively stable, particularly when evaluated over the worklife of a “typical” individual. Generally, what one finds is that:

- (1) Historically, earnings and interest returns rise and fall together (or with a time lag) in a relatively consistent and/or predictable fashion;
- (2) Interest returns are typically somewhat greater than the aggregate average earnings growth for both hourly and salaried workers, although (as expected) a smaller differential exists for the latter group;
- (3) Only the macroeconomic effects of the relationship between earnings growth and interest rates are captured in the aggregate data on Tables I through IV but additional wage growth is also obtained from the individual age-earnings profile as noted on Chart I.

While over the short term, interest earnings and wages will vary year-to-year (although highly correlated), over the long term worker's growth in earnings (in a free market economy) will largely offset the interest earnings.

The Tables which follow identify some relevant historical relationships for specific economic indicators. Charts also follow illustrating some of the data from the preceding Tables. An annotated bibliography of general economic data sources is also provided. When appropriate, given the information available for a particular loss evaluation, more specific data measures and economic studies are utilized.

TABLE I-A
EARNINGS INDICES
HOURLY

<u>Year</u>	<u>Index</u> <u>(YR-</u> <u>23=100)</u>	<u>% Change from</u> <u>Previous Year</u>	<u>Year</u>	<u>Index</u> <u>(YR-</u> <u>23=100)</u>	<u>% Change</u> <u>from</u> <u>Previous Year</u>
YR-1	200.8	2.1%	YR-31	54.3	7.6%
YR-2	196.6	2.9%	YR-32	51.0	6.5%
YR-3	191.1	2.9%	YR-33	47.6	7.2%
YR-4	185.8	3.8%	YR-34	44.6	6.8%
YR-5	179.0	3.8%	YR-35	41.9	6.3%
YR-6	172.4	3.6%	YR-36	39.3	6.7%
YR-7	166.4	4.1%	YR-37	37.0	6.3%
YR-8	159.9	3.9%	YR-38	35.3	4.7%
YR-9	153.9	3.4%	YR-39	33.9	4.1%
YR-10	148.8	2.8%	YR-40	32.6	4.2%
YR-11	144.8	2.7%	YR-41	31.4	3.5%
YR-12	141.0	2.5%	YR-42	30.6	2.7%
YR-13	137.6	2.4%	YR-43	29.5	3.7%
YR-14	134.4	3.1%	YR-44	28.8	2.4%
YR-15	130.3	3.6%	YR-45	27.9	3.5%
YR-16	125.8	4.1%			
YR-17	120.8	3.3%			
YR-18	116.9	2.5%			
YR-19	114.1	2.2%			
YR-20	111.6	3.0%			
YR-21	108.3	3.7%			
YR-22	104.4	4.4%			
YR-23	100.0	5.9%			
YR-24	91.9	8.9%			
YR-25	85.0	8.1%			
YR-26	78.5	8.3%			
YR-27	72.4	8.4%			
YR-28	67.0	8.0%			
YR-29	62.5	7.3%			
YR-30	58.5	6.8%			

Source: This chart was adapted from information regarding hours and earnings in private nonagricultural industries.
Economic Report of the President, Council of Economic Advisors.

TABLE I-B

EARNINGS INDICES

SALARY

<u>Year</u>	<u>Index</u> <u>(YR-23=100)</u>	<u>% Change from</u> <u>Previous Year</u>
YR-1	282.9	3.7%
YR-2	272.8	3.5%
YR-3	263.6	3.9%
YR-4	253.7	4.6%
YR-5	242.6	4.6%
YR-6	231.9	4.4%
YR-7	222.1	4.5%
YR- 8	212.6	4.3%
YR-9	203.8	4.1%
YR-10	195.8	4.0%
YR-11	188.3	4.0%
YR-12	181.0	4.3%
YR-13	173.6	4.7%
YR-14	165.8	5.0%
YR-15	157.9	5.5%
YR-16	149.6	5.4%
YR-17	142.0	5.2%
YR-18	135.0	5.2%
YR-19	128.3	5.9%
YR20	121.1	6.4%
YR-21	113.8	6.5%
YR-22	106.9	6.9%
YR-23	100.0	9.1%
YR-24	91.7	10.5%
YR-25	82.9	9.9%
YR-26	75.5	8.0%
YR-27	69.9	8.4%
YR-28	64.5	8.2%
YR-29	59.6	8.2%
YR-30	55.1	8.9%

Source: This chart was adapted from information found at www.worldatwork.org (previously American Compensation Association), various yearly editions.

TABLE II
COST OF LIVING FACTORS IN THE AMERICAN ECONOMY

CPI - All Items	% Change from	Medical Price Index	% Change from
(YR-23-to YR-		(YR-23-to YR-	

<u>Year</u>	<u>21=100)</u>	<u>Previous Year</u>	<u>21=100)</u>	<u>Previous Year</u>
YR-1	188.9	2.7%	310.1	4.4%
YR-2	184.0	2.3%	297.1	4.0%
YR-3	179.9	1.6%	285.6	4.7%
YR-4	177.1	2.8%	272.8	4.6%
YR-5	172.2	3.4%	260.8	4.1%
YR-6	166.6	2.2%	250.6	3.5%
YR-7	163.0	1.6%	242.1	3.2%
YR-8	160.5	2.3%	234.6	2.8%
YR-9	156.9	3.0%	228.2	3.5%
YR-10	152.4	2.8%	220.5	4.5%
YR-11	148.2	2.6%	211.0	4.8%
YR-12	144.5	3.0%	201.4	5.9%
YR-13	140.3	3.0%	190.1	7.4%
YR-14	136.2	4.2%	177.0	8.7%
YR-15	130.7	5.4%	162.8	9.0%
YR-16	124.0	4.8%	149.3	7.7%
YR-17	118.3	4.1%	138.6	6.5%
YR-18	113.6	3.6%	130.1	6.6%
YR-19	109.6	1.9%	122.0	7.5%
YR-20	107.6	3.6%	113.5	6.3%
YR-21	103.9	4.3%	106.8	6.2%
YR-22	99.6	3.2%	100.6	8.8%
YR-23	96.5	6.2%	92.5	11.6%
YR-24	90.9	10.3%	82.9	10.7%
YR-25	82.4	13.5%	74.9	11.0%
YR-26	72.6	11.3%	67.5	9.2%
YR-27	65.2	7.6%	61.8	8.4%
YR-28	60.6	6.5%	57.0	9.6%
YR-29	56.9	5.8%	52.0	9.5%
YR-30	53.8	9.1%	47.5	12.0%
YR-31	49.3	11.0%	42.4	9.3%
YR-32	44.4	6.2%	38.8	4.0%
YR-33	41.8	3.2%	37.3	3.3%
YR-34	40.5	4.4%	36.1	6.2%
YR-35	38.8	5.7%	34.0	6.6%
YR-36	36.7	5.5%	31.9	6.7%
YR-37	34.8	4.2%	29.9	6.0%
YR-38	33.4	3.1%	28.2	7.2%
YR-39	32.4	2.9%	26.3	4.4%
YR-40	31.5	1.6%	25.2	2.4%
YR-41	31.0	1.3%	24.6	2.1%
YR-42	30.6	1.3%	24.1	2.6%
YR-43	30.2	1.0%	23.5	2.6%
YR-44	29.9	1.0%	22.9	2.7%
YR-45	29.6	1.7%	22.3	3.7%

Source: Table B-60. This chart was adapted from information regarding consumer price indexes for major expenditure classes. *Economic Report of the President*, Council of Economic Advisors.

TABLE III
YIELDS ON U.S. TREASURY SECURITIES

<u>Year</u>	<u>3-Month Bills</u>	<u>6-Month Bills</u>	<u>3-Year Notes</u>	<u>10-Year Notes</u>
YR-1	1.4%	1.6%	2.8%	4.3%
YR-2	1.0%	1.1%	2.1%	4.0%
YR-3	1.6%	1.7%	10.0%	4.6%
YR-4	3.5%	3.4%	4.1%	5.0%
YR-5	5.9%	5.9%	6.2%	6.0%
YR-6	4.7%	4.8%	5.5%	5.7%
YR-7	4.8%	4.9%	5.1%	5.3%
YR-8	5.1%	5.2%	6.1%	6.4%
YR-9	5.0%	5.1%	6.0%	6.4%
YR-10	5.5%	5.6%	6.3%	6.6%
YR-11	4.3%	4.7%	6.3%	7.1%
YR-12	3.0%	3.1%	4.4%	5.9%
YR-13	3.5%	3.6%	5.3%	7.0%
YR-14	5.4%	5.5%	6.8%	7.9%
YR-15	7.5%	7.5%	8.3%	8.6%
YR-16	8.1%	8.0%	8.6%	8.5%
YR-17	6.7%	6.9%	8.3%	8.9%
YR-18	5.8%	6.1%	7.7%	8.4%
YR-19	6.0%	6.0%	7.1%	7.7%
YR-20	7.5%	7.7%	9.6%	10.6%
YR-21	9.6%	9.8%	11.9%	12.4%
YR-22	8.6%	8.8%	10.5%	11.1%
YR-23	10.7%	11.1%	12.9%	13.0%
YR-24	14.0%	13.8%	14.4%	13.9%
YR-25	11.5%	11.4%	11.6%	11.5%
YR-26	10.0%	10.0%	9.7%	9.4%
YR-27	7.2%	7.6%	8.3%	8.4%
YR-28	5.3%	5.5%	6.7%	7.4%
YR-29	5.0%	5.3%	6.8%	7.6%
YR-30	5.8%	6.1%	7.5%	8.0%
YR-31	7.9%	7.9%	7.8%	7.6%
YR-32	7.0%	7.2%	7.0%	6.8%
YR-33	4.1%	4.5%	5.7%	6.2%
YR-34	4.3%	4.5%	5.7%	6.2%
YR-35	6.5%	6.6%	7.3%	7.4%
YR-36	6.7%	6.9%	7.0%	6.7%
YR-37	5.3%	5.5%	5.7%	5.7%
YR-38	4.3%	4.6%	5.0%	5.1%
YR-39	4.9%	5.1%	5.2%	4.9%
YR-40	4.0%	4.1%	4.2%	4.3%
YR-41	3.5%	3.7%	4.0%	4.2%
YR-42	3.2%	3.3%	3.7%	4.0%
YR-43	2.8%	2.9%	3.5%	4.0%
YR-44	2.4%	2.6%	3.5%	3.9%
YR-45	2.9%	3.2%	4.0%	4.1%

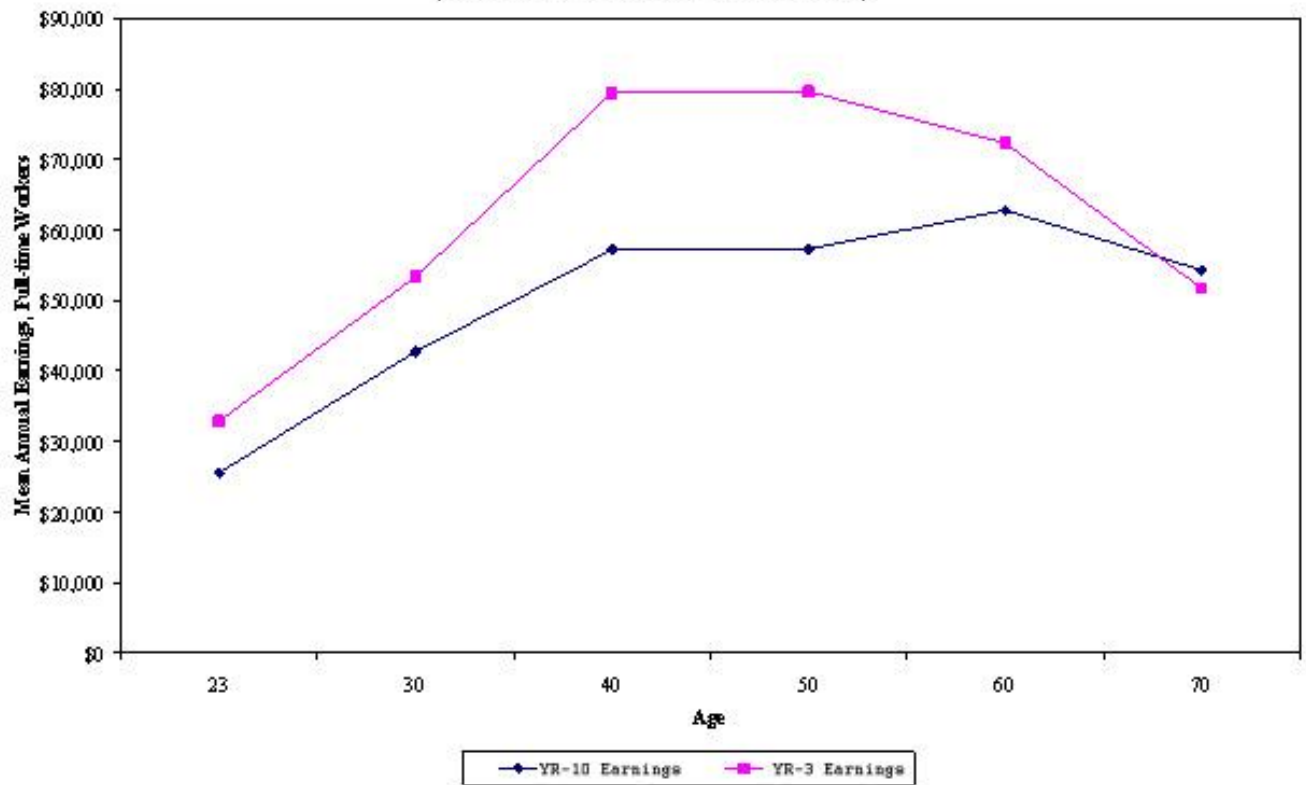
Source: Table B-73. – This chart was adapted from information regarding bond yields and interest rates. *Economic Report of the President*, Council of Economic Advisors.

TABLE IV
YIELDS ON 30-YEAR U.S. GOVERNMENT AND
HIGH GRADE MUNICIPAL BONDS

<u>Year</u>	<u>U.S. Bonds</u>	<u>Municipal Bonds</u>
YR-1	n/a	4.6%
YR-2	n/a	4.7%
YR-3	n/a	5.1%
YR-4	5.5%	5.2%
YR-5	5.9%	5.8%
YR-6	5.9%	5.4%
YR-7	5.6%	5.1%
YR-8	6.6%	5.6%
YR-9	6.7%	5.8%
YR-10	6.9%	6.0%
YR-11	7.4%	6.2%
YR-12	6.6%	5.6%
YR-13	7.7%	5.4%
YR-14	8.1%	6.9%
YR-15	8.6%	7.3%
YR-16	8.5%	7.2%
YR-17	9.0%	7.8%
YR-18	8.6%	7.7%
YR-19	7.8%	7.4%
YR-20	10.8%	9.2%
YR-21	12.4%	10.2%
YR-22	11.2%	9.5%
YR-23	12.8%	11.6%
YR-24	13.4%	11.2%
YR-25	11.3%	8.5%
YR-26	8.7%	6.4%
YR-27	7.9%	5.9%
YR-28	7.0%	5.6%
YR-29	6.8%	6.5%
YR-30	7.0%	6.9%
YR-31	7.0%	6.1%
YR-32	6.4%	5.2%
YR-33	5.6%	5.3%
YR-34	5.7%	5.7%
YR-35	6.6%	6.5%
YR-36	6.1%	5.8%
YR-37	5.3%	4.5%
YR-38	4.9%	4.0%
YR-39	4.7%	3.8%
YR-40	4.2%	3.3%
YR-41	4.2%	3.2%
YR-42	4.0%	3.2%
YR-43	4.0%	3.2%
YR-44	3.9%	3.5%
YR-45	4.0%	3.7%

Source: Table B-73. – This chart was adapted from information regarding bond yields and interest rates.
Economic Report of the President, Council of Economic Advisors.

CHART I
AGE-EARNINGS PROFILE ANALYSIS
(MALES WITH BACHELOR'S DEGREE)



BIBLIOGRAPHY OF GENERAL ECONOMIC SOURCES

Federal, state and local governments plus professional and trade associations, private agencies and academics compile and publish a wide variety of information which can be useful in an economic analysis. Although not exhaustive, the following list of government and private agencies and their publications is comprehensive and indicative of the sources which are generally referred to when performing an economic appraisal of loss. Of note, voluminous academic textbooks and/or handbooks covering an array of economic principles, as well as additional background, training and experience, have not been detailed in this bibliography.

BOARD OF GOVERNORS OF THE FEDERAL RESERVE SYSTEM

The Board of Governors compiles data on various financial and business statistics. Included are yields on securities, interest rates, price indices, and GNP. The ***Federal Reserve Bulletin*** is published monthly and the ***Federal Reserve Statistical Release of Selected Interest Rates*** is now available via their website (listed at end).

COUNCIL OF ECONOMIC ADVISORS

The Council compiles statistics including consumer and producer prices by major expenditure, productivity and wage by major industry sector, employment and unemployment figures, bond yields and interest rates. Publications include the ***Economic Report of the President*** and ***Economic Indicators***.

FEDERAL RESERVE BANK OF ST. LOUIS

The Bank collects data on the financial outlook of the economy. This includes such items as yields on securities, interest rates, general price levels, GNP and monetary components. Publications include ***U.S. Financial Data***, ***Monetary Trends***, and ***National Economic Trends***.

U.S. CHAMBER OF COMMERCE, ECONOMIC POLICY DIVISION

The Chamber's annual publication, ***Employee Benefits***, is an extensive survey of fringe benefits packages by type of benefit, industry sector, size of firm, geographic location, etc.

U.S. DEPARTMENT OF AGRICULTURE

The Consumer and Food Economics Research Division collects information relating to the economic aspects of family living, including such topics as home services, personal consumption, and cost of children. Publications issued quarterly include *Family Economics Review* now known as *Family Economics and Nutrition Review*.

U.S. DEPARTMENT OF COMMERCE

The Bureau of Census provides summary statistics on the social, political and economic organization of the United States as well as disseminating a number of special studies with statistical information by education, age, sex, occupation, labor force participation, work disability, etc. Among its publications are the *Statistical Abstract of the United States* and *Current Population Reports: Selected Studies* including *Earnings by Occupation and Education, Labor Force Statistics and Other Characteristics of Persons with a Work Disability* and *Money Income of Households, Families, and Persons in the United States*. The Bureau of Census also provides data on earnings for workers with impairments/disabilities (as these terms are defined in labor economics) through the following sources: *Survey of Income and Program Participation (SIPP)*, the *Decennial Census of the Population* and the *Current Population Survey (CPS)*. The Bureau of Economic Analysis reviews and presents in its publications various economic time series data useful to business analysts and forecasters as well as information on general business conditions. Publications include the *Business Conditions Digest* and the *Survey of Current Business*.

U.S. DEPARTMENT OF EDUCATION

The information published by the Office of Educational Research and Improvement includes statistics on graduates, teachers, finances, educational characteristics of the labor force, fields of study, earnings by educational attainment, etc. Among its publications are the *Digest of Education Statistics, Projections of Education Statistics, Education Indicators, The Condition of Education, College Costs; Basic Student Charges at Two-Year and Four-Year Institutions* (Survey Report), *Special Demographic Analysis; Education in the United States, High School and Beyond Tabulations, Educational Attainment in the United States* (various years), and *School Enrollment - Social and Economic Characteristics of Students* (various years).

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Included in the Department's publications, *Vital and Health Statistics of the United States and U.S. Decennial Life Tables*, are information regarding life expectancy by age, sex, race, and labor force participation. Another publication, *Health United States*, provides statistical information regarding health status and determinants, utilization of health resources, health care resources and health care expenditures. In addition to their own publications, the U.S. Department of Health and Human Services contracts out various projects such as a study entitled *A Labor Force Profile of Persons With Disabilities* prepared by Mathematica Policy Research, Inc. and Systemetrics/McGraw Hill. Under this department, the Social Security Administration has also published the *Survey of Disability and Work*. This survey presents information regarding the demographic characteristics of the disabled, the presence of activity limitations and

regarding the demographic characteristics of the disabled, the presence of activity limitations and mobility issues, chronic health conditions resulting in disability, labor force status and economic status.

U.S. DEPARTMENT OF LABOR

This agency, through the Bureau of Labor Statistics, collects and distributes data and statistics on labor force participation, work life expectancies, work patterns, income, budgets by household type, price indices, etc. Publications include the *Handbook of Labor Statistics*, *Occupational Outlook Handbook*, *Employment and Earnings*, *Employment and Wages*, *National Survey of Professional Administrative, Technical, and Clerical Pay*, *Area Wage Surveys*, *Occupational Injuries and Illnesses in the United States by Industry*, *Employee Benefits in Medium and Large Firms*, *Monthly Labor Review*, *Employee Benefits Survey: An MLR Reader*, *Current Wage Developments*, *CPI Detailed Report*, and *Consumer Expenditure Survey*.

EMPLOYMENT/OCCUPATIONAL RESOURCES

Supplementing the economic information available on labor market trends and characteristics is specific occupational information that can be found in publications issued by various professional and trade associations. Among these private organizations are American Medical Association, Commission on Professionals in Science & Technology, American Dental Association, and American Compensation Association. Likewise, wage information specific to occupation can be found in the Bureau of Labor Statistics state specific employment and wage estimates. Also, details regarding wages, benefits and other specific information for various employers are outlined in publications such as *Federal Employees Almanac*, *Railroad Retirement and Survivor Benefits* and *Uniformed Services Almanac* (as well as for Reserve Forces, National Guard and Retired Military).

ADDITIONAL BACKGROUND MATERIALS

In addition to federal government sources, specific state and local government data also exist, as do studies on a wide range of topics from private sources. State and local labor market data is available through government offices such as the Department of Labor as well as private organizations like the Chamber of Commerce. For the state of Colorado, sources include the *Occupational Supply & Demand Report* and *Occupational Employment Statistics*, both issued by the Colorado Department of Labor & Employment. Wage and benefit information in Colorado's municipalities and communities is available in the *Benchmark Employee Compensation Report* produced by the Colorado Municipal League (CML). Similar data is available for other regions and states. Comparative cost of living data for urban areas is available quarterly from the American Chamber of Commerce Researchers Association (ACCRA).

Studies and surveys on a wide range of topics can be found through private sources such as the Employee Benefit Research Institute (EBRI), the International Center for the Disabled, The Menninger Foundation, Global Insight, The RAND Corporation, and the Commission on Professionals in Science and Technology.

Moreover, much informative, quantitative and qualitative academic research can be found in and is reviewed from such journals as the *Journal of Human Resources*, *Journal of Labor Economics*, *Journal of Law and Economics*, *Economic Inquiry*, *Southern Economic Journal*, *American Economic Review*, *Journal of Risk and Insurance*, *Journal of Business*, *Journal of the Political Economy*, *Journal of Public Economics*, *Journal of Forensic Economics*, *Review of Social Economy*, *Empirical Economics*, *Journal of Socio-Economics*, *Social Security Bulletin*, *Population and Development Review*, *Demography*, *Industrial and Labor Relations Review*, *Applied Economics*, *Oxford Bulletin of Economics and Statistics*, *Review of Economics and Statistics*, *American Journal of Economics and Sociology*, *Quarterly Review of Economics and Finance*, *Journal of Risk and Uncertainty*, *Review of Income and Wealth*, among others.

More detailed data and analyses regarding home services can be found in the academic and government literature and surveys. These data and surveys are included in publications such as *Monthly Labor Review*, *Journal of Human Resources* and *Family Economics Review* as well as specific academic articles authored by W.H. Gauger and K.E. Walker, K.E. Walker and M.E. Woods, M.V. Leonesio, H. Paul, T. Van der Lippe and J.J. Siegers, F. Stafford and G. Duncan, M. Minton and J. Bloch, J. Peskin, among others. Specifically, studies such as *The Dollar Value of a Day* published by Expectancy Data and *The Dollar Value of Household Work* authored by W. Keith Bryant, Cathleen D. Zick, and Hyoshin Kim, contain data measuring the value of time usage for home services and associated replacement costs. *The Dollar Value of a Day (DVD)* utilizes the National Human Activity Pattern Survey (NHAPS) time-diary studied as published by the U.S. Environmental Protection Agency.

Personal consumption information has been obtained from various editions of the *Consumer Expenditure Survey* from the Bureau of Labor Statistics as well as from publications such as *Family Economics Review*, *Monthly Labor Review* and *Economic Report of the President*. In addition, various academic and research articles evaluating this phenomenon are represented in articles authored by E. Cheit, J. Burke and H. Rosen, R. Gieseeman and J. Rogers, E. Jacobs and S. Shipp, and others.

Worklife expectancies can be found in various issues of the *Journal of Legal Economics* and *Life and Worklife Expectancies* by Hugh Richards.

National forecasting information is obtained from a number of sources such as *Short-Term Outlook* and *Long-Term Outlook* published by Global Insight, *The Economic and Budget Outlook* issued by the Congressional Budget Office (CBO), and various documents obtained through the General Accounting Office (GAO).

Local forecasting information for the State of Colorado is presented in the *Colorado Economic Perspective* issued by the Office of State Planning and Budgeting as well as in *Focus Colorado: Economic & Revenue Forecast* which is a Colorado Legislative Council Staff Report. Other states have comparable information.

Financial statistics, personal income and tax data are available quarterly through the *SOI Bulletin* issued by the Department of the Treasury, Internal Revenue Service. Also, financial instruments and yield information are provided through various sources including the *Stocks, Bonds, Bills and Inflation Yearbook* published by Ibbotson Associates. Sources for information regarding businesses' financial ratios, discounting, etc. include, but are not limited to, *Valuing a Business* and *Valuing Small Business and Professional Practices*, both authored by Shannon

Pratt, *Robert Morris Associates' (RMA's) Annual Statement Studies*, *The Almanac of Business and Industrial Financial Ratios*, *Business Statistics of the United States*, *Guide to Forecasts and Projections* authored by Pallais and Holton, *Guide to Business Valuations* authored by Fishman, Pratt, et al. and *Valuation-Measuring and Managing the Value of Companies* authored by Copeland, Koller and Murrin. Information regarding the valuation of a business in a specific industry can be found in books such as *Valuation of a Medical Practice* authored by Tinsley, Sides and Anderson. Other more specific textbooks that focus on valuing damages specifically in litigation matters involving businesses can be found in a book authored by P. Gaughan titled *Measuring Commercial Damages*. A text that focuses specifically on valuing lost earnings and household services in litigation matters involving personal injury and wrongful death is *Determining Economic Damages* by Gerald D. Martin and Ted Vavoulis.

Finally, a variety of academic textbooks in the economic, finance and general business offer important theoretical and empirical information necessary to understand the dynamics of our economy. This literature provides the foundation and the basic underpinnings for an economic appraisal and include various *Principles of Economics* and more advanced *Micro/Macroeconomic* textbooks authored by Samuelson, Lipsey and Steiner, Baumol and Blinder, Ekelund and Tollison, Ferguson, Henderson and Quandt, Mansfield, and Hirshlefer; various *Managerial Economics* textbooks by Brigham, Pappas and Brigham, Maurice and Smithson, and Rooney; *Financial Theory and Corporate Policy* and *Managerial Finance* both authored by Copeland and Weston; *Financial Institutions* by Edmister; and *Fundamentals of Financial Management* by Brigham.

Also, a sampling of labor economic textbooks which focus more specifically on worker issues include *The Economics of Work and Pay* by Hammermash and Rees, *Contemporary Labor Economics* by McConnell and Brue, *Handbook of Labor Economics* by Ashenfelter and Layard, Editors, *Longitudinal Analysis of Labor Market Data* by Heckman and Singer, to name but a few.

WEBSITE RESOURCES

Many agency publications that were previously available only in hardcopy are now available online. Frequently used sites include:

Bureau of Labor Statistics	http://www.stats.bls.gov
Bureau of the Census	http://www.census.gov
Congressional Budget Office	http://www.cbo.gov
Federal Reserve Board	http://www.federalreserve.gov
Federal Reserve Bank	http://www.stls.frb.org
Internal Revenue Service	http://www.irs.gov
National Center for Education Statistics	http://www.nces.ed.gov
Social Security Administration	http://www.ssa.gov
US Bureau of Economic Analysis	http://www.bea.gov/
US Chamber of Commerce	http://www.uschamber.org
US Department of Commerce	http://www.doc.gov
US Department of Education	http://www.ed.gov
US Department of Labor	http://www.dol.gov
Employee Benefit Research Institute	http://www.ebri.org

For state government Websites http://www.state.**.us

(Replace ** with the two-letter state code, e.g., for California: <http://www.state.ca.us>)

Weed Science:

PRINCIPLES AND PRACTICES

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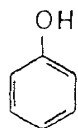
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15 Phenols

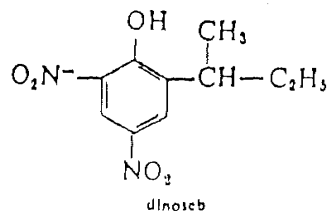


Phenol is the monohydroxy (—OH) derivative of benzene. Herbicides of this class now registered for crop use in the United States have two nitro (—NO_2) groups on the ring in the number 4 and number 6 positions. These are dinitrophenols or simply dinitros.

Historically, PCP (pentachlorophenol) was used as a herbicide in certain crops, but it is not registered now for this use in the United States. While it can be used as a preharvest desiccant in small-seeded legume crops grown for seed, it is largely used as a wood preservative.

Substituted phenolic herbicides are contact herbicides. Some have been used for more than 40 years. The sodium salt of DNOC (4,6-dinitro-*o*-cresol) was first used to remove broadleaf weeds from small grain in France about 1933. Soon after, it was introduced into the United States and promptly became the major material for annual broadleaf weed control in cereal crops, flax, and peas. However, it is not now registered for these uses in the United States. It is presently used as a plant growth regulator for blossom thinning in apples.

DINOSEB



DINOSEB

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Dinoseb is the common name for 2-*sec*-butyl-4,6-dinitrophenol. It is also often called DNBP. It has several trade names. The phenol form is usually formulated as an emulsifiable concentrate; it is also soluble in oil. It may also be formulated as water-soluble salts; the most common are the ammonium, triethanolamine, and a mixture of ethanol and isopropanolamine salts.

Dinoseb is a dark-brown solid or a dark-orange liquid, depending on temperature. As the phenol, it has a water solubility of 52 ppm, but the salts are quite soluble in water.

Toxicity to Humans and Animals

Dinoseb and its salts are dangerous poisons if taken internally, if inhaled as dusts, or if considerable quantities are absorbed through the skin. Therefore, avoid prolonged breathing of the spray drift or dusts, and avoid wearing contaminated clothing or shoes. If your skin is contaminated, wash it immediately with soap and water. Symptoms of poisoning are excessive fatigue, sweating, thirst, and fever. If these develop, send for a physician.

With normal precautions, the chemical can be applied routinely with little or no hazard to the applicators. Daily bathing and change of clothing is recommended whether the applicator thinks he is contaminated or not.

Residues on foliage normally constitute little or no hazard to livestock. In an unpublished study, a milk cow was given 1.7 g of chemical/kg body weight/day for 3 days with no ill effects. Dinoseb did not appear in the milk. If there is question, keep livestock away from sprayed foliage until a rain has removed much of the herbicide.

The acute oral LD_{50} for rats ranges from 5 to 60 mg/kg. The maximum amount tolerated in the diet for a 6-month period was 100 ppm. It is considered to be quite toxic.

Fish are sensitive to dinoseb; 1.0 ppm killed trout and sea lamprey in 14 hr, and bluegills in 5 hr (1).

Uses

Dinoseb is very toxic to growing plants, so it is used as a general contact herbicide. It is so toxic to all leaves that it lacks the selectivity of its salt derivatives. Dinoseb is valuable where mowing is impractical; for example, along fencerows, ditchbanks, and roadsides. It kills most annual weeds and removes the tops from perennial weeds. Underground parts of perennial plants are not killed except by repeated treatments. Thus, dinoseb can be used in dormant alfalfa to kill annual weeds.

TOXICOLOGICAL STUDIES ON LABORATORY ANIMALS OF CERTAIN ALKYLDINITROPHENOLS USED IN AGRICULTURE*

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THE dinitrophenols are used extensively in agriculture for the control of insects, fungi and weeds.

The older literature pertaining to the use of the dinitrophenols as insecticides has been reviewed by Kagy and Richardson (1), who point out that a preparation containing the potassium salt of dinitro-*o*-cresol was marketed as early as 1892. Since that time the dinitrophenols have been used extensively in dormant sprays for the control of mites, aphids, scale insects, and other pests in overwintering stages. During the last ten years 2-cyclohexyl-4,6-dinitrophenol and its compound with dicyclohexylamine have gained wide acceptance as insecticides; and especially as acaricides for use in the greenhouse, field and orchard.

The dinitrophenols, particularly dinitro-*o*-cresol and its derivatives, are used as eradicator fungicides for the control of fungi which are pathogenic to a number of plant species.

Dinitro-*o*-cresol, 2-*sec*-butyl-4,6-dinitrophenol, and their salts are used extensively in weed control. These materials may be applied as selective weed killers in field crops and pastures, or as contact herbicides in such locations as roadsides and right-of-ways.

The widespread use of the dinitrophenols in the agricultural field has led, naturally, to the question of the problems that may be encountered in their handling and use. The answer to this question depends, to a large extent, upon the physiological effects produced by these materials.

In the case of 2,4-dinitrophenol, there have been many reports dealing with its effect upon laboratory animals and man. This extensive literature has been reviewed by Horner (2) with special emphasis upon the role of 2,4-dinitrophenol in the production of cataracts in man. On the other hand, relatively little information is available on the toxicity of the other dinitrophenols. The report by Ambrose (3) on dinitro-*o*-cresol and that by Hrenoff and Leake (4) on 2-cyclohexyl-4,6-dinitrophenol essentially cover the work that has been published on these materials.

The present experimental work was undertaken

*Received for publication August 21, 1947.

in order to obtain toxicological information which would be useful in evaluating the actual hazards associated with the use of the dinitrophenols, and in formulating safe handling procedures.

COMPOUNDS INVESTIGATED

The chemical and physical properties of the compounds used in this toxicological study are listed in Table 1. The solubility determinations were made by adding an excess of the material to the solvent and stirring for several hours at 25°C. The excess solid was then filtered off and the amount dissolved was determined by titration of the nitro groups with titanium chloride.

SKIN IRRITATION AND ABSORPTION—RABBITS AND GUINEA PIGS

Rabbits

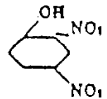
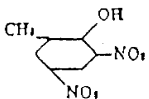
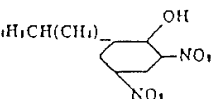
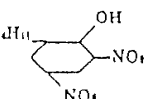
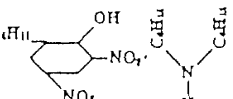
The effect of each of the dinitrophenols upon the skin was determined on white rabbits by a method previously described (5). The materials were all tested as 3 per cent solutions in 95 per cent ethanol. In some instances, other concentrations and vehicles were used. Heat was used when necessary to dissolve the test material. Routinely, 20 applications were made to the ear and 20 applications were bandaged onto the shaven abdomen over a period of four weeks. The absorption of lethal quantities of the test material or the development of marked skin irritation interrupted this routine in some cases.

2,4-Dinitrophenol. A 3 per cent alcoholic solution of 2,4-dinitrophenol produced no irritation on the ear and only a very slight irritation on the abdomen, characterized by mild hyperemia, edema, and exfoliation. There was no indication that toxic quantities of 2,4-dinitrophenol were absorbed through the skin under the conditions of this test.

Dormant spray oil containing 4 per cent of 2,4-dinitrophenol was no more irritating to the skin than the oil alone, which produced marked irritation when bandaged onto the abdomen for two or three days. Lethal quantities of 2,4-dinitrophenol were not absorbed through the abdominal skin from three applications in the oil.

4,6-Dinitro-*o*-cresol. Seven applications of a 3

TABLE 1
CHEMICAL AND PHYSICAL PROPERTIES OF COMPOUNDS INVESTIGATED

PROPERTY	COMPOUNDS				
Name*	2,4-Dinitrophenol	4,6-Dinitro-o-cresol	2-sec-Butyl 4,6-dinitrophenol	2-Cyclohexyl-4,6-dinitrophenol	2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine
Synonym	4,6-Dinitrophenol	2,4-Dinitro-o-cresol	2,4-Dinitro-o-sec-butylphenol	2,4-Dinitro-o-cyclohexylphenol	Dicyclohexylamine salt of 2,4-dinitro-o-cyclohexylphenol
Molecular Formula	$C_6H_4O_2N_2$	$C_7H_6O_2N_2$	$C_{12}H_{14}O_2N_2$	$C_{11}H_{12}O_2N_2$	$C_{11}H_{12}O_2N_2$
Structural Formula					
Formula Weight	184.04	198.13	240.21	266.23	447.56
M.P., °C.	113.2-113.9	86.0-86.9	37.9-39.3	104.1-105.7	191.5-195.8
N Found, %	14.87	13.95	11.55	10.08	9.26
N Theoretical, %	15.22	14.14	11.66	10.52	9.39
Purity of Compd., %					
From N det'n.	97.7	98.7	99.1	95.8	98.6
By titration**	98.9	98.7	97.7	99.6	97.2
Crystal Form	orthorhombic	triclinic	monoclinic	monoclinic	triclinic
Appearance	yellow crystals	yellow crystals	dark amber crystals	yellow crystals	orange crystals
Solubility in grams/100 grams at 25°C					
Water	0.0597	0.025	0.0734	0.072	0.0515
95% Ethanol	3.64	3.69	21.46	1.56	1.76
Oil***	1.67	5.98	8.77	1.84	0.00

* According to Chemical Abstracts.

** Titration of nitro groups with titanium chloride.

*** Oil commonly used in Dormant Sprays.

per cent alcoholic solution of 4,6-dinitro-o-cresol resulted in death from absorption through the skin; but caused no irritation on the ear and only slight irritation of the abdominal skin.

A 5 per cent solution in olive oil was also tested and found to be similar to the alcoholic solution in irritating properties; however, the amount of 4,6-dinitro-o-cresol absorbed from the olive oil solution during the course of 20 applications was insufficient to cause death.

A 4 per cent solution of 4,6-dinitro-o-cresol in Dormant spray oil was no more irritating than the oil alone; although in the case of three different rabbits, one application of this Dormant spray oil solution bandaged onto the shaven abdomen killed the animal within twenty-four hours.

2-sec-Butyl-4,6-dinitrophenol. A 3 per cent alcoholic solution of 2-sec-butyl-4,6-dinitrophenol failed to cause any significant irritation when repeatedly applied to the rabbit ear. However, when it was bandaged onto the shaven abdomen of 3 different rabbits, death occurred after 1, 3 and 8 exposures, respectively. No irritation of the abdominal skin was observed in any instance.

A 10 per cent solution of 2-sec-butyl-4,6-dinitrophenol in butylcarbitol acetate was applied to three rabbits. In each case death occurred within twenty-four hours without evidence of any irritation to the ear or abdominal skin.

2-Cyclohexyl-4,6-dinitrophenol. Alcohol containing 2-cyclohexyl-4,6-dinitrophenol in a concentration of 3 per cent produced no irritation on the ear, but caused a moderate irritation on the abdomen, characterized by moderate hyperemia and exfoliation, and some denaturation. This irritation was severe enough to warrant the termination of the experiment after 7 applications.

A 5 per cent solution of 2-cyclohexyl-4,6-dinitrophenol in olive oil produced only slight irritation of the ear, as shown by mild hyperemia and exfoliation, and a slightly greater response on the abdomen with some blistering as well as hyperemia and exfoliation.

Dormant spray oil containing 4 per cent of the test material appeared to be only slightly more irritating than the oil alone. Lethal quantities of 2-cyclohexyl-4,6-dinitrophenol were not absorbed from 2 applications of the Dormant spray oil solution, 7 applications of the alcoholic solution, or 20 applications of the olive oil solution, bandaged onto the shaven abdomen.

2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine. A 3 per cent solution of 2-

cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine in 1:4 acetone-alcohol (acetone used to effect complete solubility) failed to cause any appreciable irritation when applied repeatedly to the ear or when bandaged repeatedly to the shaven abdomen.

Tested in a like manner, a 20 per cent solution of the material in olive oil produced no irritation. Lethal quantities of 2-cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine were not absorbed from either of these solutions during the course of the experiments.

TABLE 2
SUMMARY OF TOXICITY FROM SKIN ABSORPTION
FOLLOWING SINGLE APPLICATION—GUINEA
PIGS

COMPOUND	"SURVIVAL DOSE"*	"LETHAL DOSE"***
	g./kg.	g./kg.
2-sec-Butyl-4,6-dinitrophenol.....	0.1	0.5
4,6-Dinitro-o-cresol.....	0.2	0.5
2,4-Dinitrophenol.....	0.2	0.7
2-Cyclohexyl-4,6-dinitrophenol.....	1.0 or more	>1.0
2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine.....	1.0 or more	>1.0

* Largest dose survived by all animals treated.

** Smallest dose causing death of all animals treated.

Guinea pigs

Guinea pigs of both sexes were used to determine the toxicity of the dinitrophenols from absorption through the intact skin. The animals used in this work were of heterogeneous stock procured from a commercial supplier and maintained on Purina Rabbit Chow (complete ration), alfalfa hay, and cabbage. A single dose of one of the dinitrophenols in alcoholic solution was applied to the clipped abdomen of each experimental animal. Each guinea pig was restrained on an animal board in such a manner that the treated area could be kept wet with ethanol during the four-hour period following the application of the test material in order to facilitate its absorption. At the end of this period, the surviving animals were removed from the boards, bandaged so as to prevent oral ingestion, caged, and observed until it was certain that they had fully recovered.

The results of this study on 108 guinea pigs are summarized in Table 2 and shown in detail in Table 3.

Summary of Skin Irritation and Absorption

These experiments on rabbits have shown that the dinitrophenols investigated are not significantly irritating to the skin.¹ Even the most irritating one of the group, 2-cyclohexyl-4,6-dinitrophenol, required prolonged exposure to cause appreciable irritation. None of the materials caused any epithelial hyperplasia or follicular changes.

In the skin irritation tests on rabbits it was apparent that some of these materials, particularly, 2-sec-butyl-4,6-dinitrophenol and 4,6-dinitro-o-cresol, were readily absorbed through the intact skin in quantities sufficient to cause death.

from the stock colony in this laboratory, although some were purchased from the Breeding and Laboratory Institute, Brooklyn.

Aliquots of olive oil solutions of the materials were emulsified with 5-10 per cent gum arabic solution and administered by means of a stomach tube (8FS 16" all rubber catheter). The volume of oil given to each rat was always less than 3 ml. and was usually of the order of 1 ml. All of the rats that survived were observed until it was certain that they had fully recovered (usually about two weeks). Deaths that resulted from the administration of the dinitrophenols are believed to

TABLE 3
MORTALITY RESULTING FROM SINGLE APPLICATION TO ABDOMINAL SKIN—GUINEA PIGS

QUANTITY APPLIED TO SKIN	COMPOUNDS (APPLIED IN ALCOHOLIC SOLUTIONS)									
	2,4-Dinitrophenol		4,6-Dinitro-o-cresol		2-sec-Butyl-4,6-dinitrophenol		2-Cyclohexyl-4,6-dinitrophenol		2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine	
	No. treated	No. died	No. treated	No. died	No. treated	No. died	No. treated	No. died	No. treated	No. died
<i>1./kg.</i>										
0.1	5	0	5	0	5	0	—	—	—	—
0.15	—	—	—	—	5	1	—	—	—	—
0.2	5	0	5	0	5	4	—	—	—	—
0.3	5	1	5	1	5	5	—	—	—	—
0.4	5	1	5	3	5	4	—	—	—	—
0.5	5	2	5	5	5	5	—	—	—	—
0.6	—	—	—	—	5	5	—	—	—	—
0.7	5	5	—	—	—	—	—	—	—	—
1.0	5	5	2	2	1	1	5	0	5	0
Totals....	35		27		36		5		5	

In order to obtain a better estimation of the relative toxicity of these dinitrophenols from skin absorption, the quantitative tests on guinea pigs were carried out. These experiments have demonstrated that the following compounds, listed according to decreasing toxicity, can readily be absorbed through the intact skin in lethal amounts: 2-sec-butyl-4,6-dinitrophenol; 4,6-dinitro-o-cresol; and 2,4-dinitrophenol. On the other hand, neither 2-cyclohexyl-4,6-dinitrophenol nor its compound with dicyclohexylamine are absorbed through the skin to an appreciable extent.

ORAL ADMINISTRATION—SINGLE DOSE BY
STOMACH TUBE—RATS

The toxicity of the dinitrophenols when given in single oral doses was determined on young mature white rats of both sexes. Most of the animals were

be due chiefly to their pyretic effect; as a rule, death occurred an hour or two after the feeding or not at all. The detailed results obtained on the 674 rats used in this study are given in Table 5 and are summarized in Table 4.

It is evident that all of the dinitrophenols investigated are rapidly acting materials of a fairly high order of acute oral toxicity. However, the toxicity of 2-cyclohexyl-4,6-dinitrophenol or its compound with dicyclohexylamine is definitely lower than that of 2-sec-butyl-4,6-dinitrophenol or 4,6-dinitro-o-cresol.

ORAL ADMINISTRATION IN THE DIET FOR
SIX MONTHS—RATS

Experimental Procedure

The modified Sherman diet (6), which has been used successfully for several years in this labora-

tory as the stock ration for rats, served as the control and basic diet in all of the experiments.

TABLE 4
SUMMARY OF ACUTE ORAL TOXICITY—RATS

COMPOUND	"SURVIVAL" DOSE*	"LETHAL" DOSE**
	g./kg.	g./kg.
2-sec-Butyl-4,6-dinitrophenol...	0.005	0.060
4,6-Dinitro-o-cresol.....	0.010	0.050
2,4-Dinitrophenol.....	0.027	0.100
2-Cyclohexyl-4,6-dinitrophenol..	0.030	0.180
2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexyl- amine.....	0.060	0.600

* Largest dose survived by all animals fed.

** Smallest dose causing death of all animals fed.

Dried meat residue (or dried extracted liver)..... 12% by weight
Dried brewer's yeast..... 5% by weight
Calcium carbonate..... 1% by weight
Iodized table salt..... 2% by weight

For several years dried meat residue was used in the stock diet, however, when this product was no longer available, dried extracted liver was substituted (March, 1944) and found to be satisfactory.

The experimental diets (see Table 6) were prepared by thoroughly mixing the dinitrophenols with the stock diet on a per cent by weight basis. The test material was added to the diet either directly or by means of a flour concentrate. In either case thorough mixing was obtained by the use of a mechanical mixer, and the actual concen-

TABLE 5
MORTALITY RESULTING FROM ADMINISTRATION OF SINGLE ORAL DOSE—RATS

SINGLE ORAL DOSE	COMPOUNDS (GIVEN IN OLIVE OIL EMULSIFIED IN CUM ARABIC)									
	2,4-Dinitrophenol		4,6-Dinitro-o-cresol		2-sec-Butyl-4,6-dinitrophenol		2-Cyclohexyl-4,6-dinitrophenol		2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine	
	No. fed	No. died	No. fed	No. died	No. fed	No. died	No. fed	No. died	No. fed	No. died
g./kg.										
0.005	—	—	—	—	20	0	—	—	—	—
0.010	9	0	20	0	20	1	—	—	—	—
0.020	20	0	20	3	10	1	—	—	—	—
0.023	10	0	—	—	10	2	—	—	—	—
0.025	10	0	—	—	—	—	—	—	—	—
0.027	10	0	—	—	10	0	—	—	—	—
0.030	30	11	20	9	10	4	10	0	—	—
0.040	20	18	20	15	10	5	10	1	—	—
0.050	20	17	20	20	10	7	10	3	—	—
0.060	20	19	—	—	20	20	10	5	10	0
0.070	30	15	—	—	—	—	25	13	—	—
0.080	40	18	—	—	—	—	20	12	—	—
0.100	20	20	—	—	—	—	40	22	5	1
0.120	—	—	—	—	—	—	20	14	—	—
0.140	—	—	—	—	—	—	10	7	—	—
0.160	—	—	—	—	—	—	10	8	—	—
0.180	—	—	—	—	—	—	10	10	—	—
0.200	—	—	—	—	—	—	10	10	—	—
0.400	—	—	—	—	—	—	—	—	5	3
0.600	—	—	—	—	—	—	—	—	10	10
Totals....	239		100		120		185		30	

The following ingredients were used in the preparation of this stock diet:

Whole wheat, freshly ground..... 55% by weight
Dried whole milk..... 25% by weight

tration of the test material in the diet checked by chemical analysis. Each flour concentrate was prepared by adding wheat flour to an alcoholic solution of the test material to form a thick paste

TABLE 6
EXPERIMENTS IN WHICH MALE RATS RECEIVED DIETS CONTAINING DINITROPHENOLS

COMPOUND IN DIET ^(a)		SOURCE OF RATS	DATE STARTED ON DIET	NO. OF RATS STARTED	SURVIVAL FOR ENTIRE EXPTL. PERIOD	LENGTH OF EXPTL. PERIOD	NO. OF RATS EXAMINED AT END OF EXPT.				
Name	Conc. (wt. %)						Hematology	Bone marrow counts	Organ weights	Blood urea-N	Histopathology
2,4-Dinitrophenol	0.00	B-L ^(c)	5-22-45	20	per cent	days	10**	7	14	14	7
	0.01	B-L	"	15	80	178			12	12	8
	0.02	B-L	"	15	80	179			12	12	8
	0.05	B-L	"	15	66	179	9**	6	10	9	9
	0.10	B-L	"	15	93	179	14		14	14	13
	0.20	B-L	"	10	60	24			6	6	6
4,6-Dinitro-o-cresol	0.00	B-L	3-23-45	20	80	182	10**	8	16	16	8
	0.002*	B-L	"	20	90	179			18	17	10
	0.005*	B-L	"	20	100	182			20	20	10
	0.01*	B-L	"	20	90	182	10**	8	18	18	9
	0.02*	B-L	"	20	80	181			16	16	12
	0.05*	B-L	"	10	90	182	9		9	9	9
	0.05	B-L	3-31-45	12	42	77			5	5	5
	0.10	B-L	7-9-45	10	40	10			4	4	4
	0.10*	B-L	7-9-45	10	50	10			5	5	5
2-sec-Butyl-4,6-dinitrophenol	0.00	B-L	3-2-45	30	70	189	10**	9	21	21	21
	0.005*	B-L	"	20	90	189			18	17	17
	0.01*	B-L	"	20	80	189	10**	8	16	15	15
	0.02*	B-L	"	20	85	189	8	8	17	16	16
	0.05*	B-L	"	10	60	21			6	6	6
2-Cyclohexyl-4,6-dinitrophenol	0.00 ^(b)	Dow	8-18-43	20	70	195	10***	14	14		6
	0.02	Dow	"	20	95	194	10***		19		9
	0.05	Dow	"	20	65	194	10**	12	13		7
	0.10	Dow	"	20	55	195			11		11
2-Cyclohexyl-4,6-dinitrophenol compd. with dicyclohexylamine	0.00 ^(b)	Dow	"	20	70	195	10***	14	14		6
	0.05	Dow	"	20	65	195	10***		13		6
	0.10	Dow	"	20	80	194	10**	15	16		9
	0.20	Dow	"	20	60	196			12		12
Totals.....				472			Approx. 600 exams.	95	355	252	258

^(a) Compound added directly to the control diet unless otherwise indicated.

^(b) One control group for both compounds.

^(c) Breeding and Laboratory Institute, Brooklyn.

* Flour concentrate containing compound added to the control diet.

** Examined bimonthly during experimental period.

*** Examined monthly during experimental period.

which was then dried, ground, passed through an 80-mesh sieve, and analyzed. The use of these concentrates facilitated the accurate addition of

small quantities of the test materials to the basic diet.

The diets containing the dinitrophenols were

made up from freshly prepared stock diet when needed. No diet preparations over a month old were used during the course of these experiments. The rats were fed from stainless-steel hoppers which were weighed and refilled three times a week.

White male rats from the stock colony in this laboratory ("Dow") were used in the experiments on 2-cyclohexyl-4,6-dinitrophenol and its compound with dicyclohexylamine. These rats were the progeny of animals obtained from the Wistar Institute in 1938. Since sufficient "Dow" animals were not available, white male rats were purchased from the Breeding and Laboratory Institute, Brooklyn, ("B and L") for the work on the other dinitrophenols.

The "Dow" rats were maintained on the stock diet from the time of weaning until about two months of age when they were divided according to body weights into well matched groups and started on the experimental diets. The rats from the Breeding and Laboratory Institute were received when about twenty-five to thirty days old, although the exact ages were not known, maintained for three to four weeks on the stock diet, and then divided according to body weights into matched groups and started on the experimental diets.

Five rats were caged together, the "Dow" rats in solid bottom cages with wood shavings and sawdust as litter, and the "B and L" rats in wire bottom cages. The animals had free access to food and water at all times. In addition, each rat was given approximately 3 grams of cabbage twice weekly.

The general design of the experiments is presented in Table 6. The following information for each experimental diet is given: concentration of the test material in the diet, method of adding test material to the diet, source of the rats used, date started, number of rats started in each group, length of experimental period, and survival.

The experiments with "Dow" rats on 2-cyclohexyl-4,6-dinitrophenol and its compound with dicyclohexylamine were started at the same time using only one group of controls; while the experiments with "B and L" rats on 2,4-dinitrophenol, 4,6-dinitro-*o*-cresol, and 2-*sec*-butyl-4,6-dinitrophenol were each started separately, making it necessary to use 3 groups of controls.

All of the rats were weighed twice a week throughout the experimental period. Records were kept of the body weight, general appearance,

and estimated average daily food consumption of each animal. Animals that died were examined for gross pathological lesions.

During the course of the experiments, periodic hematological examinations were made on several groups of animals as indicated in Table 6. The following determinations were made routinely: erythrocyte count, hemoglobin concentration, total leucocyte count and differential count.

At the end of each experiment all of the surviving rats were starved overnight, weighed, killed by decapitation, and examined. The liver, kidneys, heart, and testes from each rat were weighed; and tissues from representative animals in each group were saved for histopathological studies. Hematoxylin and eosin stained sections of the following organs were prepared: lung, heart, liver, kidney, spleen, adrenal, pancreas, testis, stomach, and bone marrow. The number of animals examined is given in Table 6.

The concentration of urea-N in the blood was determined at the time of autopsy by the diacetyl monoxime procedure (7) on the rats that received 2,4-dinitrophenol, 4,6-dinitro-*o*-cresol and 2-*sec*-butyl-4,6-dinitrophenol.

Bone marrow counts were made on many of the rats which had been examined periodically for hematological changes (see Table 6). The number of nucleated cells per cu. mm. of bone marrow was estimated by the method described by Farrar (8) using a red-blood-cell diluting pipette and 1 per cent acetic acid as the diluting fluid. The total cell count was determined in a similar manner using Hayem's solution (9).

Experimental Results

Growth curves for each group of rats on the diets containing the dinitrophenols and on the controls are given in Figure 1. The length of time that each experimental diet was fed and the survival on each diet are given in Table 6. The average final body weights (after overnight starvation) and the average organ weights of the rats in each group that survived for a period of six months are presented in Table 7, together with the standard error of the mean (S.E.) in each case. The *t*-test (10) was used in comparing the mean values obtained on the experimental groups with those of the controls; probability values (*P*) of 0.05 or less indicating a significant difference.

No evidence of corneal opacity, cataract formation, or other pathological changes were found in

the eyes of the rats receiving any of the dinitrophenols included in these studies. The hair of all of the animals on the experimental diets was stained, the intensity of the staining being approximately proportional to the concentration of the test material in the diet. This staining probably

accordance with the practice followed in this laboratory of immediately killing every animal showing definite signs of pulmonary or ear infection. In these six-month experiments there was no indication that the mortality rate was appreciably increased by the dinitrophenols in the diets.

TABLE 7
BODY WEIGHTS AND ORGAN WEIGHTS OF MALE RATS THAT SURVIVED FOR SIX MONTHS
ON DIETS CONTAINING DINITROPHENOLS

COMPOUND IN DIET		No. of rats	BODY WEIGHT (g.)	LIVER (g.)	KIDNEYS (g.)	HEART (g.)	TESTES (g.)
Name	Concn., (wt. %)		Mean \pm S.E. ^(a)	Mean \pm S.E.	Mean \pm S.E.	Mean \pm S.E.	Mean \pm S.E.
2,4-Dinitrophenol	0.00	14	314 \pm 7	7.86 \pm 0.21	2.18 \pm 0.05	1.08 \pm 0.02	3.18 \pm 0.08
	0.01	12	306 \pm 7	8.13 \pm 0.11	2.36 \pm 0.04**	1.10 \pm 0.02	3.04 \pm 0.17
	0.02	12	314 \pm 8	8.31 \pm 0.27	2.37 \pm 0.08*	1.07 \pm 0.03	3.38 \pm 0.13
	0.05	9	286 \pm 7*	7.89 \pm 0.32	2.39 \pm 0.12*	1.03 \pm 0.02	3.02 \pm 0.17
	0.10	14	269 \pm 5**	8.08 \pm 0.24	2.38 \pm 0.07*	1.01 \pm 0.02*	3.15 \pm 0.12
4,6-Dinitro-o-cresol	0.00	16	300 \pm 8	7.78 \pm 0.27	2.16 \pm 0.09	1.05 \pm 0.03	2.85 \pm 0.12
	0.002	18	292 \pm 8	7.08 \pm 0.28	2.00 \pm 0.09	1.02 \pm 0.03	2.77 \pm 0.08
	0.005	20	293 \pm 8	7.23 \pm 0.25	1.99 \pm 0.05	1.00 \pm 0.03	2.74 \pm 0.09
	0.01	18	304 \pm 8	7.55 \pm 0.28	2.01 \pm 0.06	1.01 \pm 0.02	2.58 \pm 0.15
	0.02	16	277 \pm 7*	6.86 \pm 0.22*	1.82 \pm 0.05**	0.94 \pm 0.03*	2.61 \pm 0.07
	0.05	9	247 \pm 7**	7.14 \pm 0.19	2.09 \pm 0.07	0.96 \pm 0.04	2.49 \pm 0.16
2-sec-Butyl-4,6-dinitrophenol	0.00	21	278 \pm 4	7.13 \pm 0.14	1.90 \pm 0.05	0.95 \pm 0.01	2.59 \pm 0.06
	0.005	18	286 \pm 5	6.83 \pm 0.12	1.86 \pm 0.04	0.95 \pm 0.02	2.69 \pm 0.07
	0.01	16	281 \pm 5	7.47 \pm 0.23	1.90 \pm 0.07	0.96 \pm 0.03	2.76 \pm 0.10
	0.02	17	266 \pm 6	7.85 \pm 0.24**	2.06 \pm 0.07	0.96 \pm 0.03	2.67 \pm 0.08
2-Cyclohexyl-4,6-dinitrophenol	0.00 ^(b)	14	341 \pm 10	9.16 \pm 0.42	2.13 \pm 0.06	1.01 \pm 0.03	2.57 \pm 0.09
	0.02	19	322 \pm 5	8.88 \pm 0.21	2.24 \pm 0.06	1.06 \pm 0.02	2.59 \pm 0.09
	0.05	13	322 \pm 12	9.11 \pm 0.35	2.22 \pm 0.08	1.05 \pm 0.03	2.62 \pm 0.09
	0.10	11	291 \pm 14**	8.97 \pm 0.40	1.98 \pm 0.08	0.90 \pm 0.03*	2.40 \pm 0.09
2-Cyclohexyl-4,6-dinitrophenol compd. with dicyclohexylamine	0.00 ^(b)	14	341 \pm 10	9.16 \pm 0.42	2.13 \pm 0.06	1.01 \pm 0.03	2.57 \pm 0.09
	0.05	13	316 \pm 8	9.19 \pm 0.33	2.18 \pm 0.07	0.98 \pm 0.03	2.57 \pm 0.08
	0.10	16	314 \pm 9*	9.16 \pm 0.32	2.29 \pm 0.07	1.06 \pm 0.02	2.53 \pm 0.11
	0.20	12	289 \pm 8**	8.75 \pm 0.25	2.10 \pm 0.05	0.96 \pm 0.03	2.43 \pm 0.20

^(a) S.E. = Standard Error of the Mean.

^(b) One control group for both compounds.

* P = 0.05 - 0.01 (as determined by the t-test (10)).

** P = < 0.01

came from contact with the food and apparently did no harm to the animals.

In all of the experiments which lasted for six months, the survival was essentially the same in all groups of rats, controls as well as those on the diets containing the dinitrophenols (Table 6). Most of the deaths, that occurred during the course of these experiments, were shown by autopsy to be due to pulmonary infection. Other rats were sacrificed in

The daily food intake of the control rats and of the rats in the experimental groups that grew equally as well as the controls was found to be from 10 to 20 grams per rat. It may be calculated that these rats, weighing from 200 to 350 grams, ingested quantities of the dinitrophenols of the order of 0.002-0.00054, 0.005-0.00135, 0.01-0.0027, 0.02-0.0054, 0.05-0.0135, 0.10-0.027, and 0.20-0.054 g./kg./day when maintained on diets con-

taining 0.002, 0.005, 0.01, 0.02, 0.05, 0.10, and 0.20 per cent of the test materials, respectively.

No doubt there was considerable individual variation in the quantity ingested depending upon the body weight and food intake of each rat. During the first few weeks on the experimental diets the young rats actually received greater quantities of the dinitrophenols on a g./kg./day basis than later when they were approaching maturity.

The animals that made poor weight gains usually showed an obvious dislike for the experimental diet, ate rather sparingly, and wasted a great deal of the food by pawing and scratching at the hopper; in these cases it was impossible to obtain an accurate estimation of the food consumption.

The hematological examinations which were made during the course of these experiments are indicated in Table 6. In every case, the erythrocyte counts, hemoglobin concentrations, leucocyte counts, and differential counts obtained on the animals receiving the dinitrophenols agreed satisfactorily with those obtained at the same time on their own controls. Similarly, there was satisfactory agreement between the bone marrow counts obtained at autopsy on the rats that had been maintained for six months on diets containing the dinitrophenols and the values obtained on their own controls. Thus, there was no indication that the feeding of diets containing 2,4-dinitrophenol, 4,6-dinitro-o-cresol, 2-sec-butyl-4,6-dinitrophenol, 2-cyclohexyl-4,6-dinitrophenol, or its compound with dicyclohexylamine at the concentrations shown in Table 6 for a period of six months produced any change in the bone marrow or blood picture of male rats. For the sake of clarity, further discussion of the experimental results is given separately for each of the dinitrophenols included in this investigation.

2,4-Dinitrophenol. Rats in the group of 10 animals on the diet containing 0.20 per cent 2,4-dinitrophenol lost weight rapidly and four of them died after seven, twelve, sixteen, and twenty-one days, respectively. The six survivors were killed and examined after twenty-four days on the diet, at which time they were very thin and weak. Gross examination of each animal revealed marked emaciation, an empty gastrointestinal tract, a slightly enlarged, dark spleen and small testes. Microscopic examination showed slight congestion and cloudy swelling of the liver, very slight paren-

chymatous degeneration of the epithelium of the renal tubules, slight congestion and hemosiderosis of the spleen, and testicular atrophy. No significant pathological changes were observed in the lung, heart, adrenal, pancreas, or stomach. The concentration of urea-N in the blood of these animals averaged 31.7 mg. per cent. It is difficult to distinguish clearly between the ill effects produced in these animals by dinitrophenol and those due to decreased food consumption.

The growth curve of the group of rats that received the diet containing 0.1 per cent 2,4-dinitrophenol fell 10 to 15 per cent below that of the controls throughout the experimental period of six months (Figure 1). The difference between the average final body weight of these animals and that of their controls was highly significant ($P < 0.001$). During the course of the experiment these animals showed no discernible ill effects other than slight emaciation. At autopsy, the only changes noted in the experimental group as compared with the controls was a slight depletion of the body fat, a very slight increase in the average weight of the kidneys and a very slight decrease in the weight of the heart (Table 7). Two of the 14 animals examined gave blood urea-N values of 32.8 and 36.6 mg. per cent; the other animals in this group had an average blood urea-N of 21.6 as compared with 19.4 mg. per cent for the controls. No appreciable changes were found upon microscopic examination of sections of the lung, liver, kidney, heart, spleen, adrenal, pancreas, testis, stomach, and bone marrow from these animals.

The growth curve of the group of rats that received the diet containing 0.05 per cent 2,4-dinitrophenol fell 5 to 10 per cent below that of the controls throughout the six-month experimental period (Figure 1). The difference between the average final body weight of these animals and that of their own controls was quite significant ($P = 0.01$). At autopsy the only changes observed in the experimental animals as compared with the controls was a very slight depletion of body fat, and a very slight increase in the average weight of the kidneys (Table 7). Blood urea-N values of 38.2 and 44.8 mg. per cent were found in two of the nine experimental animals. The other rats in this group had an average blood urea-N of 19.5 as compared with 19.4 mg. per cent for the controls. No significant pathological changes were found upon microscopic examination of the tissues.

In the case of the groups that received the diets containing 0.02 and 0.01 per cent 2,4-dinitrophenol, course of these experiments no discernible ill effects were noted in these animals; and at autopsy the

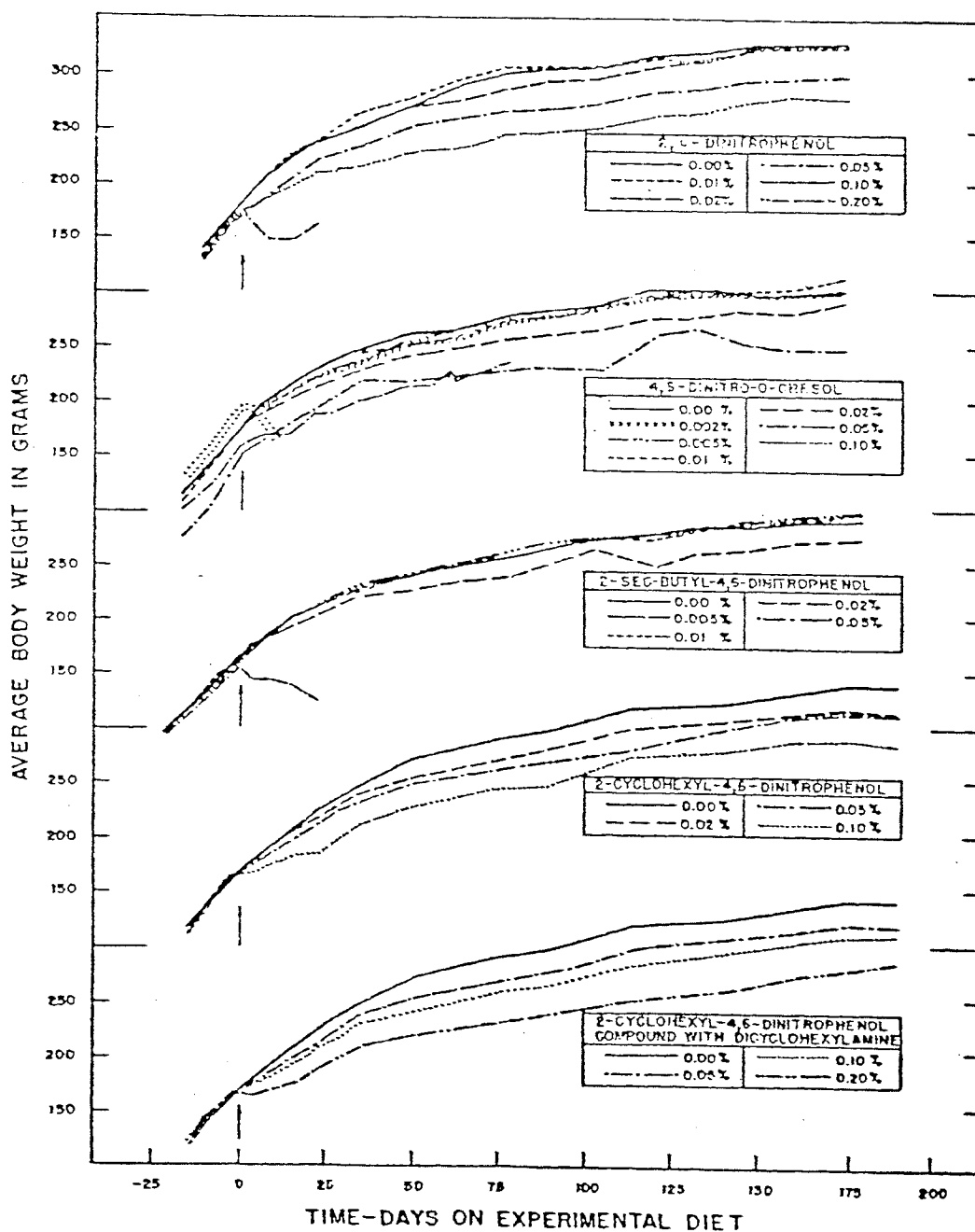


FIG. 1. Growth curves of male rats on diets containing dinitrophenols.

the growth curves were essentially the same as that of the controls throughout the six-month experimental period (Figure 1). During the only change observed in the experimental groups as compared with the controls was a very slight increase in the average weight of the kidneys.

The average blood urea-N was 22.8 and 18.2 mg. per cent for the groups on the 0.02 and 0.01 per cent diets, respectively, as compared with 19.4 mg. per cent for the controls. No pathological changes were found upon microscopic examination of sections of the lung, liver, kidney, heart, spleen, adrenal, pancreas, and testis from these animals.

4,6-Dinitro-o-cresol. The two groups of rats on the diets containing 0.10 per cent 4,6-dinitro-o-cresol, one prepared from the flour concentrate and the other by direct mixing, lost weight rapidly (Figure 1), and appeared weak, hungry, thin and unkempt. The surviving rats were killed on the tenth day of the experiment, since about half of the rats in each group had died by this time (Table 6). Gross examination of each animal revealed marked emaciation, an empty gastrointestinal tract, and a slightly enlarged dark spleen. The average blood urea-N concentration in these rats was 44.4 mg. per cent. Microscopic examination showed cloudy swelling of the liver, very slight degenerative changes in the renal tubules, and slight congestion of the spleen. No appreciable changes were observed in the lungs, heart, adrenals, pancreas or testes. In an experiment such as this, it is difficult to differentiate between the effects produced by the test material and those due to decreased food intake.

Both groups of rats on the diets containing 0.05 per cent 4,6-dinitro-o-cresol made poor weight gains (Figure 1) and appeared hungry, thin and unkempt throughout the course of the experiment. The surviving rats on the diet prepared by direct mixing with 4,6-dinitro-o-cresol were killed and examined after seventy-seven days (Table 6). No appreciable change in the organ weights was noted in these animals. Two of the five rats gave blood urea-N values of 34.4 and 35.0 mg. per cent, the other three an average value of 24.4 per cent. Congestion and hemosiderosis of the spleen was noted in three animals. No appreciable changes were observed upon microscopic examination of the lung, heart, kidney, liver, adrenal, pancreas, testis and stomach. The group receiving the diet prepared from the flour concentrate were allowed to continue on the experiment until the end of the six-month period. At autopsy depletion of the body fat was observed, but no gross changes were evident in the viscera. The average weights of the liver, kidneys, heart, and testes for the experimental animals were essentially the same as those for the controls even though the average body

weight of the experimental group was much lower than that of the controls (Table 7). Four of the nine experimental animals showed an average blood urea-N of 30.4 mg. per cent, the other 5 an average of 21.9 mg. per cent. No significant changes were observed upon microscopic examination of the tissues from these animals.

The growth curve of the group of rats on the diet containing 0.02 per cent 4,6-dinitro-o-cresol fell 7 to 9 per cent below that of the controls throughout the experimental period of six months (Figure 1). This depression in growth is probably significant, since a comparison, by means of the t-test (10), of the body weights of the experimental animals with those of the controls at frequent intervals during the 6-month period yielded P values of 0.05 or less in most instances. The general appearance of these animals was good during the course of the experiment and at autopsy there were no evident ill effects; although the average organ weights in the case of the liver, kidneys, and heart were slightly lower than those for the controls (Table 7). The average blood urea-N in this group was 16.1 as compared with 15.8 mg. per cent for the controls. No pathological changes were observed upon microscopic examination of the tissues from these animals.

In the case of the groups that received the diets containing 0.01, 0.005, and 0.002 per cent 4,6-dinitro-o-cresol, the growth curves were essentially superimposed on that of the controls throughout the six-month experimental period (Figure 1). No ill effects were observed in these animals during the course of the experiment or at autopsy. The organ weights obtained on these experimental animals compared favorably with those of the controls (Table 6). The average blood urea-N concentration was 14.0, 17.8 and 18.1 mg. per cent for the rats on the 0.01, 0.005, and 0.002 per cent diets, respectively, as compared with 15.8 mg. per cent for the controls. No histopathological changes were found upon examination of the tissues from these animals.

2-sec-Butyl-4,6-dinitrophenol. The group of 10 rats on the diet containing 0.05 per cent 2-sec-butyl-4,6-dinitrophenol lost weight rapidly and four of the animals died after five, ten, and thirteen days, respectively. The six survivors were killed and examined after twenty-one days on the diet. Examination of these animals showed marked emaciation, an empty gastrointestinal tract and an average blood urea-N concentration of 55.0 mg. per

cent. Microscopic examination of their tissues revealed slight degenerative changes in the renal tubules, and slight cloudy swelling of the liver, but no appreciable changes in the lung, heart, spleen, adrenal, pancreas, or testis. Here again, it is difficult to distinguish between the effects due to the test material and those associated with inanition.

The growth curve of the group of rats on the diet containing 0.02 per cent 2-sec-butyl-4,6-dinitrophenol fell 3 to 8 per cent below that of the controls during the experimental period of six months (Figure 1). This depression in growth is probably significant since a comparison of the body weights of the experimental rats with those of the controls at frequent intervals during the course of the experiment yielded P values slightly below 0.05 in most cases. No discernible ill effects were observed in these animals, either during the course of the experiment or at autopsy. The average blood urea-N was 20.3 as compared with 17.5 mg. per cent for the controls. The organ weights did not vary appreciably from that of the controls except for a slight increase in the weight of the liver (Table 7). Microscopic examination of the tissues from these animals failed to reveal any appreciable changes as compared with the controls.

The growth curves of the groups of rats that received the diets containing 0.01 and 0.005 per cent 2-sec-butyl-4,6-dinitrophenol were superimposed on that of the controls throughout the six-month experimental period (Figure 1). These animals showed no evidence of ill effects either during the course of the experiment or at autopsy. The average blood urea-N concentration in the animals on the 0.01 and 0.005 per cent diets were 20.9 and 17.3 mg. per cent, respectively, as compared with 17.5 mg. per cent for the controls. The organ weights of the experimental animals compared favorably with those of the controls (Table 7); and no histopathological changes were found upon examination of their tissues.

2-Cyclohexyl-4,6-dinitrophenol. The growth curve of the group of rats on the diet containing 0.10 per cent 2-cyclohexyl-4,6-dinitrophenol fell 10 to 15 per cent below that of the controls throughout the six-month experimental period (Figure 1). This depression in growth is quite significant as shown by frequent comparisons of body weights during the course of the experiment which consistently yielded P values much below 0.05. The general appearance of these animals was good and at autopsy there were no evident ill effects other

than a slight loss in body fat. The organ weights of the experimental animals agreed well with those of the controls except for heart weights which were slightly lower (Table 7). Slight cloudy swelling of the liver was the only change observed upon microscopic examination of the tissues.

In the case of the groups of rats on the diets containing 0.05 and 0.02 per cent 2-cyclohexyl-4,6-dinitrophenol the growth curves fell 3 to 10 per cent below that of the controls throughout the experimental period (Figure 1). It is very doubtful that this slight depression in growth is significant, since analyses of the body weights at frequent intervals during the course of the experiment yielded values of P below 0.05 in only a few instances; in no case was a P value of less than 0.014 encountered. The organ weights obtained on these animals compared favorably with those of the controls (Table 7). No histopathological changes were found upon examination of the tissues from these animals.

2-Cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine. The group of rats receiving the diet containing 0.20 per cent 2-cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine showed a definite depression in growth throughout the experimental period (Figure 1); their final average body weight falling 15 per cent below that of the controls ($P = <0.001$). Except for slight emaciation, these experimental animals showed no evident ill effects, either during the course of the experiment or at autopsy. Their organ weights compared favorably with those of the controls (Table 7), and no histopathological changes were observed other than slight cloudy swelling of the liver.

The growth curves of the groups of rats on the 0.10 and 0.05 per cent diets fell 5 to 9 and 7 to 11 per cent respectively, below that of the controls during the experimental period of six months (Figure 1). The significance of this depression in growth is questionable since comparisons at frequent intervals of the body weights of the rats on the 0.05 per cent diet with those of the controls gave values of P slightly above 0.05 in most instances; while similar studies on the group receiving the 0.10 per cent diet yielded P values only slightly below 0.05 in most cases, with an occasional value above 0.05. No discernible ill effects were apparent in these experimental animals either during the course of the experiment or from organ weight and

histopathological studies conducted at its termination.

Summary of Feeding Experiments with Rats

Male rats maintained for six months on diets containing 0.01 per cent 2-sec-butyl-4,6-dinitrophenol, 0.01 per cent 4,6-dinitro-o-cresol, 0.02 per cent 2,4-dinitrophenol, 0.05 per cent 2-cyclohexyl-4,6-dinitrophenol, and 0.05 per cent 2-cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine showed no appreciable ill effects as determined by frequent gross observations, growth curves, periodic blood counts, analyses for blood urea-N, organ weights, and histopathological examinations.

Effects that may be attributed to the action of the dinitrophenols as metabolic stimulants were observed in rats that received diets containing greater quantities of these materials. Thus, depression in body weight, chiefly at the expense of body fat, was the characteristic finding rather than appreciable organic injury. No cataracts were produced in any of the rats receiving the dinitrophenols, nor were there any changes in the bone marrow or blood picture.

In the case of each of the dinitrophenols investigated, it is evident that there is very little summation of toxic effects upon prolonged ingestion, as judged by a comparison of the quantity that caused death after a single oral dose with the quantity that produced no appreciable ill effects when administered daily in the diet for a period of six months.

ORAL ADMINISTRATION IN THE DIET FOR SHORT TIME—DUCKLINGS

In view of the unfortunate human experience with 2,4-dinitrophenol, there have been many attempts to produce cataracts in laboratory animals by the administration of this material. However, all of these were unsuccessful until Robbins (11) found that cataracts formed very quickly in ducklings or chicks following the feeding of a diet containing the sodium salt of 2,4-dinitrophenol.

In order to obtain comparative information concerning the production of cataracts by 2,4-dinitrophenol, 4,6-dinitro-o-cresol, 2-sec-butyl-4,6-dinitrophenol, and 2-cyclohexyl-4,6-dinitrophenol, the following experimental work was undertaken.

Experimental Procedure

Five-day old white Pekin ducklings were purchased from a commercial hatchery, maintained on Purina Duck Startena for about a week, and then started on diets prepared by thoroughly mixing definite quantities of the dinitrophenols with the Startena. The 8 to 10 ducklings in each of the experimental groups were examined frequently for body weight changes, observable ill effects, and particularly cataract formation.

Diets containing the following concentrations of the dinitrophenols were used: 0.25 per cent sodium salt of 2,4-dinitrophenol; 0.25 per cent 4,6-dinitro-o-cresol; 0.25, 0.10, and 0.03 per cent 2-sec-butyl-4,6-dinitrophenol; and 0.25 and 0.10 per cent 2-cyclohexyl-4,6-dinitrophenol.

Experimental Results

The per cent mortality in each experimental group and the incidence of cataracts are tabulated in Table 8.

Within twenty-four hours all of the ducklings receiving the diet containing 0.25 per cent sodium salt of 2,4-dinitrophenol showed bilateral cataracts. This concentration was sufficient to cause considerable retardation in growth and even a few deaths within the experimental period of thirty-five days. Since the appearance of the cataracts and the changes occurring in the eye during the course of the experiment were similar to those reported by Robbins (11), a detailed description is unnecessary.

Similarly, cataracts were produced within twenty-four hours in the ducklings on the diet containing 0.25 per cent 4,6-dinitro-o-cresol. This concentration proved rapidly fatal to the birds.

The ducklings on the diet containing 0.25 per cent 2-sec-butyl-4,6-dinitrophenol died within three days without showing cataracts. Those on the 0.10 per cent diet died within four days with the appearance of cataracts in one animal on the third day. Even at the level of 0.03 per cent in the diet, 2-sec-butyl-4,6-dinitrophenol was not well tolerated, 50 per cent of the ducklings dying within five days; nevertheless cataracts were observed in one bird on the fifth day and in another on the eighth, when the experimental birds were accidentally killed.

No cataracts were observed in the ducklings that received diets containing 2-cyclohexyl-4,6-dinitrophenol. The birds on the diet containing 0.25 per cent of the material died within four days; while

of the ten ducklings that received the 0.10 per cent diet one died on the second day, one on the third, two on the fourth, two on the fifth, two on the ninth, and one on the thirty-eighth, at which time the surviving bird was killed.

Summary of Feeding Experiments with Ducklings

The production of cataracts in ducklings by the administration of the sodium salt of 2,4-dinitrophenol, first reported by Robbins (11), has been

phenols is based upon information obtained from experimental work on animals and from extensive field experience in the agricultural use of these materials.

Physiological Action

The predominant physiological action of this class of compounds is that of a metabolic stimulant. This action is the same whether the material is absorbed through the skin or is absorbed following inhalation or oral ingestion. This characteristic

TABLE 8
PER CENT MORTALITY AND INCIDENCE OF CATARACTS IN YOUNG DUCKLINGS
ON DIETS CONTAINING DINITROPHENOLS

NO. OF DAYS ON DIET	CONTROL DIET		SODIUM SALT OF DINITROPHENOL		4,6-DINITRO- O-CRESOL		2-SEC-BUTYL-4,6-DINITROPHENOL						2-CYCLOHEXYL- 4,6-DINITROPHENOL			
	0.00%		0.25%		0.25%		0.25%		0.10%		0.05%		0.25%		0.10%	
	M	C	M	C	M	C	M	C	M	C	M	C	M	C	M	C
1	0	0	0	100	56	100	56	0	0	0	0	0	11	0	0	0
2	0	0	0	100	100		56	0	63	0	20	0	11	0	10	0
3	0	0	0	100			100		88	100	40	0	56	0	20	0
4	0	0	0	100					100		50	0	100	0	40	0
5	0	0	0	100							50	20			60	0
6	0	0	10	100							50	20			60	0
7	0	0	10	100							50	20			60	0
8	0	0	10	100							50**	40			60	0
9	0	0	10	100											60	0
10	0	0	10	100											80	0
15	0	0	10	100											80	0
18	0*	0	30	100											80	0
25			30	100											80	0
30			30	100											80	0
35			40*	100											50	0
38															90*	0

M—Per cent mortality.

C—Per cent of living ducklings with cataracts.

* All surviving ducklings killed.

**Surviving ducklings accidentally killed.

substantiated. Furthermore, it has been demonstrated that cataracts can be produced in this species as readily by 4,6-dinitro-o-cresol as by 2,4-dinitrophenol, and only slightly less readily by 2-sec-butyl-4,6-dinitrophenol. On the other hand, cataracts were not produced in ducklings by the administration of 2-cyclohexyl-4,6-dinitrophenol in the diet for as long as thirty-eight days.

DISCUSSION OF PRACTICAL HANDLING
PROBLEMS

The following discussion of the health problems associated with the handling and use of the dinitro-

physiological effect makes it possible to use the increase in basal metabolic rate as an indication of absorption following exposure. Increased body temperature, profuse sweating, and nausea may also be observed in some cases. A serious effect attributed to 2,4-dinitrophenol following its clinical use was the production of cataracts in some individuals.

Skin Contact

Contact with the dinitrophenols incident to their use in agriculture does not present a significant problem from skin irritation. The rare individual

who is hypersensitive to this class of compounds should not work with these materials.

Neither 2-cyclohexyl-4,6-dinitrophenol nor its compound with dicyclohexylamine are absorbed through the skin to an appreciable extent and, consequently, there is no significant problem of skin absorption associated with the handling and use of these materials.

On the other hand, both 4,6-dinitro-o-cresol and 2-sec-butyl-4,6-dinitrophenol are very readily absorbed through the skin and, therefore, present many problems in safe handling. Strict precautions must be observed in order to avoid contact of the skin with liquid concentrates (greater than 5 per cent) of 4,6-dinitro-o-cresol, 2-sec-butyl-4,6-dinitrophenol, or their salts. Should some of the concentrate come in contact with the skin, it must be removed immediately by very thorough washing of the contaminated area with soap and water. Clothing contaminated with the liquid concentrate must be removed immediately and washed before it is worn again. In some cases, it may be necessary to wear suitable protective clothing in order to avoid skin contact with liquid concentrates of these materials.

The low concentrations (usually less than 1 per cent) of 4,6-dinitro-o-cresol and 2-sec-butyl-4,6-dinitrophenol that are commonly found in diluted sprays ready for field use, should not present a significant handling problem from skin absorption; nevertheless, it is advisable to avoid excessive contamination of the clothing and prolonged wetting of the skin with sprays containing these materials.

Appreciable skin absorption should not result from contact with dusts or dry mixes containing the dinitrophenols, except in the case of preparations containing very high concentrations (above 30 per cent) of 4,6-dinitro-o-cresol, 2-sec-butyl-4,6-dinitrophenol, or their salts. In the handling of such preparations reasonable care should be taken to avoid unnecessary skin contact.

It should be remembered that the staining of the skin by a dinitrophenol compound gives no indication of the quantity absorbed or of the actual hazard involved, but merely shows that there has been some contact with the material.

Inhalation

The systemic toxicity of the dinitrophenols is sufficiently high that any one of them, under certain conditions, may present a health hazard

from the inhalation of dusts or sprays. Nevertheless, the practical handling problems presented by preparations containing either 2-cyclohexyl-4,6-dinitrophenol or its compound with dicyclohexylamine are much less serious than those encountered with preparations containing 4,6-dinitro-o-cresol or 2-sec-butyl-4,6-dinitrophenol.

The inhalation of either liquid or dry mix concentrates (greater than 5 per cent) of any of these compounds should be avoided. In some cases suitable respirators may be necessary to afford adequate protection. The low concentrations of the dinitrophenols commonly found in preparations ready for field use should not present a significant problem, although reasonable care should be taken to avoid the breathing of excessive amounts of the dust or spray.

Ingestion

The oral intake of toxic quantities of the dinitrophenols should not present a significant practical handling problem. Persons handling these materials should exercise reasonable care to avoid the contamination of food or anything else that may be taken into the mouth. Care should be taken to wash well before eating.

Disposal of Wastes

The improper disposal of the sludge or residue left after a spraying operation may lead to serious consequences. The ingestion of these wastes by cattle or other livestock must be prevented by adequate safeguards. The careless dumping of such wastes in ponds, streams, or irrigation ditches may be deleterious to aquatic life as well as contaminate the water for other uses.

Residues on Fruits and Vegetables

During the many years that dusts and sprays containing dinitrophenols have been used, no significant health problems have arisen from residues remaining on fruits and vegetables. Under the usual conditions of use, there is ample time for the removal of the residue from the fruit before harvest by volatilization and by the leaching action of rain. In addition, the experimental results reported in this paper indicate clearly that a much greater margin of safety is provided by the use of 2-cyclohexyl-4,6-dinitrophenol or its compound with dicyclohexylamine than by 4,6-dinitro-o-cresol or 2-sec-butyl-4,6-dinitrophenol.

Foliage Treated with Weed-killers

Field experience with the selective weed-killers containing dinitrophenols has shown that when these sprays are used as recommended, livestock may be pastured upon recently treated foliage without evident ill effects. On the other hand, foliage that has been heavily or excessively sprayed with either selective or contact weed-killers may be dangerous; livestock should be kept away from even small areas treated in such a manner.

SUMMARY AND CONCLUSIONS

Studies on rabbits have shown that none of the dinitrophenols investigated are appreciably irritating to the skin.

Experiments on rabbits and guinea pigs have demonstrated that the following compounds, listed according to decreasing toxicity, can readily be absorbed through the skin in lethal amounts: 2-sec-butyl-4,6-dinitrophenol, 4,6-dinitro-o-cresol, and 2,4-dinitrophenol. On the other hand, neither 2-cyclohexyl-4,6-dinitrophenol nor its compound with dicyclohexylamine is absorbed through the skin to an appreciable extent.

It has been determined by experimental work on rats that all of the dinitrophenols investigated are rapidly acting materials of a fairly high order of acute oral toxicity. The following values for "Survival Dose" and "Lethal Dose," respectively, were obtained for each of the compounds: 2-sec-butyl-4,6-dinitrophenol, 0.005 and 0.060 g./kg.; 4,6-dinitro-o-cresol, 0.010 and 0.050 g./kg.; 2,4-dinitrophenol, 0.027 and 0.100 g./kg.; 2-cyclohexyl-4,6-dinitrophenol, 0.030 and 0.180 g./kg.; and

2-cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine, 0.060 and 0.600 g./kg.

Male rats maintained for six months on diets containing 0.01 per cent 2-sec-butyl-4,6-dinitrophenol, 0.01 per cent 4,6-dinitro-o-cresol, 0.02 per cent 2,4-dinitrophenol, 0.05 per cent 2-cyclohexyl-4,6-dinitrophenol, and 0.05 per cent 2-cyclohexyl-4,6-dinitrophenol compound with dicyclohexylamine exhibited no appreciable ill effects as determined by gross observations, growth curves, periodic blood counts, analyses for blood urea-N, organ weights, and histopathological examinations. Higher concentrations in the diet produced effects that may be attributed to the action of these materials as metabolic stimulants.

In the case of each of the dinitrophenols studied, there is very little summation of toxic effects upon prolonged ingestion, as indicated by a comparison of the quantity that caused death after a single oral dose with the quantity that produced no appreciable ill effects when administered daily in the diet for a period of six months.

Cataracts were readily produced in ducklings by the administration of 2,4-dinitrophenol, 4,6-dinitro-o-cresol, or 2-sec-butyl-4,6-dinitrophenol in the diet; but not by 2-cyclohexyl-4,6-dinitrophenol when fed for as long as thirty-eight days.

A discussion is given of the practical handling problems associated with the use of the dinitrophenols, based upon information obtained from experimental work on animals and from extensive field experience in agriculture. Consideration is given to the health problems that may arise from skin contact, inhalation, or ingestion.

REFERENCES

- (1) KAGY, J. F. AND RICHARDSON, C. H.: Ovicidal and scabicide properties of solutions of dinitro-o-cyclohexylphenol in petroleum oil. *J. Econ. Ent.*, 29: 52-61, 1936.
- (2) HORNER, W. D.: Dinitrophenol and its relation to formation of cataract. *Arch. Ophth. (Chicago)*, 27: 1097-1121, 1942.
- (3) AMBROSE, A. M.: Some toxicological and pharmacological studies on 3,5-dinitro-o-cresol. *J. Pharma. and Exptl. Ther.*, 76: 245-51, 1942.
- (4) HRENOFF, A. K., AND LEAKE, C. D.: Toxicological studies on 2,4-dinitro-6-cyclohexyl-phenol, a new insecticide. *Univ. Calif. Pub. in Pharm.*, 1: 151-160, 1939.
- (5) ADAMS, E. M., IRISH, D. D., SPENCER, H. C., AND ROWE, V. K.: The response of rabbit skin to compounds reported to have caused acneiform dermatitis. *Indust. Med.*, 10: *Ind. Hyg. Sec.*, 2: 1-4, 1941.
- (6) HAWK, P. B., AND BERGEIN, O.: Practical physiological chemistry, Tenth ed., p. 692. P. Blakiston's Son and Co., Inc., Philadelphia, Pa., 1931.
- (7) BARKER, S. B.: The direct colorimetric determination of urea in blood and urine. *J. Biol. Chem.*, 152: 453-463, 1944.
- (8) FARRAR, G. E., JR.: The concentration of nucleated cells in the bone marrow of the albino rat. *Am. J. Physiol.*, 117: 662-4, 1936.
- (9) KRACKE, R. R.: Diseases of the blood, 2nd ed., pp. 655-656. J. B. Lippincott Co., Philadelphia, Pa., 1941.
- (10) FISHER, R. A.: Statistical methods for research workers. Oliver and Boyd, London 1938.
- (11) ROBBINS, B. H.: Dinitrophenol cataracts: Production in an experimental animal. *J. Pharm. and Exptl. Ther.*, 80: 264-267, 1944.

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