FINAL REPORT

Submitted December 1, 1988

Title: Bibliography: Risk Assessment, Mechanisms of Action of Non-genotoxic Agents With Carcinogenesis and Activation of Proto-oncogenes

Purchase Order 87-13125, NIOSH, and Subcommittee for Environmental Health Risk Assessment

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50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO.	2.	PB91-185215

4. Title and Subtitle Bibliography: Risk Assessment, Mechanisms of Action of Non-genotoxic Agents with Carcinogenesis and Activation of Protooncogenes	5. Report Date 1988/12/01 6.
7. Author(s) Albert, R. E.	8. Performing Organization Rept. No.
9. Performing Organization Name and Address Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, Ohio	10. Project/Task/Work Unit No. 11. Contract (C) or Grant(G) No. (C) 87-13125 (G)
12. Sponsoring Organization Name and Address	13. Type of Report & Period Covered 14.

15. Supplementary Notes

16. Abstract (Limit: 200 words) This bibliography on risk assessment, mechanisms of action of nongenotoxic agents with carcinogenesis and activation of protooncogenes was prepared from material contained in the following databases: BIOSIS; Cancerlit; Catline; Chemical Abstracts; Conference Papers Index; Current Contents; Occupational Safety and Health (NIOSH); and Toxline. It covered the English language literature for the period 1982 through 1988. Two distinct search strategies were developed. One strategy was to search for cocarcinogens, secondary carcinogens, and tumor promoters. The second plan was the activation of oncogenes or protooncogenes. A brief description was offered of each of the databases and the search strategy used for each.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms NIOSH-Publication, NIOSH-Contract, Task-Order-87-13125, Carcinogenesis, Risk-factors, Risk-analysis, Neoplasms, Genetic-factors

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages 69
	22. Security Class (This Page)	22. Price

(See ANSI-Z39.18) *See Instructions on Reverse*

OPTIONAL FORM 272(4-77)
(Formerly NTIS-35)
Department of Commerce

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1) Project Personnel

Roy E. Albert, M.D.	Principal Investigator
Martha Radike, Ph.D.	Selection of Literature
David Warshawsky, Ph.D.	Personal Contact
Sherrie Kline, M.L.S.	Online Search
Leva Wilson	Secretarial Support

December 1, 1988

2) Information Sources

A. Online Search and Strategies

The English language literature was searched from 1982-1988 for tumor promotion on the following online databases: BIOSIS; Cancerlit; Catline; Chemical Abstracts; Conference Papers Index; Current Contents; Occupational Safety and Health (NIOSH); and Toxline. For databases such as NIOSH's Occupational Safety and Health, which cannot be easily limited by language, foreign language articles were weeded out after references were printed.

Because of variations in file content and structure, and in database vendor search software, it was impossible to set up a single search strategy to be processed in all databases. Two distinct search strategies were developed. The first, processed according to our original plan, was to search for cocarcinogens, secondary carcinogens and tumor promoters. In databases with extremely large retrieval in this area (such as Cancerlit), we printed only references which discussed risk. The second topic was the activation of oncogenes or protooncogenes. In some cases this topic was also restricted in order to limit retrieval. Details of these strategies are listed on Table I. They are given in the Dialog search system format, which was used for the greatest number of databases. Changes were made when necessary to adapt the strategies to the search software of the other systems - BRS Information Technologies, National Library of Medicine and STN International.

Because of its broad coverage and high degree of relevancy, we searched the Cancerlit file first and used it as our point of reference. Although it is impossible to weed out previously retrieved citations during an online session, we checked each subsequent printout against previous retrieval to insure that no reference would be photocopied more than once.

Our initial search strategies retrieved many thousands of references, and we are unable to give an exact count of the total number of papers published on this topic, nor on the total number of unique references retrieved in these searches. Because the various databases cover different types of materials and must be searched in a variety of ways, it is difficult to make direct comparisons. For example, a search of the basic "tumor promoter" terms on Cancerlit retrieved nearly 7000 English language references to "risk." Conference Papers Index (CPI), on the other hand, which is a much smaller database and contains no abstracts, produced less than 300 titles with the broader search strategy. All relevant references from CPI, therefore, were probably retrieved, while some papers from Cancerlit were likely lost in narrowing down the search. The large number of databases searched, however, compensates to some extent for this problem.

Another problem encountered was the wide variation in terminology. Unlike searching for a chemical or a specific disease entity, we were not able to find one or two phrases which are invariably used by all authors when discussing a subject. There is no particular keyword or descriptor which will retrieve all relevant papers across all databases. Also, some of the terms used to narrow down the searches were quite nonspecific, such as "risk" and "mechanism." There are many different ways to express these concepts. While

these ideas may often be implied in an article, they might not be specifically indicated in the title of abstract. These concepts, especially "mechanism," are usually not represented by a particular subject descriptor.

We have given a break-down by database of these retrieval for each search strategy. It should be noted that some databases, especially Occupational Safety and health and Toxline, may contain multiple listings for the same reference. The figures on the attached tables for references retrieved refer to total number of citations, not necessarily unique citations. The figures for the number of copies requested reflect the number of papers requested which had not previously been copied, and not the total number of relevant papers from the database.

Table I

Strategy A

Basic tumor promoter strategy: Searches titles, abstracts, keyword phrases, descriptors

Cocarcinogen? or Co(w)carcinogen?
OR
Secondary (w) carcinogen?
OR
(multi or two or second) (w) stage (w) carcinogen?
OR
(sequential or multistage or progressor) (w) carcinogen?
OR
(tumor? or tumour? or carcinogen? or
hepatocarcinogen? or cancer or neoplas?)
(3N) (promot? or enhanc? or potential?
or acelerat? or synerg? or conversion?
or epigenetic)

AND

risk? or hazard?

These additional terms used to narrow down searches as indicated on the attached sheets.

Strategy B

Basic oncogene strategy searches titles, abstracts

(Activat? or mechanism?) (5N)
(oncogen? or protooncogen?)

Notes: ? = Truncation. Any number of letters may follow in the same work; e.g. cocarcinogen? = cocarcinogen or cocarcinogens or cocarcinogenesis, etc.

(w) = adjacency. Used to search for two words next to each other; e.g. secondary (w) carcinogen = secondary carcinogen (as a phrase)

(3N) = within 3 words, in any order; e.g. "tumor promoter" or "promotion of a tumor" or "hepatocarcinogenic potentiation" or "hepatocarcinogens which may be potentiated," etc.

Datebase Name: **BIOSIS**
Dates Searched: 1982-1/88 update
Coverage: journal articles, meeting abstracts, book chapters

Strategy A (tumor promoters, cocarcinogens, etc)
Search terms in title, abstract, keywords: 6039 (not printed)
Search terms in title only: 2002 (not printed)
Search terms in title, abstract, keywords + risk/hazard in title, abstract, keywords
139 titles printed
39 complete citations printed
24 copies requested

Strategy B (oncogenes)
Search terms in title, abstract, keywords: 456 (not printed)
Search terms in title only: 229 (not printed)
Search terms in title, abstract, keywords + risk/hazard in title, abstract, keywords
4 titles printed
4 complete citations printed
2 copies requested

Database Name: **Cancerlit**
Dates Searched: 1982-4/88 update
Coverage: journal articles, meeting papers, dissertations, book chapters

Strategy A
Search terms in title, abstract, keywords: 6682 (not printed)
Search terms in title: 1816 (not printed)
Search terms in title, abstract, keywords & risk/hazard:
464 complete citations printed
253 copies requested

Strategy B
Search terms in title, abstract, keywords: 767 (not printed)
Search terms in title, abstract, keywords + risk/hazard 26 citations printed
13 copies requested
Search terms in title only: 211 titles printed
84 complete citations printed
33 copies requested

Datebase Name: **Catline**
Dates Covered: 1982-2/88 update
Coverage: books, conference proceedings

Strategy A:
Search terms in title, descriptors: 22 complete citations printed
(no abstracts available) 10 publications requested

Strategy B:
Search terms in title, descriptors: 28 complete citations printed
17 publications requested

Additional strategy:
Carcinogen? or neoplasm? + risk
33 complete citations requested
8 publications requested

Database Name: **Chemical Abstracts**
Dates Searched: 1982-1/88
Coverage: journal articles, conference proceedings, monographs

Strategy A:
Search terms in title, keywords: 2836 (not printed)
Search terms in title, keywords + hazard/risk
70 complete citations printed
31 copies requested

Strategy B:
Search terms in title, abstract, keywords: 171 titles printed
68 complete citations printed
65 copies requested

Database Name: **Conference Papers Index**
Dates Searched: 1982-3/87 (last update at time of search)
Coverage: published and unpublished meeting papers, abstracts not available online

Strategy A
Search terms in title, keywords: 296 titles printed
88 complete citations printed
77 copies requested

Strategy B
Search terms in title, keywords: 23 citations printed
8 copies requested

Database Name: **Current Contents**
Dates Searched: 10/12/87-4/12/88
Coverage: journal articles

Note: Current Contents database is set up very differently from other files in that the searchable unit is not a single article, but the table of contents of a complete journal issue. It is very difficult to search this file and retrieve relevant references without also getting many false drops. We searched this database twice; on the update processed 4/12, there was a problem with the BRS software, and we were able to print out only half of the titles. Because of this problem and the nature of the database, it is impossible to give meaningful figures on retrieval. There are, however, many very recent, up-to-date references which were retrieved, and we copied 83 articles listed on Current Contents printouts.

Database Name: **Occupational Safety & Health (NIOSH)**
Dates Searched: 1982-8/87
Coverage: journal articles, meeting abstracts, monographs, government documents

Strategy A
Search terms in title, abstract, keywords: 357 (not printed)
Search terms in title: 93 titles printed
30 complete citations printed
25 copies requested

Search terms in title, abstracts, keywords + risk/hazard:
56 titles printed
43 complete citations printed
25 copies requested

Strategy B
Search terms in title, abstract, keywords:
8 citations printed
6 copies requested

Database Name: **Toxline**
Dates Searched: 1982-2/88 update
Coverage: journal articles, book chapters, dissertations, government reports

Strategy A
Search terms in title, abstract: 1803 (not printed)
(Note: proximity searching not available. Searched for terms in same sentence)
Search terms in title, abstract + hazard/risk:
711 titles printed
380 complete citations printed
152 copies requested

Strategy B
Search terms in title, abstract: 202 titles printed
136 complete citations printed
71 copies requested

B. Individuals, Agencies, Organizations

A telephone survey was conducted to elicit unpublished data concerning "secondary carcinogens" promoters and non-genotoxic carcinogens. Of 32 telephone contacts made, 23 responded. Of these, 10 gave input to the report; 13 had no additional information. In addition, two personal contacts were made by Dr. Warshawsky.

Personal Contact - 2 Phone Contact - 23 No Return Call - 6

Personal contact:

Moolgavhan 10/15/87
Emil Pfitzer 1/20/88

Phone contact:

Gene Poynter 8/18/88 - no information
Irene Lowinski 8/18/88 - Symposium in Texas on Skin Carcinogenesis
M. McClain 8/18/88 - liver thyroid (EPA document - adrenal- Am. J. Tox. Vol 7 (1), 1988)
James Swenberg 8/18/88 No call back
Emil Pfitzer 8/18/88 No call back
Tom Slaga 8/18/88 No call back
Richard T. Robertson 8/18/88
8/19/88 - will call with information endocrine tumors
Kenneth Bishoff 8/18/88 No call back
James Trosko 8/18/88 Sent information
Mel Anderson 8/18/88 No information
Peter Preuss 8/18/88 Call back 8/23/88 No information
Tony Lee 8/19/88 No information
Richard Niemeier 8/19/88 No information
David Rall 8/19/88 - Call back 9/14/88 by Mr. Huff - Annual Report will be sent by Hugh Lee
David Hoel 8/19/88 - M. Hogen called 8/19/88 Paper in hand
Richard Adamson 8/29/88 - Out of office, will call or send information
Curtis Travis 8/19/88 Out on Travel
Donald Gardner 8/18/88 - No information
Dan Kreuski 8/18/88 - Call back 8/22/88 - EPA report
Pat Durkin 8/18/88 No information 8/19/88
Perry Gehring 8/18/88 No information - Call Watanabe
Freh Homburger 8/18/88 - 8/18/88 - sent information
E. Huberman 8/18/88 - 8/19/88 send paper
Robert Langenbach 8/18/88-8/19/88 No information
Peter Magee 8/18/88 No information
S. Moolgavhan 8/18/88 - No information - kidney tumors - unleaded gasoline
H. Pitot 8/18/88 called 8/23/88 - Iverson book
Ray Tenant 8/19/88 8/23/88 sent information
H. Rosenkranz 8/18/88 - 8/29/88 No information

Did not call (10) / or no answer (3)

L. Tomatis - IARC
Helis Miido
Tom Camerion NCI
Bob DeMato P&G
Jim McDonald - Merick
Art Tischler - Tufts
R. McClellan
Robert Neal No answer
Rausher
Phil Watanabe
Ann Kennedy No answer
Ron Hart
David Clayson 8/18/88 no answer

3) Difficulties Encountered

As initially directed, the first literature searches were based on promoters, cocarcinogens etc. related to risk assessment rather than mechanism of action which was suggested later. The early searches were not discarded or repeated and citations appear in the references related to risk assessment and non-genotoxic enhancers of carcinogenesis.

A category titled "Reviews" has been added to many sections of the bibliography. In the format initially established for the final report, a review could be cited in human (in vivo, in vitro) sections and in animal (in vivo, in vitro) sections. One citation was placed in a review section for each major heading.

The literature search for "mechanisms through which agents (or their metabolites) affect carcinogenesis by activating proto-oncogenes" was not successful in identifying chemicals related to proto-oncogene activation. We decided to focus on oncogene activation while avoiding (if possible) oncogenes introduced into cells by viruses. In some cases, the activity of protein products of amplified and activated oncogenes are discussed.

TABLE I. Articles Retrieved - Non-Genotoxic Carcinogens
(Interim Report, Nov. 1, 1988)

	Human							
	In Vivo				In Vitro			
Category	Jrnls	Proc	Books (Chap)	Unpubl	Jrnls	Proc	Books (Chap)	Unpubl.
I. Promotion	17	15	4		10	4	1	
Co-carcinogens Enhancers	17	8	1		4			
Secondary/ Indirect		2						
Toxicity/ Cell Prolif.	1	1				2		
Hormones	14	3			1			
Solid State	6	5	1			5		
Cell/Cell Interaction							1	1
Genetic Suscept.								
II. Oncogenes	9	2	2		31	9	7	

TABLE II. Articles Retrieved - Non-Genotoxic Carcinogens
(Interim Report, Nov. 1, 1988)

	Animal							
	In Vivo				In Vitro			
Category	Jrnls	Proc	Books (Chap)	Unpubl	Jrnls	Proc	Books (Chap)	Unpubl.
I. Promotion	62	42	7	4	29	26	6	1
Co-carcinogens Enhancers	21	7			13	1	1	1
Secondary/ Indirect	1	4		2				1
Toxicity/ Cell Prolif.	11	5			0	1		
Hormones	2	4			2	1		
Solid State	6	2	6		2	1	3	
Cell/Cell Interaction					1	4	2	1
Genetic Suscept.								
II. Oncogenes	14	12	3		38	26	11	

TABLE III. Articles Retrieved - Non-Genotoxic Carcinogens
(Interim Report, Nov. 1, 1988)

Category	Review Articles			
	Journals	Proceedings	Books (Chapter)	Unpublished
I. Promotion	14	23	8	4
Co-carcinogens Enhancers	2		3	
Toxicity/ Cell Proliferation	1			
Cell/Cell Communication			2	1
Hormones	1	2	2	
Solid State	1			
Genetic Susceptibility	1		4	
II. Oncogenes	13	1	4	

4) Bibliography: Risk Assessment, Mechanisms of Action of Non-genotoxic Agents Associated with Carcinogenesis and Activation of Proto-oncogenes

I. Mechanisms Through Which Agents Affect Carcinogenesis But Do Not Initiate The Carcinogenic Process

A. Promotion mechanisms

1) Human, in vivo

Journal articles

Browne, K. (1983). Asbestos-related mesothelioma: epidemiological evidence for asbestos as a promoter. Arch. Environ. Health 38:261-66.

Carroll, K.K. et al. (1986). Fat and cancer. Cancer (Suppl) 58:1818-25.

Guillem, J.G. et al. (1987). Nutrition in the prevention of neoplastic disease in the elderly. Clin. Geriat. Med. 3:373-87.

Hecker, E. (1987). Tumour promoters of the irritant diterpene ester type as risk factors of cancer in man. Botanical Journal of the Linnean Society 94:197-219.

Lane, H.W. and Carpenter Jr., J.T. (1987). Breast cancer: incidence, nutritional concerns, and treatment approaches. J. Am. Diet. Assoc. 87:765-69.

Lin, R.S. et al. (1985). Occupational exposure to electromagnetic fields and the occurrence of brain tumors. J. Occup. Med. 27:413-19.

Lipsett, M.B. (1983). Hormones, medications, and cancer. Cancer 54:2426-29.

McPherson-Kay, R. (1987). Fiber, stool bulk, and bile acid output: implications for colon cancer risk. Prev. Med. 16:540-44.

Montesano, R. and Slaga, T.J. (1983). Initiation and promotion in carcinogenesis: an appraisal. Cancer Surveys 2:613-21.

Moolgavkar, S.H. (1986). Carcinogenesis modeling: from molecular biology to epidemiology. Ann. Rev. Public Health 7:151-69.

Nair, P. and Turjman, N. (1983). Role of bile acids and neutral sterols in familial cancer syndromes of the colon. Dis. Colon Rectum 26:629-32.

Oshima, A. et al. (1984). Follow-up study of HBs Ag-positive blood donors with special reference to effect of drinking and smoking on development of liver cancer. Int. J. Cancer 34:775-79.

Paustenbach, D.J. et al. (1986). A critical examination of assumptions used in risk assessments of dioxin contaminated soil. Regulat. Toxicol. Pharmacol. 3:284-307.

Rosen, P. (1987). The significance of proto-oncogenes in carcinogenesis. Medical Hypotheses 22:23-26.

Schottenfeld, D. (1984). Chronic disease in the workplace and environment: cancer. Arch. Environ. Health 39:150-57.

Shu, H.P. et al. (1987). A critical evaluation of the use of mutagenesis, carcinogenesis, and tumor promotion data in a cancer risk assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Regul. Toxicol. Pharmacol. 7:57-88.

Tartter, P.I. et al. (1984). Cholesterol, weight, height, Quetelet's index, and colon cancer recurrence. J. Surg. Oncol. 27:232-35.

Proceedings

Armstrong, B.K. (1985). Saccharin/Cyclamates: Epidemiological evidence. IARC Sci. Publ. 65:129-43.

Hecker, E. et al. (1984). Irritant diterpene ester promoters of mouse skin: contributions to etiologies of environmental cancer and to biochemical mechanisms of carcinogenesis. In Cellular Interactions by Environmental Tumor Promoters. Edited by H. Fujiki et al. Japan Sci. Soc. Press, Tokyo, pp. 3-36.

Hecker, E. (1984). Cocarcinogens of the tumour-promoter type as potential risk factors of cancer in man. A first complete experimental analysis of an etiological model situation and some of its consequences. IARC Sci. Publ. 56:441-63.

Hill, M.J. (1985). Mechanisms of colorectal carcinogenesis. Int. Cong. Series 685:149-63.

Kolonel, L.N. et al. (1986). Studies of nutrients and their relationship to cancer in the multiethnic population of Hawaii. In Essential Nutrients in Carcinogenesis. Edited by L.A. Poirier et al. Plenum Press, NY, Adv. Exptl. Med. Biol. 206, pp. 35-43.

Mettlin, C. (1984). Diet and the epidemiology of human breast cancer. Cancer 53 (Suppl.):605-11.

Moolgavkar, S.H. (1983). Model for human carcinogenesis: action of environmental agents. Environ. Health Perspect. 50:285-91.

Purchase, I.F.H. (1987). Carcinogenic risk assessment: a toxicologist's view. In Nongenotoxic Mechanisms in Carcinogenesis. Edited by B.E. Butterworth and T.J. Slaga. Banbury Report 25, Cold Spring Harbor Laboratory, NY, pp. 175-86.

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Rogers, A.E. and Conner, M.W. (1986). Alcohol and cancer. In Essential Nutrients in Carcinogenesis. Edited by L.A. Poirier et al. Plenum Press, NY, Adv. Expt. Med. Biol. 206, pp. 473-95.

Thompson, M. (1984). Aetiological factors in gastrointestinal carcinogenesis. Scand. J. Gastroenterol. (Suppl) 104:77-89.

Weisburger, J.H. et al. (1982). Mechanisms of promotion in nutritional carcinogenesis. Carcinogenesis 7:175-82.

Weisburger, J.H. and Horn, C. (1982). Nutrition and cancer: mechanisms of gentotoxic and epigenetic carcinogens in nutritional carcinogenesis. Bull. N.Y. Acad. Med. 58:296-312.

Weisburger, J.H. et al. (1983). Bile acids, but not neutral sterols, are tumor promoters in the colon in man and in rodents. Environ. Health Perspect. 50:101-107.

Weisburger, J.H. and Wynder, E.L. (1984). The role of genotoxic carcinogens and of promoters in carcinogenesis and in human cancer causation. Acta Pharmacol. Toxicol. 55 (Suppl. 2):53-68.

Books

Creasey, W.A., Editor (1985). Alcohol and coffee. In Diet and Cancer. Lea & Febiger, Philadelphia, PA, pp. 161-73.

Higginson, J. (1984). Existing risks for cancer. In Reducing the Carcinogenic Risk in Industry. Edited by P.F. Deisler, Jr. Marcel Dekker, Inc., NY, pp. 1-19.

Gibson, E.S. et al. (1986). Industrial mutagenicity testing: assessing silica's role in lung cancer among foundry workers. In Silica, Silicosis, and Cancer: Controversy in Occupational Medicine. Edited by D.F. Goldsmith et al. Praeger Scientific, NY, pp. 167-76.

Kolonel, L.N. and Le Marchand, L. (1986). The epidemiology of colon cancer and dietary fat. In Dietary Fat and Cancer. Edited by I.P. Clement. Alan R. Liss, Inc., pp. 69-91.

2) Human, in vitro

Journal articles

Akiyama, T. et al. (1988). Tumor promoter and epidermal growth factor stimulate phosphorylation of the c-erbB-2 gene product in MKN-7 human adenocarcinoma cells. Molec. Cell. Biol. 8:1019-26.

Apte, R.N. and Keisari, Y. (1987). Differential stimulation of mononuclear phagocyte IL 1 production and and oxidative burst by tumor-promoting and non-tumor-promoting agents. Immunobiol. 175:470-81.

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Proceedings

Friedman, E.A. (1983). Promotion of human premalignant epithelial cells. In Human Carcinogensis. Edited by C.C. Harris and H.N. Autrup, Academic Press, NY, pp. 325-68.

Lotem, J. and Sachs, L. (1982). Regulation of growth and differentiation by phorbol esters and the mechanisms of tumor promotion. Carcinogenesis 7:385-90.

Sivak, A. (1984). An evaluation of assay procedures for detection of tumor promoters. Acta Pharmacol. Toxicol. 55 (Suppl. 2):69-88.

Thompson, M. (1984). Aetiological factors in gastrointestinal carcinogenesis. Scand. J. Gastroenterol. (Suppl) 104:77-89.

Books

Trosko, J.E. and Chang, C.C. (1985). Implications for risk assessment of genotoxic and non-genotoxic mechanisms in carcinogenesis. In Methods for Estimating Risk of Chemical Injury: Human and Non-human Biota and Ecosystems. Edited by V.B. Vouk et al. John Wiley & Sons, NY, pp. 181-200.

3) Animal, in vivo

Journal articles

Akhurst, R.J. et al. (1988). Localized production of TGF-β mRNA in tumour promoter-stimulated mouse epidermis. Nature 331:363-65.

Appel, K.E. et al. (1986). Approaches to the health risk assessment of PCDD/PCDF. Chemosphere 15:1825-34.

Argyris, T.S. (1985). Promotion of epidermal carcinogenesis by repeated damage to mouse skin. Am. J. Ind. Med. 8:329-37.

Boyland, E. (1987). Estimation of acceptable levels of tumour promoters. Br. J. Ind. Med. 44:422-23.

Boyland, E. (1985). Methyl groups or additional aromatic groups donate tumour promoting activity. Brit. J. Ind. Med. 42:784-86.

Busser, M.T. and Lutz, W.K. (1987). Stimulation of DNA synthesis in rat and mouse liver by various tumor promoters. Carcinogenesis 8:1433-37.

Butterworth, B.E. et al. (1987). The potential role of chemically induced hyperplasia in the carcinogenic activity of the hypolipidemic carcinogens. Toxicol. Ind. Health 3:129-49.

Caldwell, M.E. and Brewer, W.R. (1983). Plants with potential to enhance significant tumor growth. Cancer Res. 43:5775-77.

Carroll, K.K. et al. (1986). Fat and cancer. Cancer (Suppl) 58:1818-25.

Chu, K.C. et al. (1987). Differentiating among proposed mechanisms for tumor promotion in mouse skin with the use of the multievent model for cancer. J. Natl. Cancer Inst. 79:789-96.

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Cohen, L.A. et al. (1984). Influence of dietary medium-chain triglycerides on the development of N-methylnitrosourea-induced rat mammary tumors. Cancer Res. 44:5023-28.

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Deml, E. and Oesterle, D. (1987). Dose-response of promotion by polychlorinated biphenyls and chloroform in rat liver foci bioassay. Arch. Toxicol. 60:209-11.

Diwan, B.A. et al. (1985). Tumor-promoting effects of di(2-ethylhexyl)phthalate in JB6 mouse epidermal cells and mouse skin. Carcinogenesis 6:343-47.

Estensen, R.D. (1984). Phorbol myristate acetate: is a tumor promoter acting as a hormone? J. Expt. Pathol. 1:71-77.

Fournier, A. and Murray, A.W. (1987). Application of phorbol ester to mouse skin causes a rapid and sustained loss of protein kinase C. Nature 330:767-69.

Fujiki, H. and Sugimura, T. (1987). New classes of tumor promoters: teleocidin, aplysiatoxin, and palytoxin. Adv. Cancer Res. 49:223-64.

Fukushima, S. et al. (1987). Promotion by L-ascorbic acid of urinary bladder carcinogenesis in rats under conditions of increased urinary K ion concentration and pH. Cancer Res. 47:4821-24.

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