Interagency Agreement (IAA) between NIEHS/National Toxicology Program (NIEHS/NTP) and FDA/National Center for Toxicological Research (FDA/NCTR)

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Office of Scientific Coordination,
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Disclaimer

The views and opinions expressed by the presenter should not be interpreted as current or future official position or policy of the U.S. Food & Drug Administration, or any other U.S. Government agency.

Any mention of a company, trade-name, or product is only for clarification, and should not be interpreted as endorsement.

Purpose of Presentation

" … to update the NTP Board of Scientific Counselors regarding the 23½ year history, (and some perspectives of the future) of the Interagency Agreement (IAA) between the NIEHS/National Toxicology Program (NIEHS/NTP) and FDA/National Center for Toxicological Research (FDA/NCTR)."

U.S. Food & Drug Administration

MISSION: FDA is responsible for **protecting the public health** by assuring the **safety, efficacy and security** of **human and veterinary drugs, biological products, medical devices**, our nation's **food supply, cosmetics**, and products that **emit radiation**.

FDA is also responsible for advancing the public health by helping to **speed innovations** that make **medicines more effective, safer, and more affordable** and by helping the public get the accurate, science-based **information** they need to use medicines and foods to maintain and improve their health. FDA also has responsibility for regulating the **manufacturing, marketing and distribution of tobacco products** to protect the public health and to reduce tobacco use by minors. ***(bold and color for emphasis by presenter)***

U.S. Food & Drug Administration

(list is not exhaustive)

Foods, including:

- dietary supplements (including vitamins)
- bottled water
- food additives (including colorants)
- infant formulas
- food contact materials
- other food products (*USDA → some meat, poultry, and egg products*)

Drugs (human), including:

- prescription drugs (both brand-name and generic)
- non-prescription (over-the-counter) drugs

Biologics, including:

- vaccines
- blood and blood products
- cellular and gene therapy products
- tissue and tissue products
- allergenics

Medical Devices, including:

- simple items (*eg* tongue depressors and bedpans)
- complex technologies (*eg* heart pacemakers, diagnostic devices)
- dental devices
- surgical implants and prosthetics

Electronic Products emitting radiation, including:

- microwave ovens
- x-ray equipment
- laser products
- ultrasonic therapy equipment
- mercury vapor lamps
- sunlamps

Cosmetics, including:

- color additives found in makeup and other personal care products
- skin moisturizers and cleansers
- nail polish and perfume

Veterinary Products, including:

- veterinary drugs and devices
- livestock feeds
- pet foods

Tobacco Products, including:

- cigarettes
- tobacco for cigarettes, pipes, cigars, etc.
- roll-your-own tobacco
- smokeless tobacco
- tobacco 'devices'
- (May 2016 ; Deeming Rule for other products)

U.S. Food & Drug Administration

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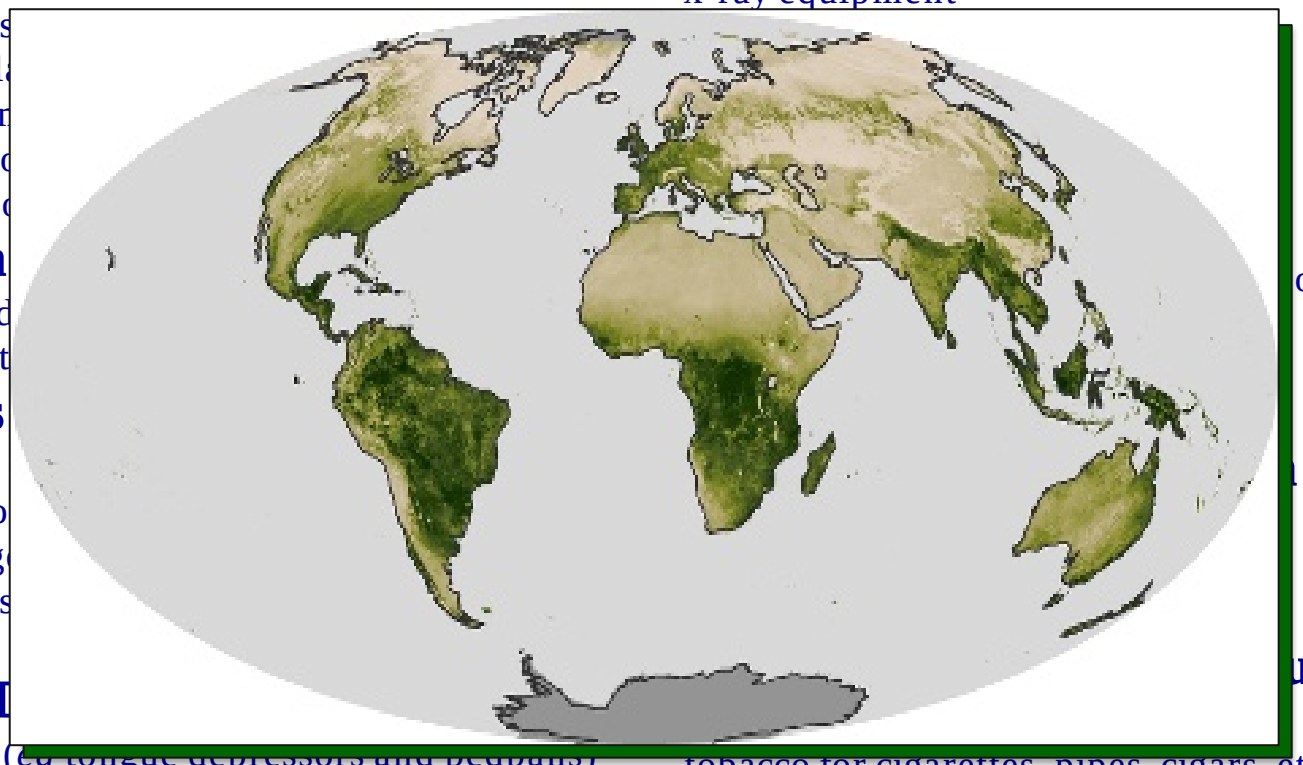

Electronic Products emitting radiation, including:

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- smokeless tobacco
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(May 2016 ; Deeming Rule for other products)

National Center for Toxicological Research:

FDA Research Resource

- *Established January 1971*
- *Non-regulatory national resource owned and managed within DHHS by FDA*
- *Conduct integrated, toxicological research*
- *Foster interagency, academic, and industrial collaboration in support of risk-assessment needs related to public health.*

National Center for Toxicological Research

Mission –

… conduct toxicological studies, and scientific research to develop and support innovative tools and evaluation of approaches that FDA uses to protect and promote individual and public health.

FDA Jefferson Arkansas Campus; homes of FDA/NCTR and FDA/Office of Regulatory Affairs/ Arkansas Regional Laboratory

NCTR Research Strategy

Hazard Quantification
(hazard identification/quantification, mechanism of action, etc.)

Biomarkers *(exposure or effect; genomics, proteomics, metabolomics)*

Bio-imaging *(MRI, CT, microPET, SEM, histopathology)*

Organotypic models *(3D & stem cells)*

Microbiome *(preclinical studies)*

Precision/Personalized Medicine

Nanotoxicology *(hazard identification/quantification; standards)*

Inhalation Toxicology *(tobacco constituents)*

Modeling *(PK, PBPK, PD, QSAR)*

Bioinformatics *(preclinical hazard identification; data mining)*

Regulatory Science Training

Interagency Agreement (IAA) between FDA/NCTR and NIEHS/NTP

The missions of NTP and NCTR sometimes overlap when an FDA-regulated product (or contaminant) is nominated to (considered by) NTP for toxicology studies.

Interagency Agreement (IAA) between FDA/NCTR and NIEHS/NTP

Interagency Agreement (IAA) established December 1992 to facilitate cooperation between FDA/NCTR and NIEHS/NTP:
(1) on compounds of interest to FDA and NIEHS/NTP;
(2) to facilitate FDA regulatory decisions.

Initiated 10 Dec 1992

Dr. J.E. Henney (FDA); Dr. K.L. Olden (NIEHS)

Nigel J. Walker, PhD, NTP Project Officer
Paul C. Howard, PhD, FDA Project Officer

Goals of IAA

(1) **Conduct toxicological studies** at NCTR on FDA-regulated or FDA-interest chemicals/compounds.

(2) **Ensure design** and conduct of toxicological studies are consistent with ***regulatory needs*** and goals of FDA and NIEHS/NTP.

(3) **Provide oversight** and ensure studies are conducted in the most rigorous scientific manner.

(4) **Ensure communication** of study data from the studies are available to enable regulatory agencies (U.S. and worldwide) to make science-based, safety assessment and risk management decisions.

Interagency Agreement (IAA):

How do we accomplish study design that meets regulatory needs, best science & design practices, etc.?

(Example of good communication)

Toxicology Study Selection and Review Committee:

semi-annual; NTP, FDA/NCTR, FDA-regulatory centers.

(goal: best science; maximum information for regulators)

Interagency Agreement (IAA):

How do we accomplish study design that meets regulatory needs, best science & design practices, etc.?

Toxicology Study Selection and Review Committee:

semi-annual; NTP, FDA/NCTR, FDA-centers … well … sometimes we end up in a scrum!

Goals of IAA

(1) **Conduct toxicological studies** at NCTR on FDA-regulated or FDA-interest chemicals/compounds.

(2) Ensure design and conduct of toxicological studies are consistent with *regulatory needs* and goals of FDA and NIEHS/NTP.

(3) **Provide oversight** and ensure studies are conducted in the most rigorous scientific manner.

(4) **Ensure communication** of study data from the studies are available to enable regulatory agencies (U.S. and worldwide) to make science-based, safety assessment and risk management decisions.

Interagency Agreement:

Public Health impact by providing hazard identification and dose response data for accurate risk assessment.

Technical Reports (GLP) or other reports (n=19)

- Fumonisin B_1 (TR496)
- Chloral hydrate (TR502, TR503)
- Riddelliine (TR 508)
- Urethane ± ethanol (TR510)
- α-Hydroxy (glycolate) and ß-Hydroxy (salicylate) acids (TR524)
- Malachite Green (TR527)
- Genestein (TR539, TR545)
- Ethinyl Estradiol (TR547, TR548)
- Aloe Vera (TR553, TR547)
- Retinyl Palmitate (TR568)
- AIDS Therapeutics (AZT +/- combinations; TR569, GMM14, GMM16)
- Acrylamide (TR575)
- Glycidamide (TR588)

Peer-reviewed scientific publications since 1992 (n>260)

Programs of Study under IAA

Dietary Supplements Program

Food Contaminants Program

Enhancing Toxicology Program

Endocrine Active Agents Program

Drug & Device Program

AIDS Therapeutics Program

Nanoscale Materials Program

Phototoxicology Program

Dietary Supplements Program

Bitter Orange, *Citrus aurantium*
combination with caffeine and exercise

Usnea lichen, Usnic Acid
hepatotoxic in rats and mice

Glucosamine, Chondroitin
biochemical alterations in diabetic rats

Aloe vera
gastrointestinal carcinogen, rats

Currently under study

OXICOLOGICAL SCIENCES 131(1), 26–39 (2013)
oi:10.1093/toxsci/kfs275
Advance Access publication September 11, 2012

Clear Evidence of Carcinogenic Activity by a Whole-Lea
of *Aloe barbadensis* Miller (Aloe vera) in F344/N F

Mary D. Boudreau,*,1 Paul W. Mellick,† Greg R. Olson,† Robert P. Felton,‡ Brett T. Thorn,‡ and Fr

*Division of Biochemical Toxicology, Food and Drug Administration; †Toxicologic Pathology Associates; and ‡Division of Bioin

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Key Words:
chronic; gastr
Aloe vera; *Alo*

Aloe barba
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Toxicologic Pathology, 39: 1065-1074, 2011

ISSN: 0192-6233 print / 1533-1601 online
DOI: 10.1177/0192623311422081

Aloe vera Non-Decolorized Whole Leaf
Intestinal Tumors in F344 Rats Shar
Pathways with Human Sporadic C

ARUN R. PANDIRI[1,2], ROBERT C. SILLS[1], MARK J. HOENERHOFF[1], SHYA
HUE-HUA L. HONG[1], GORDON P. FLAKE[1], DAVID E. MALARKEY[1], G
NIGEL J. WALKER[6], AND MARY D. BO

[1]*Cellular and Molecular Pathology Branch, National Toxicology Progra*
Health Sciences (NIEHS), Research Triangle Par
[2]*Experimental Pathology Laboratories, Inc., Research Tri*
[3]*Biostatistics Branch, NIEHS, Research Triangle P*
[4]*Toxicologic Pathology Associates, Jeffers*
[5]*National Center for Toxicological Research (NCTR*
[6]*NTP/NIEHS, Research Triangle Park, N*

ABSTRACT

Aloe vera is one of the most commonly used botanicals for various prophyla
demonstrated a dose-dependent increase in large intestinal tumors in F344 rats ch
non-decolorized whole leaf extract (AVNWLE) in drinking water. The morphological a
tumors in the F344 rats were compared to human colorectal cancer (hCRC) literature.
induced large intestinal tumors with hCRC. The commonly mutated genes (*Kras, Ctnn*
and TGF-β) important in hCRC were evaluated within AVNWLE-induced large int
tumors indicated eight of twelve adenomas (Ads) and four of twelve carcinomas (Cas
mutations in exons 1 and 2 of the *Kras* gene (two of eight Ads, two of four Cas), and
Cas). No *Tp53* (exons 5–8) mutations were found in Ads or Cas. Molecular pathways
were also altered in AVNWLE-induced Ads and Cas. In conclusion, the AVNWLE-
larities with hCRC at the morphological and molecular levels.

Keywords: *Aloe vera*; colon; F344 rat; human; colorectal tumors.

INTRODUCTION

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of in

NTP TECHNICAL REPORT
ON THE
TOXICOLOGY AND CARCINOGENESIS
STUDIES OF A NONDECOLORIZED
WHOLE LEAF EXTRACT OF
ALOE BARBADENSIS MILLER (ALOE VERA)
IN F344/N RATS AND B6C3F1 MICE
(DRINKING WATER STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

August 2013

NTP TR 577

NIH Publication No. 13-5910

National Institutes of Health
Public Health Service
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food Contaminants Program

Fumonisin B1

led to worldwide regulatory levels

Malachite Green

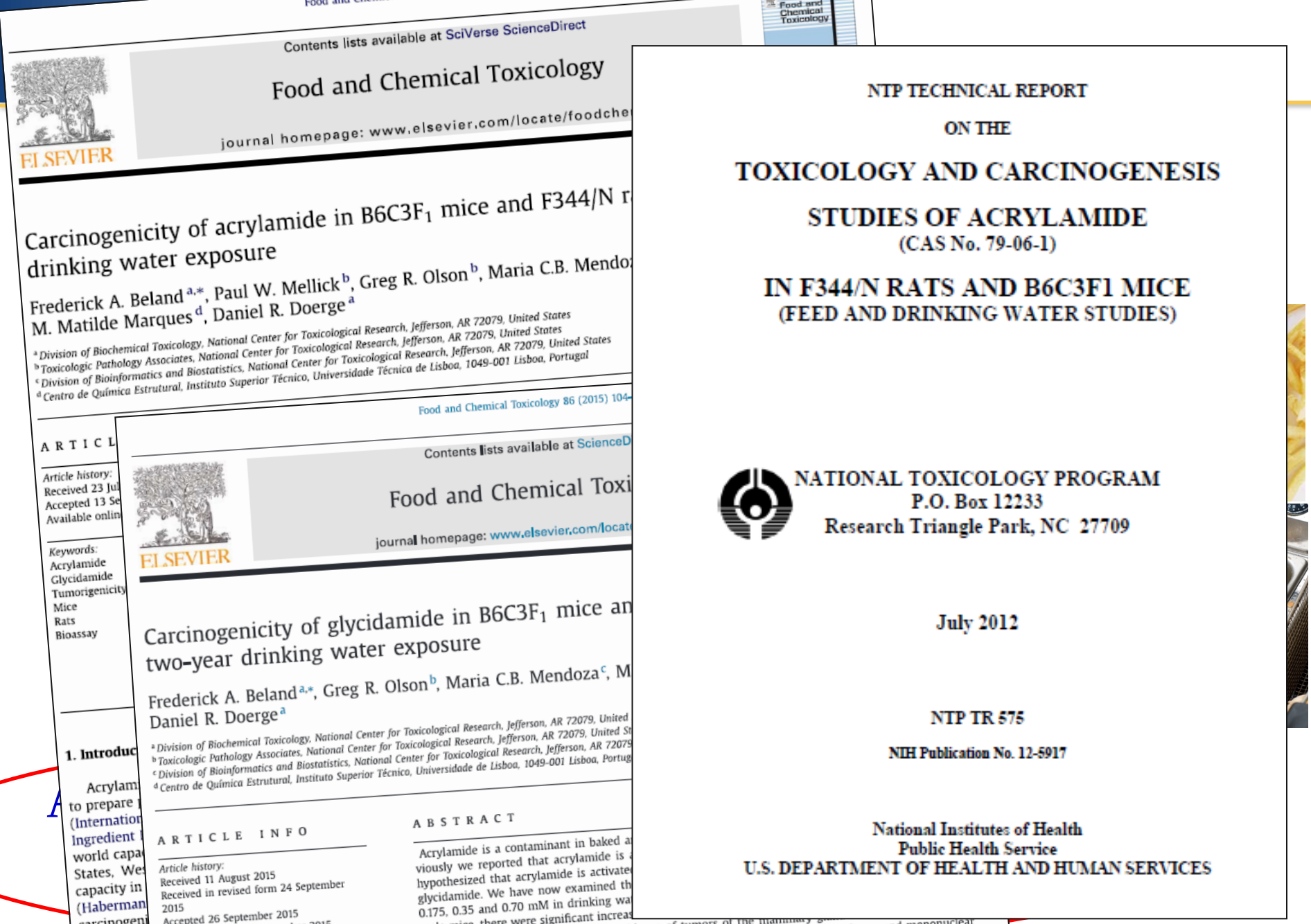
reinforced US ban on imports

Urethane ± Ethanol

no synergism, no regulatory action required

Acrylamide, Glycidamide

critical study for Risk Assessment, worldwide



Contents lists available at SciVerse ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodche

Carcinogenicity of acrylamide in B6C3F$_1$ mice and F344/N r
drinking water exposure

Frederick A. Beland[a,*], Paul W. Mellick[b], Greg R. Olson[b], Maria C.B. Mendo
M. Matilde Marques[d], Daniel R. Doerge[a]

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[b] Toxicologic Pathology Associates, National Center for Toxicological Research, Jefferson, AR 72079, United States
[c] Division of Bioinformatics and Biostatistics, National Center for Toxicological Research, Jefferson, AR 72079, United States
[d] Centro de Química Estrutural, Instituto Superior Técnico, Universidade Técnica de Lisboa, 1049-001 Lisboa, Portugal

Food and Chemical Toxicology 86 (2015) 104-

Contents lists available at ScienceD

Food and Chemical Toxi

journal homepage: www.elsevier.com/locat

Carcinogenicity of glycidamide in B6C3F$_1$ mice an
two-year drinking water exposure

Frederick A. Beland[a,*], Greg R. Olson[b], Maria C.B. Mendoza[c], M
Daniel R. Doerge[a]

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[b] Toxicologic Pathology Associates, National Center for Toxicological Research, Jefferson, AR 72079, United St
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Received in revised form 24 September 2015
Accepted 26 September 2015
Available online 30 September 2015

Keywords:
Acrylamide
Glycidamide

ABSTRACT

Acrylamide is a contaminant in baked a
viously we reported that acrylamide is
hypothesized that acrylamide is activate
glycidamide. We have now examined th
0.175, 0.35 and 0.70 mM in drinking wa
male mice, there were significant increas
Female mice also had an increased incidence of tumors of the mammary gl
female rats, there were significant increases in thyroid gland and oral cavity neoplasms and mononuclear
cell leukemia. Male rats also had increases in tumors of the epididymis/testes and heart, while female
rats demonstrated increases in tumors of the mammary gland, clitoral gland, and forestomach. A simi-
lar spectrum of tumors was obtained in mice and rats administered acrylamide. These data indicate that,
glycidamide is efficiently metabolized to glycidamide and that the

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF ACRYLAMIDE

(CAS No. 79-06-1)

IN F344/N RATS AND B6C3F1 MICE

(FEED AND DRINKING WATER STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

July 2012

NTP TR 575

NIH Publication No. 12-5917

National Institutes of Health
Public Health Service
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food Contaminants Program (continued)

Furan

extending dose-response data

Melamine + Cyanuric Acid

establishing the dose-recovery LOAEL

Bisphenol A (CLARITY)

extensive 2-yr bioassay, tissues to NIEHS collaborators (U01)

Arsenic

PK, PBPK, and bioassay for low levels of As

Currently under study

Commentary

Consortium-Based Science: The NIEHS's Multipronged, Collaborative Approach to Assessing the Health Effects of Bisphenol A

Linda S. Birnbaum,[1] John R. Bucher,[2] Gwen W. Collman,[3] Darryl C. Zeldin,[4] Anne F. Johnson,[5] Thaddeus T. Schug,[6] and Jerrold J. Heindel[6]

[1]National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH), Dep... Services (DHHS), Research Triangle Park, North Carolina, USA; [2]Division of the Natio... Research, and [4]Division of Intramural Research, NIEHS, NIH, DHHS, R... Triangle Park, North Carolina, USA; [6]Division of Extra... DHHS, Research Triangle Park, North C...

Background: plastic and... that BPA e... understand... cal's potenti...

Objectives: Toxicology... approach to ... inform decisi...

Discussion: N... research grants... mechanisms of... a round-robin ... with the Food a... a chronic toxicit... more integrated,... potential human ...

Key words: bisp...
Environ Health Pe...
25 September 2012

Bisphenol A (BPA) ... carbonate plastics, ... products. Manufactu... pounds of BPA every... the most common in... duced worldwide (Rub... with BPA are used in ... ucts, including food an... toys, eyeglasses, compute... and medical equipment. ... ing the chemical are used ... in metal coatings for fo... dairy equipment, office e...

Reproductive Toxicology 58 (2015) 33–44

Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

Review

NIEHS/FDA CLARITY-BPA research program update

Jerrold J. Heindel[a,*], Retha R. Newbold[b], John R. Bucher[b], Luísa Camacho[c], K. Barry Delclos[c], Sherry M. Lewis[f], Michelle Vanlandingham[c], Mona I. Churchwell[c], Nathan C. Twaddle[c], Michelle McLellen[c], Mani Chidambaram[c], Matthew Bryant[c], Kellie Woodling[c], Gonçalo Gamboa da Costa[c], Sherry A. Ferguson[d], Jodi Flaws[e], Paul C. Howard[f], Nigel J. Walker[b], R. Thomas Zoeller[g], Jennifer Fostel[b], Carolyn Favaro[h], Thaddeus T. Schug[a]

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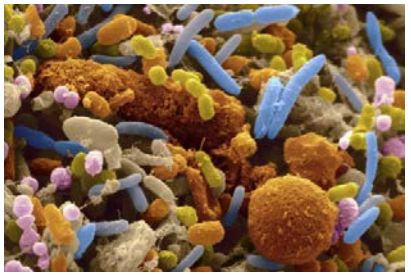
[g] Biology Department, University of Massachusetts, Amherst, MA 01003, United States
[h] Team Vistronix, NTP Computer and User Support, National Institute of Environmental Health Sciences/National Institutes of Health, ... of the National Toxicology Program, Research Triangle Park, NC 27709, United States

... of numerous consumer products resulting in ... the body of BPA toxicology ... assessment

Enhancing Toxicology Program

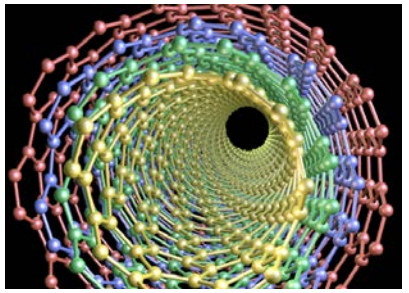
Microbiome

examining the role of microbiome in rodent bioassay



Nanotechnology Standards

developing standards and standard approaches for nanomaterial toxicological evaluation



Currently under study

Endocrine Active Agents Program

Genistein

multigeneration study; established effects

Ethinyl Estradiol

multigeneration study; established effects

Nonylphenol

renal toxicity

Drug & Device Program

Ketamine

established brain apoptosis rat, behavior changes in rodents, NHP

Chloral Hydrate

none to equivocal hazard

AIDS Therapeutics (AZT, 3TC, NVP)

some and equivocal evidence of carcinogenesis


Neuroscience 132 (2005) 967–977
THE ROLE OF THE N-METHYL-D-ASPARTATE RECEPTOR IN KETAMINE-INDUCED APOPTOSIS IN RAT FOREBRAIN CULTURE
C. WANG,[a*] N. SADOVOVA,[c] X. FU,[b] L. SCHMUED,[a]
A. SCALLET,[a] J. HANIG[d] AND W. SLIKKER[a*]
Key words: NMDA receptor, ketamine, antagonist, antisense oligonucleotide, neurodegeneration, apoptosis.
Ketamine, a noncompetitive N-methyl-D-aspartate (NMDA) receptor ion channel blocker, has been used as a general pediatric anesthetic for surgical procedures in infants and toddlers. Ketamine is a nonbarbiturate, dissociative anes-
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Who We Are
SmartTots is a collaborative effort of the IARS, the U.S. FDA and many others who are working to make anesthesia safer for infants and children.
Read More

Drug & Device Program (continued)

Oxybenzone

established reproductive/developmental toxicity with two assays (NTP & NCTR)

Cellular Telephone Radiation

NTP – chronic bioassay

NCTR – neuro-immunohistochemistry; in vitro

Triclosan

topical PK and carcinogenesis

Toxicologic Pathology, 42: 1165-1167, 2014

ISSN: 0192-6233 print / 1533-1601 online
DOI: 10.1177/0192623314534920

Regulatory Forum Opinion Piece*: New Testing Paradigms for Reproductive and Developmental Toxicity—The NTP Modified One Generation Study and OECD 443

Paul M. D. Foster[1]

[1]*Division of the National Toxicology Program, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina, USA*

Abstract

The National Toxicology Program (NTP) has developed a new flexible study design, termed the modified one generation (MOG) reproduction study. The MOG study will encompass measurements of developmental and reproductive toxicity parameters as well as enable the setting of appropriate dose levels for a cancer bioassay through evaluation of target organ toxicity that is based on test article exposure that starts during gestation. This study design is compared and contrasted with the new Organization for Economic Co-operation and Development (OECD) 443 test guideline, the extended one generation reproduction study. The MOG study has a number of advantages, with a focus on F_1 animals, the generation of adequately powered, robust data sets that include both pre and postnatal developmental toxicity information, and the measurement of effects on reproductive structure and function in the same animals. This new study design does not employ the use of internal triggers in the design structure for the use of animals already on test and is also consistent with the principles of the 3R's.

Keywords: developmental pathology; endocrine disrupters; female reproduction; male reproduction; reproductive system; safety assessment.

One of the major roles of the National Toxicology Program (NTP) has been in the development of new toxicology test methods. Following 2 workshops (King-Herbert and Thayer 2006; Thayer and Foster 2007) that focused on the NTP selection of a new rat strain for all of its toxicological studies and that there would be a greater emphasis on early life test article exposures in the conduct of its cancer bioassays, it became apparent that there was a need for some dose range finding studies that involved early life test article exposure (gestation, lactation, and continuing exposure through adulthood). At the same time, NTP also showed that they could markedly increase the power to detect postnatal developmental effects (including those consequent to *in utero* exposure) in their developmental and reproductive toxicity (DART) studies by simply retaining more of the offspring from each litter post weaning (on most DART littering studies, only 1 male and female from each litter is retained) that would normally be culled or only given a cursory examination (Blystone et al. 2010).

Taken together, the program realized that in performing the necessary setting of dose levels and identification of target organ toxicity in order to undertake a perinatal cancer bioassay, it was possible at the same time to use animals already produced following exposure during gestation and lactation to develop additional, high-quality DART information in a single design, which we have termed the modified one generation (MOG) study (http://ntp.niehs.nih.gov/ntp/About_NTP/BSC/2011/April/MOGDesign.pdf). The design basically com-

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The author(s) received no financial support for the research, authorship, and/or publication of this article.

Address correspondence to: Paul M. D. Foster, Division of the National Toxicology Program, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC 27709, USA; foster2@niehs.nih.gov.

Nanoscale Materials Program

Nanotechnology Core Facility

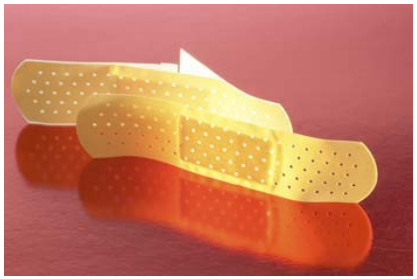
valuable resource to FDA and NIEHS

Nanoscale Silver

definitive 90-day toxicity study

Nanoscale Quantum Dots and TiO2

defined lack of dermal penetration



TOXICOLOGICAL SCIENCES 111(1), 37–48 (2009)
doi:10.1093/toxsci/kfp139
Advance Access publication July 2, 2009

Quantitative Determination of Skin Penetration of PEG-Coated CdSe Quantum Dots in Dermabraded but not Intact SKH-1 Hairless Mouse Skin

Neera V. Gopee,*·† Dean W. Roberts,*·† Peggy Webb,*·† Christy R. Cozart,* Paul H. Siitonen,* John R. Latendresse,‡
William W. Yu § Vicki L. Colvin,§ Nigel J. Walker,¶ and Paul C. Howard*·†·1

*National Cen
Arkansas 72079;
Houston, Texas

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glycol coated
37 nm diamet
into intact, ta
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OXFORD
SOT | Society of Toxicology
www.toxsci.oxfordjournals.org

TOXICOLOGICAL SCIENCES, 150(1), 2016, 131–160
doi: 10.1093/toxsci/kfv318
Advance Access Publication Date: January 5, 2016
Research Article

Differential Effects of Silver Nanoparticles and Silver Ions on Tissue Accumulation, Distribution, and Toxicity in the Sprague Dawley Rat Following Daily Oral Gavage Administration for 13 Weeks

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Phototoxicology Program

Alpha Hydroxy Acids (glycolic acid)
established no hazard

Beta Hydroxy Acids (salicylic acid)
established no hazard

Aloe Vera
established no hazard

Retinyl Palmitate
some hazard identified

Phot

Alpha
esta

Beta H
estal

Aloe V
estab

Retinyl
some

NTP TECHNICAL REPORT

ON THE

PHOTOCOCARCINOGENESIS

STUDY OF

RETINOIC ACID AND RETINYL PALMITATE

[CAS Nos. 302-79-4 (All-*trans*-retinoic acid)
and 79-81-2 (All-*trans*-retinyl palmitate)]

IN SKH-1 MICE

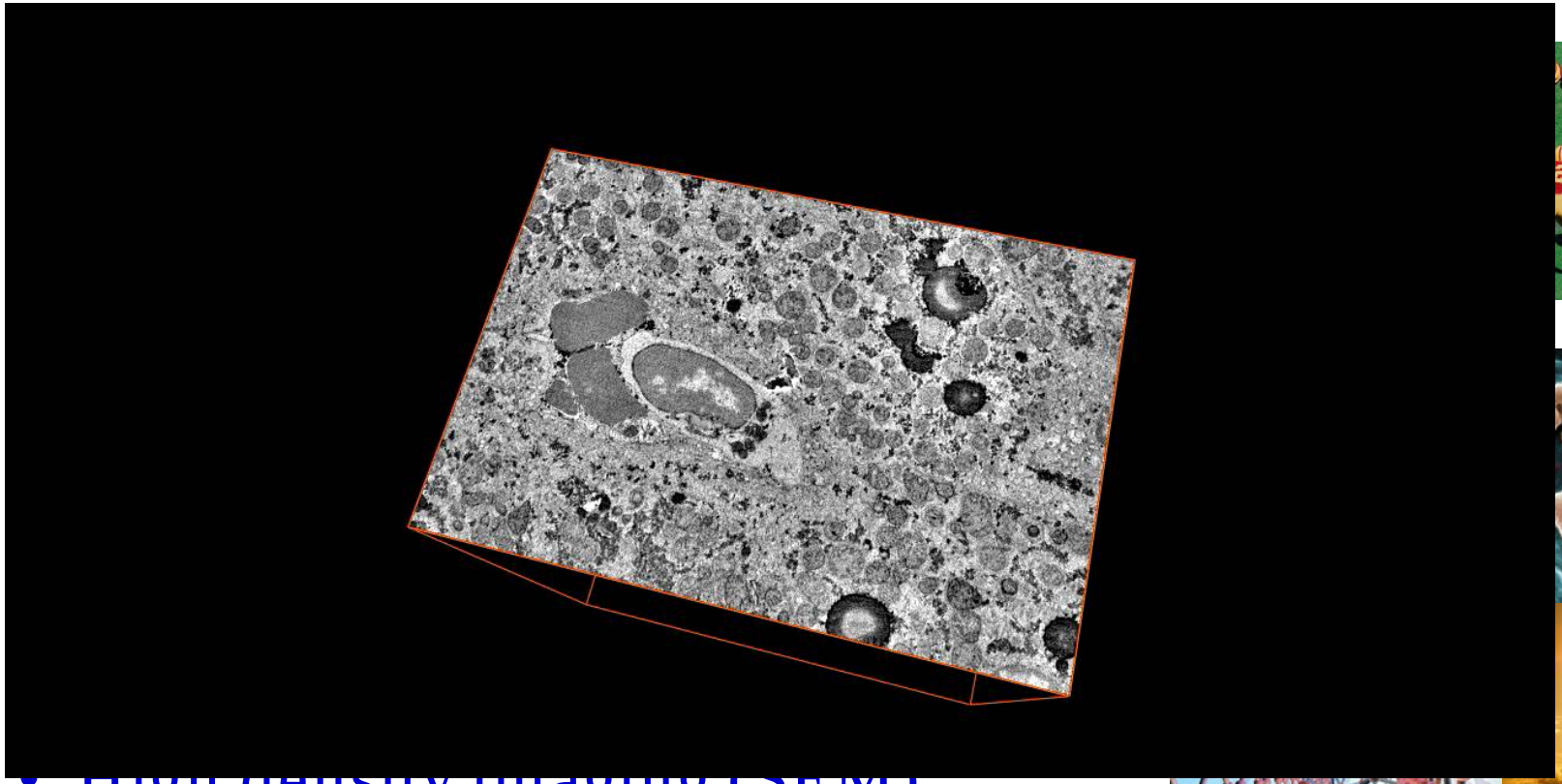
(SIMULATED SOLAR LIGHT
AND TOPICAL APPLICATION STUDY)

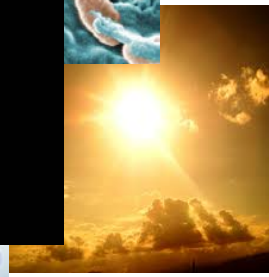
NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

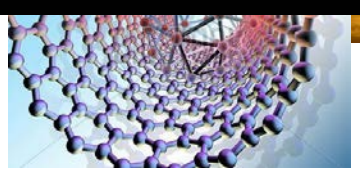
August 2012

NTP TR 568

IAA: Taking Advantage of Unique Resources at FDA/NCTR







- High density imaging (SEM)
- Sequential imaging efforts
- Rodent (and higher-order) learning

IAA: Impact on FDA and Future Direction

IMPACT

- Results used for regulatory decisions (*e.g.* *a*crylamide)
- Study results generating debate regarding public risk (*e.g.* BPA, retinyl palmitate, aloe vera)

FUTURE DIRECTION

- Continue with studies of high interest/concern to FDA and NTP (*e.g.* arsenic, botanicals/dietary supplements, food contaminants, endocrine active compounds)
- Examine new methods/approaches for utility to inform NTP and FDA regarding hazard and risk [*e.g.* microbiome, advanced sequential imaging (electron microscopy; neuropathology), organotypic models, nanotechnology]

NIEHS/NTP & FDA/NCTR
Interagency Agreement

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Assoc. Dir. NTP

Nigel Walker,
NTP PO

Robert Califf,
Comm. FDA

William Slikker,
Director NCTR

Paul Howard,
NCTR PO

NIEHS/NTP and FDA/NCTR Interagency Agreement:

23½ years of providing data, protecting Public Health