

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Contact

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Education

- 1968 - 1974 Student at the Agricultural University of Wageningen, The Netherlands. *M.Sc. degree in Human Nutrition* awarded in 1974.
- 1974 - 1978 Ph.D. Student, *Shell Toxicology Laboratory* in Sittingbourne, United Kingdom
- 1979 *Ph.D. degree in Agricultural Sciences* awarded by the Agricultural University of Wageningen, The Netherlands, on a thesis entitled „*The Relationship between Microsomal Enzyme Induction and Liver Tumour Formation*“ (under supervision of Prof. Dr. J. H. Koeman)

Professional Experience

- 1978 - 1980 Scientist at the Institute of Toxicology and Pharmacology of the *University of Marburg*, Germany
- 1980 - 1985 Scientist at the *German Cancer Research Center* in Heidelberg, Germany
- 1985 - 1986 Senior Toxicologist in the Department of Agrochemical Toxicology of *Sandoz Ltd* in Muttenz, Switzerland
- 1986 - 1992 Head of the General Toxicology Department and Member of the Directorate at *RCC, Research and Consulting Company Ltd* in Itingen, Switzerland
- 1992 - present Independent Consultant in Toxicology in Pratteln, Switzerland (1992 - 1998) and Sissach, Switzerland (1998-2002), now based in Zutphen, the Netherlands

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Achievements

1974 - 1985

Mechanistic research on the induction of mouse liver tumours by non-genotoxic compounds. The organochlorine insecticide dieldrin served as a model substance. The most important results of these investigations were

1. The demonstration in a chronic mouse study of a relationship between dieldrin-induced increases in liver DNA and mouse liver tumour formation [*Cancer Research* 41, 3615-3620 (1981)];
2. The discovery that the dose-response relationship for liver tumour formation in mice by the *non-genotoxic* carcinogen dieldrin is consistent with Haber's Rule, i.e., the product of exposure concentration [c] and duration [t] produces a constant toxic effect, $c \cdot t = \text{constant}$ [*Carcinogenesis* 6, 1457-1462 (1985)];
3. The demonstration of a close association of tumour formation with nuclear polyploidisation in mouse hepatocytes [*Carcinogenesis* 8, 265-269 (1987)].

1985 - 1992

Direction of numerous general toxicity and carcinogenicity studies with pharmaceuticals and agrochemicals. Successful management of the general toxicology department of a major European contract research laboratory leading to rapid expansion of services. First introduction in the world of computerised dosing equipment in general and reproduction toxicity studies in 1988.

1992 - present

Consultancy services to leading companies in the chemical industry with an acknowledged record of achievement. The consultancy offers comprehensive services in product safety assessment including

Design of safety evaluation programmes,
Human safety assessment,
Interaction with regulatory agencies (product defense),
Preparation of EU expert reports and US NDAs, Preparation of preclinical assessments, investigator's drug brochures, INDs,
Data interpretation and evaluation (report preparation),
Design, monitoring and report review of toxicity studies,
Preparation of manuscripts for publication in scientific journals (including editorials),
Coaching and training of junior toxicologists.
Presentations in Radio and TV programmes/documentaries.
The consultancy has so far been commissioned by the following companies or institutions:

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Achievements – continued

<p>Switzerland Ciba Geigy Pharma AG Sandoz Pharma AG Sandoz Agro AG EPS AG F. Hoffmann - La Roche AG Novartis Pharma AG Oekoskop Novartis Consumer Health AG Novartis Crop Protection AG RCC AG Permamed AG Papiliorama Swiss Television DRS</p> <p>England Zeneca Agrochemicals Ltd Hydrogen Talentmark</p> <p>Israel Makhteshim Ltd Intec Pharma Ltd</p> <p>Austria Monsanto GmbH Austrian Television ORF</p>	<p>Germany Knoll AG BASF AG Henkel KGaA Cognis Deutschland GmbH Verband der Chemischen Industrie e.V. West-German Television WDR North-German Television NDR Zweites Deutsches Fernsehen ZDF</p> <p>The Netherlands Yamanouchi Europe B.V. Shell International B.V. TNO Pharma B.V. NOTOX B.V. / WIL Research Solvay Pharmaceuticals B.V. Kinesis Holding B.V. DSM Dutch Society for Nature & Environment Dutch Radio NOS</p> <p>Belgium UCB S.A. (Pharma Sector) PAN Europe</p> <p>France INVENTIVA SAS</p>
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1992 - 1998	Secretary of the Toxicology Section of the Swiss Society of Pharmacology and Toxicology
1996 - 2000	Member of the Board of Directors of the Swiss Register of Toxicologists.
1995	Chairman of the Task Force of the Swiss Society of Pharmacology and Toxicology on Guidelines for Training and Registration of Toxicologists in Switzerland. The recommendations of the Task Force were adopted by the Society for the establishment of a Swiss Register of Toxicologists (with EUROTOX certification) and a post-graduate training programme for toxicologists in Switzerland.
2002 - 2004	The demonstration in outbred and inbred rat strains that (spontaneous) carcinogenesis is genetically determined and that non-genotoxic carcinogens operate by facilitating the expression of tumour predisposition in target cells [<i>Regulatory Toxicology and Pharmacology</i> , <u>36</u> , 86-95; <u>40</u> , 18-27; <u>40</u> , 293-304].

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Achievements – continued

2009 – 2016
Discovery that the Druckrey-Küpfmüller equation $d t^n = \text{constant}$ (where d = daily dose and t = exposure time to effect, with $n \geq 1$) for genotoxic carcinogens also applies to non-genotoxic compounds, such as the toxicity of neonicotinoid insecticides to arthropods (*Toxicology* 276, 1-4) and neurotoxicity induced by organic mercury (*Toxicology* 347, 1-5). Publication of books on the hazards of neonicotinoid insecticides to insects and the food chain. Review of current pesticide risk assessment and proposals for new approaches (*Toxicology* 309, 39– 51; *J Environment Analytic Toxicol* S4:001; *Sci. Rep.* 4, 5566; DOI:10.1038/srep05566 (2014)) that were subsequently adopted by the European Food Safety Authority (EFSA). Instrumental role in bringing about bans on neonicotinoids in Europe.

Scientific Publications

- 1979 H. A. Tennekes. Ph.D. Thesis
The relationship between microsomal enzyme induction and liver tumour formation.
Agricultural Research Report 890, Centre for Agricultural Publishing & Documentation, Wageningen
- 1978 H. A. Tennekes and A.S. Wright.
The relationship between biotransformation pathways of chemicals and hepatic tumorigenesis in various strains and species.
In: Primary Liver Tumours, pp. 305-318, MTP Press (UK)
- 1979 H. A. Tennekes, A. S. Wright and K.M. Dix.
The effects of dieldrin, diet and other environmental components on enzyme function and tumor incidence in livers of male CF-1 mice.
Arch. Toxicology Suppl. 2, 197-212
- 1981 H. A. Tennekes, A. S. Wright, K. M. Dix, and J. H. Koeman.
Effects of dieldrin, diet and bedding on enzyme function and tumor incidence in livers of male CF-1 mice.
Cancer Research 41, 3615-3620
- 1982 H. A. Tennekes, L. Edler, and H. W. Kunz
Dose-response analysis of the enhancement of liver tumor formation in CF-1 mice by dieldrin.
Carcinogenesis 3, 941-945
- 1982 W. Kunz, G. Schaudé, M. Schwarz, and H. A. Tennekes. *Quantitative aspects of drug-mediated tumor promotion in liver, and its toxicological implications*
In: *Carcinogenesis* 7, 111-125, Raven Press, New York

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Scientific Publications - continued

- 1982 D. Schrenk, M. Schwarz, H. A. Tennekes, and W. Kunz.
A novel pathway of nitrosamine metabolism in liver microsomes: denitrosation of nitrosamines by cytochrome P-450.
In: Biological Reactive Intermediates II, pp. 1157-1163, Plenum Publishing Corporation, New York
- 1982 D. Kitta, M. Schwarz, H. A. Tennekes, H. Uehleke and W. Kunz.
Covalent binding of CCl₄-intermediates to reduced pyridine nucleotides in mouse liver.
In: Biological Reactive Intermediates II, pp. 769-777, Plenum Publishing Corporation, New York
- 1983 H. W. Kunz, H. A. Tennekes, R. E. Port, M. Schwarz, D. Lorke, and G. Schaudé
Quantitative aspects of chemical carcinogenesis and tumor promotion in liver
Env. Health Persp., 50, pp. 113-122
- 1985 H. Tennekes, B. van Ravenzwaay, and H. W. Kunz.
Quantitative aspects of enhanced liver tumour formation in CF-1 mice by dieldrin.
Carcinogenesis 6, 1457-1462
- 1985 H. W. Kunz, M. Schwarz, H. Tennekes, R. Port, and K. Appel.
Mechanism and dose-time response characteristics of carcinogenic and tumor promoting xenobiotics in liver.
In: Tumorpromotoren, BGA Schriften 6, pp. 76-97, MMV Medizin Verlag, München
- 1987 B. van Ravenzwaay, H. Tennekes, M. Stöhr, and W. Kunz.
The kinetics of nuclear polyploidisation and tumour formation in livers of CF-1 mice exposed to dieldrin.
Carcinogenesis 8, 265-269
- 2002 B. van Ravenzwaay and H. Tennekes.
A Wistar rat strain prone to spontaneous liver tumor development. Implications for carcinogenic risk assessment
Regulatory Toxicology and Pharmacology 36, 86-95
- 2004 H. Tennekes, C. Gembardt, M. Dammann and B. van Ravenzwaay.
The stability of historical control data for common neoplasms in laboratory rats: adrenal gland (medulla), mammary gland, liver, endocrine pancreas and pituitary gland.
Regulatory Toxicology and Pharmacology 40, 18-27

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Scientific Publications - continued

- 2004 H. Tennekes, W. Kaufmann, M. Dammann and B. van Ravenzwaay.
The stability of historical control data for common neoplasms in laboratory rats and the implications for carcinogenic risk assessment.
Regulatory Toxicology and Pharmacology 40, 293-304
- 2004 A.O. Gamer, E. Leibold, K. Deckardt, B. Kittel, W. Kaufmann, H.A. Tennekes, and B. van Ravenzwaay.
The effects of styrene on lung cells in female mice and rats. Food Chem Toxicol. 42(10),1655-67
- 2007 K. Deckardt , I. Weber, U. Kaspers, J. Hellwig, H. Tennekes, and B. van Ravenzwaay.
The effects of inhalation anaesthetics on common clinical pathology parameters in laboratory rats.
Food Chem Toxicol. 45(9),1709-18
- 2009 G. Coelho Palermo Cunha, B. van Ravenzwaay, H. A. Tennekes, W. Mellert, S. Schulte and S. Burkhardt
Effects of an ultraviolet B radiation absorber on photocarcinogenesis in hairless albino mice
Skin Pharmacology and Physiology 22, 166-176
- 2010 H. Tennekes, V.A. Gretton, and T. Stedeford.
Hazard and risk assessment of chemical carcinogenicity within a regulatory context.
In: Cancer Risk Assessment: Chemical Carcinogenesis, Hazard Evaluation, and Risk Quantification (Edited by Ching-Hung Hsu and Todd Stedeford), pp. 37-65. John Wiley and Sons, Hoboken, NJ 07030-5774
- 2010 H. A. Tennekes
The significance of the Druckrey-Küpfmüller equation for risk assessment - The toxicity of neonicotinoid insecticides to arthropods is reinforced by exposure time
Toxicology 276, 1-4
- 2010 H. A. Tennekes
The Systemic Insecticides: A Disaster in the Making
ETS Nederland BV, Zutphen, The Netherlands
- 2011 H. A. Tennekes
Das Ende der Artenvielfalt – Neuartige Pestizide töten Insekten und Vögel
Bund fuer Umwelt und Naturschutz Deutschland (BUND) – Friends of the Earth Germany, Berlin

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Scientific Publications - continued

- 2011 H. Tennekes
The significance of the Druckrey-Küpfmüller equation for risk assessment - The toxicity of neonicotinoid insecticides to arthropods is reinforced by exposure time: Responding to a Letter to the Editor by Drs. C. Maus and R. Nauen of Bayer CropScience AG
Toxicology 280, 173-175
- 2011 H. A. Tennekes and F. Sánchez-Bayo
Time-Dependent Toxicity of Neonicotinoids and Other Toxicants: Implications for a New Approach to Risk Assessment
J Environment Analytic Toxicol S4:001. doi:10.4172/2161-0525.S4-001
- 2013 R. Mason, H. Tennekes, F. Sánchez-Bayo, P. Uhd Jepsen
Immune Suppression by Neonicotinoid Insecticides at the Root of Global Wildlife Declines
Journal of Environmental Immunology and Toxicology 1, 3-12
- 2013 H. A. Tennekes and F. Sánchez-Bayo
The molecular basis of simple relationships between exposure concentration and toxic effects with time
Toxicology 309, 39– 51
- 2013 F. Sánchez-Bayo, H. A. Tennekes, K. Goka
Impact of systemic insecticides on organisms and ecosystems
In: *Insecticides - Development of Safer and More Effective Technologies* (Ed. Stanislav Trdan), pp. 365-414. InTech Open Science
ISBN:980-953-307-514-8
- 2014 H. Tennekes
Wirkung der Neonicotinoide. Umweltgau in der Insektenwelt
Oekoskop (Fachzeitschrift der Ärztinnen und Ärzte für Umweltschutz)
Nr. 1/14, 5-8
- 2014 S. Mellching-Kollmuss, K.C. Fussell, R. Buesen, M. Damman, S. Schneider, H. Tennekes, B. van Ravenzwaay.
Anti-androgenicity can only be evaluated using a weight of evidence approach
Regul. Toxicol. Pharmacol. 68, 175-92
- 2014 G. Rondeau, F. Sánchez-Bayo, H.A. Tennekes, A. Decourtye, R. Ramirez-Romero, N. Desneux
Delayed and time-cumulative toxicity of imidacloprid in bees, ants and termites.
Sci. Rep. 4, 5566; DOI:10.1038/srep05566
(www.nature.com/scientificreports)
- 2015 F. Sánchez-Bayo, H. A. Tennekes
Environmental Risk Assessment of Agrochemicals — A Critical Appraisal of Current Approaches
In: *Toxicity and Hazard of Agrochemicals*, Prof. Marcelo Larramendy (Ed.), ISBN: 978-953-51-2145-9, InTech.

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Scientific Publications - continued

- 2015 H. A. Tennekes
Een ingrijpende herziening van de risico analyse van chemische producten is dringend noodzakelijk
TCDD 3, 12-13
- 2015 H. Tennekes, J. Hoppichler
Chemikalien: Menge und Zeit machen das Gift
Oekoskop (Fachzeitschrift der Ärztinnen und Ärzte für Umweltschutz) 15-4, 19-22
- 2016 J. Pletz, F.Sánchez-Bayo, H. A. Tennekes
Dose-response analysis indicating time-dependent neurotoxicity caused by organic and inorganic mercury—Implications for toxic effects in the developing brain
Toxicology doi:10.1016/j.tox.2016.02.006
- 2016 H. A. Tennekes, J. Pletz, F. Sánchez-Bayo
Development of a Dose-Response Model For Risk Assessment of Receptor-Mediated Effects
Internal Medicine Review, Vol.1 (2)
- 2016 H. A. Tennekes
A Critical Appraisal of the Threshold of Toxicity Model for Non-Carcinogens
J Environ Anal Toxicol 6:408
- 2017 H. A. Tennekes
Dose: Time-to-effect analyses can identify hazardous chemicals at an early stage of product development
Environ Risk Assess Remediat 1 :65-70
- 2017 Sánchez-Bayo F., Tennekes H.A.
Assessment of ecological risks of agrochemicals requires a new framework
Environ Risk Assess Remediat. 1(3): 20-28
- 2017 Tennekes H.A.
The Importance of Dose-Time-Response Relationships for Hazard Identification and Limitation of Animal Experiments.
Open Acc J of Toxicol. 1(5): 555572.
DOI: 10.19080/OAJT.2017.01.555572.

Unpublished Study Reports now in the Public Domain

- 1987 Tennekes, H., Horst, K., Luetkemeier, H., Vogel, W., Schlotke, B. & Terrier, C.H.
Triazophos. Subchronic oral toxicity, 13 week feeding study in rats.
Unpublished report No. 071818 from RCC Research & Consulting Company AG, Itingen, Switzerland, 10 December 1987. Aventis document A37398. Submitted to WHO by Aventis CropScience, Frankfurt am Main, Germany.

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Unpublished Study Reports now in the Public Domain - Continued

- 1987 Tennekes, H., Horst, K., Luetkemeier, H., Wilson, J., Vogel, W., & Terrier, Ch.
Thirteen week oral toxicity (feeding) study with Bentazone Technical (ZNT No. 86/48) in the rat.
Unpublished report by RCC Research & Consulting Company AG, Itingen, Switzerland, submitted to WHO by BASF, Limburgerhof, Germany.
- 1989 Tennekes, H., Stucki, P., Luetkemeier, H., Biedermann, K., Bloch, M., Chevalier, H., Vogel, O. & Terrier, C.
Chronic toxicity and oncogenicity (feeding) study with CME 134 in the rat.
Project 064192. Document No. 134AB-437-009. Unpublished report from RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by Shell International Chemical Co. Ltd, London, United Kingdom.
- 1989 Tennekes, H., Horst, K., Luetkemeier, H., Vogel, W., Vogel, O., Armstrong, J., Ehlers, H.A., Muller, E., Terrier, C.
TPTH-technical (Code: HOE 029664 OF ZD97 0004: Oncogenicity 80-week feeding study in mice.
Unpublished report 047002 (A40467) from RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by Hoechst AG, Frankfurt-am-Main, Germany.
- 1989 Tennekes, H., Horst, K., Luetkemeier, H., Vogel, W., Schlotke, B., Vogel, O., Ehlers, H.A., Muller, E., Terrier, C.
TPTH-technical (Code: HOE 029664 OF ZD97 0007): Chronic toxicity/oncogenicity 104-week feeding study in rats.
Unpublished report 046980 (A40468) of RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by Hoechst AG, Frankfurt-am-Main, Germany.
- 1990 Tennekes, H., Janiak, T., Probst, D., Luetkemeier, H., Vogel, O., Westen, H., Biedermann, K. & Heusner, W.
Triazophos. Chronic toxicity/oncogenicity feeding study in rats.
Unpublished report No. 071537 from RCC Research & Consulting Company AG, Itingen, Switzerland, 24 December 1990. Aventis document A44716. Submitted to WHO by Aventis CropScience, Frankfurt am Main, Germany.
- 1991 Tennekes, H., Janiak, T., Probst, D., Luetkemeier, H., Vogel, O., Schlotke, B., Biedermann, K., & Heusner, W.
Pyrazophos substance technical. Chronic toxicity/oncogenicity feeding study in rats.
Unpublished report No. 071526 from RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by Hoechst.

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Unpublished Study Reports now in the Public Domain - Continued

- 1991 Tennekes, H., Janiak, T., Probst, D., Luetkemeier, H., Vogel, O., Schlotke, B., Biedermann, K., & Heusner, W.
Pyrazophos substance technical. Chronic toxicity addendum to RCC project 071526 satellite feeding study in rats with a supplementary test concentration.
Unpublished report No. 209226 from RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by Hoechst.
- 1991 Tennekes, H., Janiak, T., Stucki, H.P., Probst, D., Luetkemeier, H., Vogel, O., Schlotke, B., Biedermann, K. & Heusner, W.
28-Day range-finding (feeding) study with chlorfenvinphos in the mouse.
RCC Project No. 243202. Unpublished report from RCC Research & Consulting Company AG, Itingen, Switzerland. Submitted to WHO by American Cyanamid Co., Princeton, NJ, USA
- 1992 Tennekes, H., Schmid, H. & Probst, D.
Sub-chronic oral toxicity 13-week feeding study in mice with Hoe 099730 substance, technical.
RCC Research & Consulting Company Ltd, Itingen, Switzerland. Report No. 291025. A48186. Unpublished report submitted to WHO by Hoechst Schering AgrEvo GmbH, Germany.
- 1992 Tennekes, H., Probst, D. & Luetkemeier, H.
Sub-chronic oral toxicity 13-week feeding study in rats with Hoe 099730 substance, technical.
RCC Research & Consulting Company Ltd, Itingen, Switzerland. Report No. 291093. A48187. Unpublished report submitted to WHO by Hoechst Schering AgrEvo GmbH, Germany.
- 1992 Schmid, H., Tennekes, H., Janiak, T., Probst, D., Luetkemeier, H., Pappritz, G., Marki, U., Vogel, O., Heusner, W.
Ethylenthiourea 104 week chronic toxicity (feeding) study in rats.
Unpublished study No. 256803 from RCC Research & Consulting Company Ltd, Itingen, Switzerland.. Submitted to WHO by Rohm and Haas Company, Spring House, Pennsylvania, USA.
- 1994 Tennekes, H.
The genetic toxicology of captan.
Unpublished review commissioned by Zeneca Agrochemicals. Submitted to U.S. EPA.
- 1995 Tennekes, H.
The genetic toxicology of folpet.
Position paper commissioned by Makhteshim Chemical Works Ltd, Beer-Sheva, Israel. Submitted to WHO.

Curriculum Vitae

H. A. Tennekes, M.Sc., Ph.D., FRSM

Memberships

Dutch Society of Toxicology

Swiss Society of Pharmacology and Toxicology

British Toxicology Society

Association of European Toxicologists and Toxicological Societies (EUROTOX)

International Union for the Conservation of Nature (IUCN)/Commission on Ecosystem Management (CEM)

Society of Toxicologic Pathology

American Chemical Society

Overseas Fellow, Royal Society of Medicine

Memberships Editorial Board Scientific Journals

Editor-in-Chief, Journal of Environmental Risk Assessment and Remediation

Editorial Board Member, Annals of Clinical Toxicology

Editorial Advisory Board Member, The Open Toxicology Journal

Editorial Board Member, Toxicology: Current Research Journal

Certifications

Registered Toxicologist in Switzerland and the Netherlands (with EUROTOX certification)

_____ Date:
Dr. H.A. Tennekes