



INTERNATIONAL NEUROTOXICOLOGY ASSOCIATION

INA News January 2016

Message from the President and Past-President

Dear INA members,

We would like to start this newsletter with our best wishes for 2016, a year without an INA meeting. This newsletter will provide conference announcements for 2016 and give us the opportunity to meet each other this year.

In 2015 we had our 15th biannual meeting in Canada together with the Neurobehavioral Teratology Society (NBTS), now the Developmental Neurotoxicology Society (DNST). Over 170 scientists from around the world gathered in Montréal and with 12 symposia, 6 platform sessions, and 60 posters discussed the latest research in neurotoxicology from molecular through epidemiological studies.

Another important event in 2015 was the election of new officers. The Nominating Committee was chaired by the past-president Jordi Llorens supported by Miki Aschner and Will Boyes. They did a great job and the membership could make their choices among several outstanding researchers and long-term INA members. The new officers were announced during the business meeting in Montréal. Remco Westerink now serves as president-elect, Sandra Allen was reelected as secretary, and Pam Lein and Lucio Costa were also reelected as councilors. Welcome and welcome back to all the new officers. On behalf of the Executive Council (EC) we would like to thank the other candidates of the 2015-17 ballot (Anu Kanthasamy, Tim Shafer, Ellen Fritsche, and Marcel Leist). Thank you for your willingness to run in this election process and we're sure you'll have further opportunities to serve INA in the future.

Jan Lammers served as treasurer of INA since 2008 and our money was safe in his hands! He did a great job and we would like to thank him a lot for keeping the INA account in good shape, collecting the membership dues, raising and managing funds for several meetings, doing the reimbursement for many invited speakers, Hooisma lectures, and more. Thank you, Jan! Jan served the INA EC for many years, but he also convinced Harm Heusinkveld to run as the new Dutch treasurer in the 2015 election process. Welcome on board Harm and good luck with this tough job.

After serving INA as secretary for several years Jordi completed his turn as president-elect, president and past-president this summer. He did a great job initiating the website update, heading several local and scientific committees of INA meetings and finally bringing the new officers into the executive committee. Thank you Jordi and good luck!

For the upcoming INA meeting in June 2017, we will meet together with the Neurotoxicity Society in Florianopolis, Brazil for INA16. The request for symposium proposals will go out soon, so be ready with your best ideas for this next important meeting.

Best regards,
Ed Levin, President
Christoph van Thriel, Past-President

Message from the President-elect

I would like to gratefully acknowledge Helena Hogberg for her excellent help with the website and her willingness to serve as website editor. Since the last newsletter, we had a re-design and re-launch of the INA website and we hope all of you have already visited the new website:

<http://www.neurotoxicology.org/>. To have a vivid website we need the help of all members! Please send Helena or any other EC member your photos from INA meetings, announce jobs in your lab, write some interesting sentences about your last publication, etc. We need content from you to attract other people to join our association and to keep INA thriving.

While on the website, you will also find a renewed section 'Other Links - Services' (<http://www.neurotoxicology.org/equipment-companies-industry-labs-consulting-services/>). This section now lists a number of companies that may be of particular interest for you because they offer cells, equipment and/or services valuable for neurotoxicity testing. Notably, these companies may not only be a valuable resource for your research, they all also provide financial support to INA. Their donations will be entirely used to generate a student travel fund that will help our young members to visit our biennial meetings. So have a look on the website and check out these companies yourself; their generous support is vital to our young members! If you offer a product or service yourself and want to be listed on our website or in our newsletter, please contact me at r.westerink@uu.nl.

In addition to a renewed website, we have also two new sections in this newsletter! In "Researcher in the spotlight", Tim Shafer highlights the main findings and implications of his article "Microelectrode arrays: A physiologically based neurotoxicity testing platform for the 21st century", which is the most cited article in Neurotoxicology since 2010. In our new "Young researcher series" as part of our new Postdoc/Grad Student Section, Martje de Groot will give us some insight in her research and struggles as PhD student.

We hope you will appreciate these new sections and very much welcome your contributions for the next newsletter!

All the best, and enjoy our website and newsletter,

Remco Westerink
President-Elect

Secretary's Report

INA will have its yearly business meeting during the Society of Toxicology meeting in New Orleans, LA, USA. Please plan to attend!

Date: Tuesday March 15, 12:15-1:15 PM
Location: Hilton New Orleans Riverside (SOT Headquarters)
2 Poydras St.
Belle Chasse room

We had 8 new members in 2015:

7 full members

Dr Shekher Mohan, Marshall University, West Virginia, USA
Dr Aaron Bowman, Vanderbilt University Medical Centre, Nashville, USA
Ms Evelien Van Valen, Academic Medical Centre, Amsterdam, the Netherlands

Dr Moniek Van Hout, Enschede Hospital, the Netherlands
Dr Felix Soares, Universidade Federal de Santa Maria, Brazil
Dr Yael Abreu-Villaca, Universidade do Estado do Rio de Janeiro, Brazil
Dr Russell Carr, Mississippi State University, USA

1 student member

David Edmondson, Purdue University, West Lafayette, USA.

Our total members are currently listed at 216 members (204 full and 12 student) from 30 countries.

There are a number of members that I have written to individually and asked them to confirm their email address and to indicate that they want to stay as members. I have had no response from the members listed below. Please review this list for help in contacting them. This will help us to tidy up the membership database with only those who wish to maintain INA membership. Please send any information (new addresses, emails, etc) to Sandra Allen (Sandra.allen@regulatoryscience.com).

Dr M. Bahie Abou-Donia, Duke University, Durham, NC USA
Mr. Philip Adeniyi, University of Ilorin, Kwana State, Nigeria
Dr Elias Aizenman, University of Pittsburgh, Pittsburgh PA USA
Dr Tarinee Arkanavichien, Khon Kaen University, Khon Kaen, Thailand
Dr Peter Arlien-Soeborg, Copenhagen University, Copenhagen, Denmark
Prof Christopher Atterwill, Prognus Ltd, Bedfordshire, UK
Dr Pere Boadas-Vaello, Universitat de Girona Medical Sciences, Girona, Spain
Dr Joseph Bressler, Kennedy Krieger Institute, Baltimore, MD USA
Dr Steven Burr, MRC Applied Neurosciences Group Plymouth University, Somerset, UK
Dr Jason R Cannon, Purdue University, West Lafayette, IN USA
Dr Monique Chalansonnet, Institut National de Recherche et de Sécurité, Vandoeuvre Cedex, France
Dr Werner Classen, Novartis Pharma A.G., Basel, Switzerland
Dr Michael Collins, Loyola University, Maywood, IL USA
Dr Michael Csicsaky, Nieders. Ministerium f. Frauen Arbeit u. Soziales, Referat, Hannover, Germany
Dr David Davis, University of Southern California, Los Angeles, CA USA
Prof Jose Delgado-Garcia, University Pablo de Olavide, Sevilla, Spain
Prof Illes Desi, University Medical School Szeged, Szeged, Hungary
Dr Anne Dreiem, Institut Curie, Orsay, France
Dr Vicente Felipo, Fund. Valencia de Invest Biomed Instituto Investigaciones Citológicas, Valencia, Spain
Dr Yoram Finkelstein, Shaare Zedek Med Ctr, Jerusalem, Israel
Dr Robert Floyd, Oklahoma Medical Research Foundation, Oklahoma City, OK USA
Dr Clement Furlong University of Washington, Seattle, WA USA
Prof Halima Gamrani, Cadi Ayyad University, Marrakech, Morocco
Dr Huiming Gao, NIEHS/NIH, Research Triangle Park, NC USA
Dr Stephanie Garcia, Oak Ridge National Laboratory, Hummelstown, PA USA
Dr Santokh Gill, Health Canada, Ottawa, Ontario Canada
Dr Mercedes Gomez, Universitat Rovira i Virgili, Reus, Spain
Dr Jan Bert Gramsbergen, University of Southern Denmark, Odense, Denmark
Dr Ulla Hass, National Institute of Occupational Health, Copenhagen, Denmark
Dr Diane Henshel, Indiana University, Bloomington, IN USA
Dr Marcia Howard, Consumer Healthcare Products Association, Washington, DC USA
Dr Wanchai Itrat, Khon Kaen University, Khon Kaen, Thailand
Dr Vinay Kumar, Khanna Industrial Toxicology Research Centre, Lucknow, India
Dr Dusko Kozic, Institute of Oncology Diagnostic Imaging Center, Sremska Kamenica, Serbia
Dr Jing Liu Pope, Oklahoma State, Stillwater, OK USA
Dr Rozsa Lorencz, University of Szeged Med School, Szeged, Hungary
Dr Søren Peter Lund, National Institute Occupational Health, Copenhagen, Denmark
Dr Dennis Morse, Pfizer Global Research & Development, Ann Arbor, MI USA
Dr Kiti Muller, National Institute Occupational Health, Helsinki, Finland
Dr Laszlo Nagymajtenyi, University of Szeged, Szeged, Hungary
Dr Urs Nederhauser, Hoffman La Roche, Basel, Switzerland
Dr Per Nylen, National Institute of Occupational Health, Solna, Sweden

Dr Olalekan Ogundele, Afe Babalola University, Ado-Ekiti, Nigeria
Dr James Olopade, University of Ibadan, Oyo, Nigeria
Dr Orapin Pasurivong, Khon Kaen University, Maung, Khon Kaen, Thailand
Dr Leon Prockop, University of South Florida, Tampa, FL USA
Prof Vijayalakshmi Ravindranath, National Brain Research Centre, Manesar, Haryana, India
Dr Kenneth Reuhl, Rutgers University, Piscataway, NJ USA
Prof Rudy Richardson, University of Michigan, Ann Arbor, MI USA
Dr Gary Rockwood, USAMRICD, Aberdeen Proving Ground, MD USA
Dr Mohamed Salama, Mansoura University, Mansoura, Egypt
Dr Ana Paula dos Santos, University of Lisbon, Lisbon, Portugal
Dr Nison Sattayasai, Khon Kaen University, Muang, Khon Kaen, Thailand
Dr Jintana Sattayasai, Khon Kaen University, Muang, Khon Kaen, Thailand
Dr Kai Savolainen, Finnish Institute of Occupational Health, Helsinki, Finland
Prof Prahlad Seth, Remote Sensing Application Centre, BIOTECH Park, Lucknow, India
Prof Gisela Stoltenburg-Didinger, Charite Campus Virchow Klinikum, Berlin, Germany
Dr Hanna Tahti, University of Tampere, Tampere, Finland
Dr Richard Tasker, University of Prince Edward Island, Charlottetown, Prince Edward Island, Canada
Dr M. Amelia Tavares, Institute Biology Molecular e Celular, Porto, Portugal
Dr Desire Tshala-Katumbay, Oregon Health and Sciences University, Portland, OR USA
Dr Jintanaporn Wattanathorn, Khon Kaen University, Muang, Khon Kaen, Thailand
Dr Faith Williams, Newcastle University Medical School, Newcastle Upon Tyne, UK
Dr Robert Yokel, University of Kentucky, Lexington, KY USA
Dr Amy Zmarowski, WIL Research Europe BV, s-Hertogenbosch, the Netherlands

2015 INA Business Meeting

Minutes for INA Business Meeting June 28, 2015 4.30-5.30pm room Verdun, Hôtel Bonaventure, Montréal, Quebec, Canada

Attendees: The meeting was hosted by Christoph van Thriel and Ed Levin with approximately 30 members present including all members of the Executive Committee (Sandra Allen, Remco Westerink, Harm Heusinkveld, Jordi Llorens, Pamela Lein, Lucio Costa)

Welcome – Christoph van Thriel

Minutes from INA Business Meeting held in Phoenix, March 2014 were approved.

- 1) President's report – Christoph van Thriel
- 2) Announcement of New Officers – Christoph van Thriel
- 3) Secretary's report - Sandra Allen reported that the data-base indicated 200 full members and 32 student members from 30 countries. There was discussion concerning members that have not paid dues in recent years but staying on the membership data-base. After the meeting the situation will be reviewed with the new Treasurer and notes sent to non-paying members. Proposals to remove "members" will be discussed with the Executive Committee.
- 4) Treasurer's Report – Harm Heusinkveld presented the Treasurer's report (below). The INA bank account remains healthy but there is an issue of members not paying dues (see point 3 above).
- 5) Web site update –Helena Hogberg is doing an excellent job at maintaining the website. It was proposed (Remco Westerink) that companies and other organizations with links to the website should be requested to make payments for this and the monies used to support student attendance at meetings. Remco will make formal proposals to the Executive Committee.

- 6) Status of INA-15 meeting. Report by the INA-15 Local Organizing Committee. The meeting was progressing well and it was anticipated that the meeting would break even from a financial perspective.
- 7) Status of INA-16 meeting – Report by the INA-16 Local Organizing Committee. The meeting was likely to be joint with NTS (Jean Harry), ICOH (Kent Anger) and possibly the neurology section of Environmental Neurotoxicology (Jaques Reis). At least one of the organizing societies needs to be US based in order to benefit from EPA funding. Membership of the Local Organizing Committee and Scientific Committee need to be agreed. There was strong support from the floor of the meeting that INA-16 should be an “all inclusive” meeting as has been traditional for INA. In addition, it was requested that student awards could be made in advance of the meeting to enable them to attend.
- 8) Proposal for INA-17 in 2019 – Christoph van Thriel indicated that Dusseldorf will prepare a detailed proposal. A request to the membership for further proposals should be sent out before the end of the summer.
- 9) There was no additional any other business.
- 10) New President Ed Levin closed the meeting

Treasurer’s Report
INA Account Summary 2014

INA Treasury December 31 2013			
Dutch Accounts			€ 57,917
	€ 13,539 reserved for Hooisma Memorial Fund		
US Account (currently kept by Ed Levin)			\$ 4,251
INA Treasury December 31 2014			
Dutch Accounts			€ 52,208
	€ 13,539 reserved for Hooisma Memorial Fund		
US Account (currently kept by Ed Levin)			\$ 4,283
INA Account Summary for 2014			
Balance in the Dutch accounts of INA on December 31 2013			
INA account	€ 375.32		
INA savings	€ 46,677.56		
INA PayPal*	€ 191.06		
Subtotal		€ 47,243.94	
Jacob Hooisma Memorial Fund		€ 10,673.75	
Total			€ 57,917.69
Balance in the Dutch accounts of INA on December 31 2014			
INA account	€ 406.38		
INA savings	€ 40,687.12		
INA PayPal*	€ 214.67		
Subtotal		€ 41,308.17	
Jacob Hooisma Memorial Fund		€ 10,900.66	
Total			€ 52,208.83

* excluding the 2005 €750, 2006 €1000, and 2009 €750 donations by TNO, which are still in the INA account

Submitted by Jan Lammers, PhD
INA Treasurer

Researchers in the Spotlight

Tim Shafer (US Environmental Protection Agency) - "Microelectrode arrays: A physiologically based neurotoxicity testing platform for the 21st century" Johnstone et al., *Neurotoxicology* 2010. 31, 331-350.

I came to the EPA in 1991 as a post-doc and had a background in cellular neurophysiology using patch-clamp techniques, and was hired as a permanent scientist in 1994 to develop cellular neurophysiological approaches. My lab began working with microelectrode arrays in about 2005 to study the effects of pyrethroids. At the ion channel level, there was evidence that pyrethroids interacted with sodium, calcium and chloride channels, and we wanted a method to assess additivity that would incorporate potential effects of pyrethroids on all of these channels and any other potential targets. Because measurement of neural network activity using MEAs is a more apical measure than using patch recordings of individual ion channels, this offered an ideal approach. Dr Guenter Gross of the University of North Texas, one of the pioneers of MEA recordings in neural networks, was extremely gracious in teaching me the basics of the field. This led to a collaboration where I visited his lab several times over a 2 year period and we became good friends. It was also during this time-span that the NAS report on "Toxicity testing in the 21st century" was published. I realized that MEAs offered a potentially ideal approach for screening chemicals for potential neurotoxicity because they provided functional information at a level of physiological organization that was impacted by a diverse set of potential targets.

That realization was the genesis of the article. At that point in time, MEAs had been utilized by neuroscientists to study network physiology and to a limited extent by neurotoxicologists to study effects of individual chemicals on neural network function. I approached the other authors on the paper to see if they were interested in writing a review that would achieve several goals: 1) provide an introduction to the field to other neurotoxicologists and regulators, especially those who did not have a background in electrophysiology; 2) highlight the utility of the approach for compound screening; and 3) summarize the data available at that point where MEAs had been used to study neurotoxic compounds. I have been both pleasantly surprised and humbled by the response to the article. In hindsight, it clearly was important because it highlighted the need in the field for high-throughput methods that would provide an assessment of function.



Tim Shafer (left) and Andrew Johnstone (right)

One of the challenges identified in the article was the need for increased throughput of MEAs, and it even included examples of the early formats of higher throughput devices. Since the article was published, MEA formats of 12, 48 and 96 wells are now available and have significantly increased the rate at which compounds can be screened. My own laboratory has been active in the last 5 years in developing assays for acute neurotoxic effects, and more recently an assay to screen for the potential to cause developmental neurotoxicity. MEA recordings provide a rich dataset that includes information on spiking, bursting and coordinated activity across both time and space. Numerous different endpoints can be extracted from an MEA recording, and now the availability of multi-well MEAs means that a vast amount of data regarding chemical effects on network function can be collected in a short period of time. Going forward, I see data analysis as being one of the greatest challenges for the field. The challenge is twofold. First, the endpoints that are most informative regarding chemical effects on network function need to be identified, and second, approaches that are most useful to predicting chemical effects *in vivo* must be developed. The latter will likely necessitate the inclusion of MEA data with data from other *in vitro* assays, as well as considerations of metabolism and information regarding exposure and kinetics. I think the prospect of where the field will be in another 5 years is extremely exciting.

I want to end by giving due credit to my other co-authors on the paper, as they all made important contributions to the success of the article and it wouldn't have been possible without them. Since then, I've been equally fortunate to have the work supported via the EPA and a cooperative agreement with Axion Biosciences, and to have a group of intelligent and hardworking colleagues to move the research forward.

Postdoc/Graduate Student Section Young researcher series

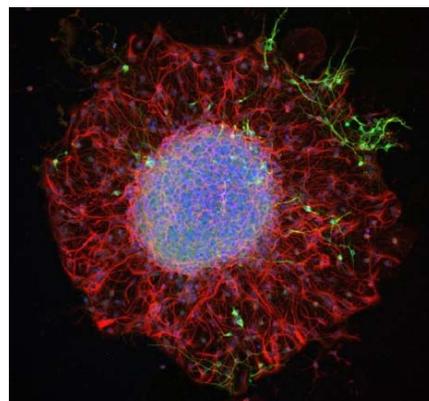
Just recently I was invited to be the first contributor to the “Young researcher series” in the renewed INA newsletter. A great opportunity of course, so I agreed to do so. So, first let me introduce myself: my name is Martje de Groot and I'm a PhD student at the Institute for Risk Assessment Sciences (IRAS), Utrecht University, the Netherlands. Well actually, by the time you read this, I will (hopefully) be a former PhD student, as on the 28th of January I will defend my thesis entitled “Novel model systems for *in vitro* neurotoxicity testing - Chemical stressors and neurotoxic hazard of extremely low frequency electromagnetic fields”. During the last 5 years I performed my research at the Neurotoxicology Research Group of Remco Westerink at IRAS. My research focused mainly on developing and characterizing different model systems for *in vitro* neurotoxicity testing. As you will probably know, traditionally neurotoxicity is often investigated *in vivo* using large numbers of experimental animals. The development of *in vitro* methods for DNT can play a major role in the reduction of animal use while increasing time- and cost-effectiveness. Moreover, these methods have the potential to provide insight into cellular and molecular mechanisms of neurotoxicity that are not readily identified in experimental animal studies. Our research has focused on developing *in vitro* systems for both the developing and aging neuronal cells.



As my PhD research was funded within the “Electromagnetic fields and Health” program of the Netherlands Organisation for Health Research and Development, I subsequently used the newly characterized *in vitro* models to investigate the potential neurotoxicity of 50 Hz extremely low frequency electromagnetic fields (ELF-EMF). As there are many uncertainties and controversies with

respect to ELF-EMF exposure and their alleged health effects and there is currently no biological mechanism to explain observed effects, the research we performed in our lab was aimed to resolve part of these uncertainties.

In my research I used a variety of different techniques, ranging from microscopy to look at morphology and neurite outgrowth and cell viability and ROS assays to assess cellular status, to single cell fluorescent microscopy to investigate calcium homeostasis or the multielectrode array (MEA) to look at spontaneous electrical activity. By doing so, we thus included both structural and functional endpoints of neurotoxicity. Our combined data using different and sensitive *in vitro* models for adult, aging/stressed and developing neuronal cells, demonstrated limited neurotoxicity of ELF-EMF only at very high exposure intensities in a developing system. Given the current ELF-EMF exposure and reference levels and taking into account experimental uncertainties such as poor reproducibility of effects, *in vitro-in vivo* extrapolation and window effects, we conclude that the neurotoxic potential of ELF-EMF exposure in humans is likely to be limited.



Looking back at the research I performed at IRAS, I think the biggest struggle during experiments has been the exposure to ELF-EMF. As I have a background in pharmaceutical sciences and toxicology, the exposure units and the complex underlying physics sometimes were a black-box to me and consequently, communicating with physicists to upgrade the system to meet my wishes or to resolve problems was equally challenging. Also, as I investigated the toxicity of a physical, instead of a chemical exposure, I sometimes felt as a bit of a “loner” in the field of toxicology, for example when giving presentation at conferences. But all in all, I think these (and other) challenges are important factors in the process of becoming a better researcher.

As for my scientific future, I am very positive. We were able to publish all my research in ‘Toxicological Sciences’ and ‘Neurotoxicology’. It feels good to be so close to my defense and getting that PhD title! Meanwhile, I recently started as a Postdoc at the Pharmacology department of Utrecht University, working on prenatal infection and behavior in the offspring. Packed with the acquired neurotoxicological knowledge and experiences, I feel confident to start this new challenge.

Best wishes,
Martje de Groot

Of Interest

Special issues: Regulatory Developmental Neurotoxicity Studies and Flame Retardants

The last volume of 2015 of *Neurotoxicology and Teratology* contains two Special Issues that may be of particular interest for INA members.

Can we improve the assessment of cognitive function in regulatory developmental neurotoxicity studies? (<http://www.sciencedirect.com/science/journal/08920362/52/part/PA>).

Assessments of cognitive function have been recommended for guideline developmental neurotoxicity studies of pesticides and environmental chemicals for more than two decades. However, the results of these tests have rarely been used as points of departure for regulatory decisions. Some have even suggested eliminating these tests from developmental neurotoxicity testing protocols. The articles in

this Special Issue discuss the strengths and limitations of the use of cognitive tests in developmental neurotoxicity testing, including:

- The regulatory context in which developmental neurotoxicity testing is carried out;
- Evaluations of the efficacy of these tests for regulatory decision-making;
- Descriptions of the state of the science of cognitive testing for regulatory purposes;
- Discussion of possible reasons for the infrequent use of these endpoints in regulatory decisions; and
- Proposals to enhance the sensitivity and practical application of these tests in this testing environment.

Discussion of these issues may provide guidance for improving developmental neurotoxicity testing in the future. The editors of *Neurotoxicology and Teratology* therefore invite comments on the utility of current cognitive test methods and ways that these methods for assessing cognitive function in guideline-based developmental neurotoxicity studies might be improved or enhanced, in order to maximize the future value of cognitive data in a regulatory context.

Submit comments in the form of correspondence to the editor at the journal's website (<http://www.journals.elsevier.com/neurotoxicology-and-teratology>) no later than 15 March, 2016.

Flame retardant chemicals: A changing landscape

(<http://www.sciencedirect.com/science/journal/08920362/52/part/PB>).

Exposure to flame retardants, particularly halogenated ones, is increasingly common today. Recent work has revealed a troubling degree of toxicity among some of these chemicals, prompting deployment of a variety of alternatives. The articles in this Special Issue describe this changing landscape of flame retardant chemicals, and provide an up-to-date evaluation of the effects and relative toxicity of many of the alternatives, including:

- Experimental studies in five animal species and two epidemiological studies in humans;
- Experimental studies of polybrominated diphenyl ethers and newer organophosphorous alternatives; and
- An extensive review that organizes the literature and provides qualitative expert judgment about the likely public health impact of these chemicals and specific research that is needed to address existing data gaps for each of them.

This Special Issue provides the field with an invaluable resource to propel research on these important chemicals at a critical time in their history. The editors of *Neurotoxicology and Teratology* encourage research toxicologists, regulators, risk managers, and the industry itself to examine this work and apply it to the benefit of public health.

Upcoming Meeting of Interest



Save the Dates! SEPTEMBER 25-28, 2016
MANGANESE  **The Second International Conference on Manganese**

DEADLINE FOR ABSTRACTS
PLATFORMS MAY 1, 2016
POSTERS JUNE 1, 2016
<http://events.mountsinaihealth.org/event/manganese2016>

The Second International Conference on the neurotoxicity and prevention of manganese health effects will be held **September 25-28, 2016** at the Icahn School of Medicine at Mount Sinai in New York City, USA. This is the 28th meeting in the International Neurotoxicology Conference series. Note the following deadlines:

Platform Abstracts **May 1, 2016**
Poster Abstracts **June 1, 2016**

This conference will bring together international experts and new researchers to present, discuss, and evaluate the most recent information on manganese. The conference will yield international state-of-the-science discussion of what is known, identify information gaps, and help define future directions for research to advance our fundamental knowledge of the causes, mechanisms, diagnosis, related new technologies, treatment and prevention of manganese (Mn)-induced or exacerbated diseases and disorders in children and adults, especially in those at risk for high exposure, such as miners and welders.

The following topics will be included: Environmental and Human exposure to Mn; Pharmacokinetics, Uptake and Distribution of Mn; New aspects of Mn toxicity in animal models and humans; Clinical Features, Imaging and Pathology of Mn in Humans; Neurobehavioral Effects of Workplace Mn Exposure in Humans; Neurobehavioral Effects of Environmental Mn Expo in Humans; Biomarkers of Mn exposure; Reproductive effects of Mn; Effects of Mn on Cellular Functions and Behavior in Animal Models; and Health Risk Assessments and Protective standards of Mn.

Website under construction. If you would like to receive further information on this conference please [click here](https://mountsinaisph.wufoo.com/forms/manganese-2016-email-updates/). (<https://mountsinaisph.wufoo.com/forms/manganese-2016-email-updates/>)

Membership News

IRAS, Mimetas and CDI receive funding for development of organ-on-a-chip for neurotoxicity testing

Dr. Remco Westerink from the Neurotoxicology Research Group (IRAS-Utrecht University, NL), the biotechnology company Mimetas (Leiden, NL) and Cellular Dynamics International (Wisconsin, USA) have received 1.6 million USD funding for their project 'NeuroScreen-3D'. They will develop and validate an organ-on-a-chip for *in vitro* human neurotoxicity testing using Mimetas OrganoPlate™ technology combined with CDI's human induced pluripotent stem cells (iPSCs). This model will allow for better predictive, high-throughput, animal-free neurotoxicity testing of medicines and chemicals.

The complexity of the central nervous system requires integration of morphological endpoints with electrophysiological parameters to evaluate neurotoxicity and seizure liability. The platform aims to replace the *ex vivo* hippocampal slice assay, which is currently used for regulatory purposes.

A panel of experts from BASF, Sanofi, GlaxoSmithKline, Abbvie, NC3Rs and renowned academic institutions has selected 'NeuroScreen-3D' as the most innovative project of the *Neuratect* CRACK IT Challenge. The *Neuratect* Challenge was organized by the UK-National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) to create a physiologically-relevant platform for assessing neurotoxicity *in vitro*.

Download the NC3Rs press release [here](#).

Dutch-German consortium for animal-free, integrated human neurotoxicity studies

A new 3-year research project, called "N3rvousSystem", has started at the Institute for Risk Assessment Sciences (Utrecht University, the Netherlands). "N3rvousSystem" aims to develop an animal-free strategy to detect adverse effects on brain development and function resulting from chemical exposures. To evaluate whether cellular assays reliably predict neurotoxicity, our *in vitro* data will be combined in pharmacokinetic models with information from literature and *in vivo* behavioral experiments to predict neurotoxicity in humans. This integrated, system biology approach will reveal which combination of experiments and methods is best suited to predict human

neurotoxicity. As such, “N3rvousSystem” will improve risk and safety assessment while also making a strong contribution to the reduction and replacement of animal experiments.

The project is funded by the joined Dutch (ZonMw) & German (BMBF) InnoSysTox program. The awarded consortium comprises a research collaboration between the Institute of Risk Assessment Sciences (IRAS; Utrecht University, the Netherlands), the Leibniz-Institut für umwelt-medizinische Forschung (IUF; Germany), the National Institute for Public Health and the Environment (the Netherlands), the Institut für Energie- und Umwelttechnik (Germany) and companies Pamgene (the Netherlands) and Tascon (Germany). Several INA members, including Remco Westerink, Harm Heusinkveld and Milou Dingemans, are closely involved in this project.

Current INA Officers

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