



INTERNATIONAL NEUROTOXICOLOGY ASSOCIATION

INA News

January 2014

President's Message

Dear INA members,

The INA-14 meeting was held as a *homecoming meeting* in Egmond aan Zee, the Netherlands (see meeting below), 25 years after the foundation of INA as an association dedicated to promote scientific knowledge regarding the action of toxic agents on the nervous system during the first meeting in Lunteren. The eventful history of INA has been vividly described in two papers: in *NeuroToxicology* written by our former presidents Will Boyes and Lucio Costa (Costa, 2013; soon to be available on the INA website), and in *Neurotoxicology and Psychophysiology* by Kent Anger, Chair of the ICOH Scientific Committee along with Will Boyes. By conducting excellent experimental as well as epidemiological studies, enthusiastic researchers from all over the world have made neurotoxicology a highly recognized area within toxicology.

Renowned INA members contributed to the detection of neurotoxic hazards from various sources (e.g., environmental and occupational exposures) and also discovered the biological mechanism(s) underlying such toxic effects. In April 2013 one of these outstanding researchers, Toshio Narahashi passed away after a life well lived. Today, his work would be described as ***translational***. He linked the severe hyperexcitatory symptoms seen in individuals poisoned by pyrethroids to the modification of voltage-gated sodium channels in the nervous system. Toshio's work is only one of the outstanding contributions of INA members to the field of neurotoxicology, there are many more people and examples of such ***translational research***.

In my experience, this is exactly the core of INA and our biannual meetings. As a small and specialized group of open-minded researchers, INA has always promoted the dialogue between behavioral and mechanistic approaches, applied and basic science, and we have taken care to nurture this culture! During the last decades the world of science changed markedly. With reduced budgets more papers have to be generated, more grant money to be procured, more PhD theses to be completed, and more excellent post-docs to be promoted for a successful career. Many of the "older" INA members managed to keep pace without losing neurotoxicology as their predominant research area. Nevertheless, the effort is extremely high and the time for the aforementioned scientific dialogue is often lacking. Especially young scientists might be swamped and need to concentrate on narrow areas within their academic discipline. That hampers the translation of research results into the "*real world*".

In contrast, decision makers in academia (e.g., National Research Council) and policy (e.g., European Union) demand scientific answers to tackle general problems like, an improved toxicological testing of chemicals, a better understanding and prevention of neurodegenerative diseases, or a healthier environment in general. In medicine slogans like "*From bench to bedside*" reflect these demands and the search for "*adverse outcome pathways*" (AOPs) in regulatory toxicology is motivated by societal challenges related to health, demographic change and wellbeing. These recent developments at the interface between science and policy confirm my belief that the traditional INA approach of bridging neurotoxic health effects with biological mechanisms is still up-to-date.

During the last meetings we had several symposia addressing alternative methods (e.g. stem cell-based *in vitro* assays) and species (e.g. zebra fish). By focusing and including these *hot topics* INA attracted new and young researchers. This was highly visible during the INA-14 David Ray Student Symposium.

I have the strong belief that the next step should be the outline of a strategy of testing the most relevant endpoints in neurotoxicology in a structured and stepwise combination of *in vitro* and *in vivo* approaches. The 2015 meeting will be held in collaboration with the Neurobehavioral Teratology Society (NBTS) in Montreal. This combination will provide the perfect environment for this next step of **translational neurotoxicology**. Thereby, the great history of INA will be continued and new challenges will be addressed.

My best wishes for 2014,
Christoph van Thriel
President 2013-2015, International Neurotoxicology Association

Past President INA-14, 2013

My term as President of INA for 2011-2013 is now finished, and it's time to write the Past-President message. This term has been that of the 14th Meeting of the Association, held at the Hotel Zuiderduin in Egmond aan Zee, The Netherlands, 9-13 June 2013. We all can be proud of this Meeting, which was a success in many aspects: scientific, organizational, and also financial.

In evaluating the Meeting, I would like to start by expressing our deepest gratitude to the leading organizers in the Local Organizing Committee, Didima de Groot (Chair), Remco Westerink, and Jan Lammers, for their impressive job. With the help of Erik de Vries and Donald Fox also in the Organizing Committee, and that of Helena Bastiaanse from Bastiaanse Communication in the Technical Secretariat, they succeeded in presenting a wonderful meeting. We enjoyed a great location that fit well in the tradition of INA Meetings, a nice social program allowing plenty of interaction among attendants, and a perfect organization that made the Meeting run so smooth that everything seemed to work on its own, with no effort behind it. And many of us are perfectly aware how much effort is required to organize an event of this size with no apparent difficulties.

The opening session of the Meeting included a remembrance of our loved member Toshio Narahashi, who recently passed away. Another highlight was the commemoration of INA's 25th Anniversary, on which occasion the INA Meeting was being held back in The Netherlands, where the first meeting of the Association took place in 1987. The lecture named after Jacob Hooisma opened the scientific program, with a lecture by another founder of INA, Peter Spencer. This was followed by ten highly interesting symposia, many of which reflected the scientific theme of the Meeting "*Neurodevelopmental basis of health and disease*", and a poster session. The scientific program was selected by a Scientific Committee including myself as Chair, with Kevin Crofton, Donald Fox, Didima de Groot, Merle Paule, Anna Price, Diane Rohlman, Christoph van Thriel, Erik de Vries, and Remco Westerink. The excellent proposals submitted by the members of the Association were a great basis for program selection. The program also included a Student's Symposium that included talks by Jenny Bauman, Vanessa Hausherr, Hester Hendriks, Anne Krug, Marieke Meijer, and Martin Schmuck. Their outstanding quality made us confident about the future of neurotoxicology. The scientific outcome of the meeting will be completed by the publication of its Proceedings in a special Issue of *Neurotoxicology* that will have a publication date of 2014.

If I talked previously about finances it is because we were certainly concerned by the general economic situation that was, and still is, having a true impact on the research budgets of many laboratories. In fact, the number of attendants, around 90, was smaller than desired, and we know of many colleagues that could not attend due to budget limitations. Compared to previous INA meetings, this meeting was shorter by one day, ending on Thursday instead of Friday, with the main aim of reducing costs. Nevertheless, Jan Lammers, with the help of a Finances Committee (Sandra Allen, Christopher van Thriel, Ellen Fritsche, Abby Li, Will Boyes, Merle Paule, Tomas Guilarte, Anna Price, Eugenio Vilanova, and Sandra Ceccatelli) and additional collaborating individuals (Michael Aschner, Donald Fox, Carey Pope, Wei Zheng and myself) succeeded in raising all necessary money, including funds to support students and award prizes. The list of generous sponsors include AutoMate Scientific, Purdue University, Elsevier Publishers, Axion Biosystems, Society of Toxicology, Seahorse Bioscience, HEKA Elektronik, Dutch Society of Toxicology, Metris bv, TNO, IBRO- WERC, NIH/NIEHS, Carey Pope, Carl Zeiss, Leica Microsystems, and ECVAM.

Overall, the INA is in good health, with stable membership and renewing leadership. For the present 2013-2015 term, Lucio Costa and Pamela Lein replaced Remco Westerink and Eugenio Vilanova as Councilors of the Executive Committee. Donald Fox ended his duty as Past-President, and Ed Levin entered the Committee as President-Elect. We are all grateful to the many hours Remco, Eugenio and especially Don devoted to the INA; we have enjoyed the fruits of these efforts, a stronger association and great meetings.

Serving as President of INA has been an honor and a pleasure, and I want to thank the membership for the opportunity. When INA started, I was a graduate student at the beginning of my thesis in the field of neurotoxicology. I think that INA and INA meetings greatly contributed to keep me in the field. This is the organization where I met so many scientists with common interests, and that allowed us to become friends in these particularly warm meetings that characterize our Association. The continuous support to students at the meetings is a key strategic action, and I'm glad to see it maintained and even increased throughout the years. And I'm also very pleased to see the immediate future in such good hands as those of Christoph van Thriel as President and Ed Levin as President-Elect. I'm sure they'll successfully drive the Association and will organize great meetings. I know they are already working hard for the next one, so I look forward to seeing you all in Montreal, 27 June - 1 July 2015.

Best Regards
Jordi Llorens

2014 INA Business Meeting

The 2014 business meeting will be held during the Society of Toxicology (SOT) meeting in Phoenix, Arizona on Monday 24 March from 1:00-2:00 pm at the Sheraton in room Ahwatukee AB. All members are invited to attend.

INA-15, 2015

In the year 2015, INA and the Neurobehavioral Teratology Society (NBTS) will have a joint meeting in Montréal, Canada from 28 June 28 to 3 July 2015. As is customary, NBTS will meet with the Teratology Society (TS) and Organization of Teratology Information Services (OTIS), and in addition the International Commission on Occupational Health (ICOH) Neurotoxicology Committee will meet at the same location. Montréal is a culturally rich city on the St. Laurence River in Quebec, Canada with diverse attractions of art, architecture, music, cuisine and nature including the Montréal Botanical Gardens, Beaux Arts Musée, Montréal Historic Old City St. Joseph's Oratory, Mount Royal Park and a wide variety of

outstanding international cuisine. The theme of the meeting will be “Neural Mechanisms of Functional Impairment Across the Lifespan.” Proposals for symposia will be solicited by the program committee as the meeting time approaches.

The Local Organizing Committee includes Ed Levin, Maryse Bouchard, Phil Bushnell, Ginger Moser, Don Fox, Merle Paule, Will Boyes, and Jordi Llorens.



The Neurobehavioral Teratology Society has been active for over 35 years. Its purpose is to understand the behavioral and neural alterations that result from genetic and environmental perturbations of the nervous system. There are approximately 160 members with several key dual members including former officers of both INA and NBTS. The two societies have overlapping and complementary interests in neurotoxicology. In addition to research concerning environmental toxicants, NBTS scientists also conduct research into the neurotoxic effects of drugs of abuse and therapeutic drugs. Research covered by NBTS includes the persisting effects of developmental exposure, but particularly since the inclusion of the Behavioral Toxicology Society, research at the NBTS meeting also includes neurotoxic effects of chemical exposures throughout the lifespan.

To learn more about NBTS, or to attend one of their meetings before 2015, please see their website www.nbts.org.

Of Interest

The Neurotoxicology Specialty Section (NTSS) of the Society of Toxicology has established the Toshio Narahashi Neurotoxicology Fellowship Award Fund to honor Dr. Narahashi's lifetime contributions to neurotoxicology research as well as his devotion to training successful neurotoxicologists. Proceeds from the Fund will be used to support annual travel stipends and awards for graduate students and postdoctoral fellows who demonstrate outstanding neurotoxicology research. Award recipients will be selected by the executive committee of the NTSS. Awards will be bestowed at the NTSS social event held during the SOT Annual Meeting. INA has pledged \$1,000 to the Toshio Narahashi Neurotoxicology Fellowship Award. If you would like to make a personal contribution (which is tax-deductible) to continue the legacy of Professor Narahashi, click on <http://www.toxicology.org/ai/csot/contribute.asp> to access the donor form. Be sure to select Toshio Narahashi Neurotoxicology Fellowship Award under named funds.

The Society of Toxicology (SOT) will hold its annual meeting in Phoenix, AZ on 23-27 March 2014. Events of special interest to neurotoxicology include: 1) INA business meeting, scheduled for Monday, March 24 at 1:00 pm; 2) The Neurotoxicology Specialty Section (NTSS) Business Meeting and Reception, which will be held Wednesday, March 26 from 6:00-7:30 PM. A short business meeting will be held at approximately 6:45 PM. If you have an item for the business meeting agenda, please contact the current NTSS President, Anumantha Kanthasamy (akanthas@iastate.edu); 3) NTSS-sponsored symposia including: *Molecular mechanisms of neuro/glial toxicity: from oxidative stress to redox signal transduction*, Chairs: Franco (University of Nebraska-Lincoln) and Block (Virginia Commonwealth University), *Is neuroimmune*

crosstalk important to neurotoxicology? Critical insight from animal and human studies, Chairs: Larson (University of Wisconsin) and McLoughlin (NIOSH), *Methylmercury's modes of action: new approaches to understanding an old problem*, Chairs: Ralston (University of North Dakota) and Aschner (Vanderbilt University), and *Neurobehavioral impacts of early-life manganese exposure: linking human and animal model studies*, Chairs: Smith (University of California Santa Cruz) and Lucchini (Icahn School of Medicine at Mount Sinai); and 4) NTSS-sponsored workshops including: *Is manganese-induced Parkinsonism mediated via dopamine neuron degeneration or dysfunction?* Chairs: Zheng (Purdue University) and Guilarte (Columbia University), *Advances in the application of imaging technologies to developmental toxicology*, Chairs: Makris (USEPA) and Sutherland (Bristol-Myers Squibb), *Application of the adverse outcome pathway (AOP) concept to neurotoxicology: a challenging approach*, Chairs: Fritsche (IUF - Leibniz Research Institute for Environmental Medicine) and Price (The Joint Research Center of the European Commission), *The promise of translational imaging in nonclinical safety assessment*. Chairs: Paul (US Food and Drug Administration) and Chen (ILSI Health and Environmental Sciences Institute).

NTSS will again have a Poster Competition for students and post-docs at the SOT meeting, using the judging procedure instituted last year. To participate in the 2014 poster competition, you will need to submit an extended abstract by February 25, 2014. The extended abstract should include the abstract originally submitted to SOT, 2-4 sentences describing the impact of the research, up to one page of key figures or data, and a 3-5 sentence conclusion (total of 3 pages). The extended abstracts will be reviewed by a committee prior to the meeting and will comprise 50% of the score. The remaining portion of the score will be based on the face-to-face interviews at your posters on Monday late afternoon. At this point we anticipate at least 3 judges will evaluate each poster. More detailed information is posted on the NTSS website: <http://www.toxicology.org/isot/ss/NTSS/awards.asp>. Eligibility requirements for the NTSS poster competition: 1) Graduate students and postdoctoral research fellows/associates must be in attendance at the 2014 annual meeting; 2) Trainees must meet SOT criteria for classification as a graduate student or postdoctoral fellow at the time of the annual meeting; 3) Graduate students and postdocs MUST be members of NTSS or show evidence of application for membership. Graduate students or postdocs giving platform presentations at the annual meeting are also eligible if they prepare a poster summarizing their talk. Advisors or mentors who are not members are strongly encouraged to join NTSS. Submission requirements: 1) An extended abstract as defined above (3 pages); 2) A letter of support from the graduate student's advisor or postdoctoral mentor outlining the independence and role of the candidate in the research must be submitted to Pamela Lein (pjlein@ucdavis.edu), Chair of the NTSS Student and Postdoctoral Awards Committee by 25 February 2014. Participants will also be required to send a PDF of their completed poster to Dr. Lein by 17 March 2013 to facilitate the judging (this presubmission of the poster need not be the final version presented at the 2013 Annual Meeting). In addition to recognition plaques for each winner, monetary prizes will be awarded for first, second and third place. Winners will be announced at the annual NTSS Business Meeting in Phoenix, AZ, USA.

Of More Interest

From Dan Richards, Communications manager at the UK's National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs):

A review by 15 pharmaceutical companies and contract research organisations that sets out recommendations to improve animal welfare in short-term tox studies based on using bodyweight loss limit of 10% as an objective measure of maximum-tolerated dose has recently been published in *Regulatory Toxicology and Pharmacology*. Analysis of data from 151 studies show bodyweight loss ranged from 15–25% in practice, but little scientific value in exceeding 10%. Bodyweight loss is used as a measure of animal welfare, with the greater the weight loss, the greater the potential for suffering. Previously there has been little regulatory or cross-industry agreement on how the maximum-tolerated

dose should be defined. Recommendations from this review are that a 10% upper limit of bodyweight loss as a primary endpoint is sufficient to determine maximum-tolerated dose in short-term toxicity studies in rats and dogs. This is the first evidence-based guidance on upper limit for body weight loss. These standardised assessment criteria will minimise the adverse effects experienced by thousands of animals used in pharmaceutical development each year.

The full press release, and associated content including blog post, can be downloaded here: <http://www.nc3rs.org.uk/news.asp?id=1932>

INA History

The history of INA was gathered by Lucio Costa and published in *NeuroToxicology* (vol 36, 89-103, 2013). Fun facts and pictures highlight the inception and growth of our society. A .pdf of the paper will soon be available on the INA website.

Upcoming Meetings of Interest

❖ **Workshop: Novel Tools and Methods for the Screening of Chemicals for Developmental Neurotoxicity** **Developmental Neurotoxicity Assessment of Mixtures in Children (DENAMIC) project**

The main objective of the workshop is to bring together people that are working in the field of chemical exposure and developmental neurotoxicity. The workshop will focus on tools and methods for screening of neurotoxic effects, but also on subclinical effects on learning (cognitive skills) and developmental disorders in children (e.g., ADHD, autism spectrum disorders). Another topic is the use of biomarkers in the field of developmental neurotoxicity. The workshop will also present and discuss findings obtained by the European Union funded project DENAMIC, which investigates neurotoxic effects of low-concentration mixtures of pesticides and a number of common environmental pollutants in children.

Workshop will be held 10-11 March 2014 in Amsterdam, the Netherlands
28 February 2014 last day for early registration
www.denamic-project.eu

❖ **Fourth International Conference on Alternatives for Developmental Neurotoxicity Testing (DNT): Toward Adverse Outcome Pathways and Fit-for-Purpose Assays for DNT** **Center for Alternatives to Animal Testing (CAAT): TestSmart DNT4**

The CAAT promotes humane science by supporting the creation, development, validation, and use of alternatives to animals in research, product safety testing, and education. They seek to effect change by working with scientists in industry, government, and academia to find new ways to replace animals with non-animal methods, reduce the numbers of animals necessary, or refine methods to make them less painful or stressful to the animals involved. Developmental neurotoxicity (DNT) from chemical exposures is a growing concern, and this conference is the fourth of a series of workshops addressing alternative methods for testing for DNT. This conference will bring together diverse stakeholders from around the globe, including research scientists, regulators, industry representatives, academics, and pediatricians.

The conference will be held 12-13 May 2014 in Philadelphia, PA, USA
10 February 2014 abstract submission and early registration deadline
<http://caat.jhsph.edu/dnt4>

❖ **First International Congress: Global Environmental Contamination (GEC-2014): Challenges for the Well-being of the Human Brain**

This conference will focus on the nervous system as a target of chemicals exposure, potential causes of dysfunction and disease, and on the broad issue of how to harness brainpower to address the issue of environmental contamination and human health.

The conference will be held 7-10 September 2014 in Luxembourg.
15 April 2014 submission of abstracts
30 May 2014 last day for pre-registration
<http://gec2014.sciencesconf.org>

Membership News

Two student members have joined INA since the meeting in June. See the minutes of the June 2013 business meeting for more details.

Current INA Officers

President	Christoph van Thriel	thriel@ifado.de
President-Elect	Ed Levin	edlevin@duke.edu
Past-President	Jordi Llorens	jllorens@ub.edu
Secretary	Sandra Allen	sandra.allen@regulatoryscience.com
Treasurer	Jan Lammers	j.lammers@ziggo.nl
Councilors	Lucio Costa	lgcosta@u.washington.edu
	Pam Lein	pjlein@ucdavis.edu
Webmaster	Eugenio Vilanova	evilanova@umh.es
Newsletter editor	Ginger Moser	moser.ginger@epa.gov

Treasurer's Report

Below is the INA 2013 account summary. Despite economic crises in large parts of the world, the financial situation of INA has improved over the last year. Reserves have increased mainly due to dues payments (although this remains relatively poor), interest on savings account and profit for the INA-14 meeting. On the other hand, the Hooisma Memorial Fund has decreased considerably due to relative high costs for the invited speaker during INA-14 (but that's what the money is meant for). Overall, INA appears to be financially healthy.

INA Treasury		
	December 31 2012	December 31 2013
Dutch accounts	€ 55,644	€ 57,917
Reserved for Hooisma Memorial Fund	€ 13,539	€10,673
US accounts	\$ 4,667	\$4,252
Currently kept by Ed Levin		

Business Meeting Minutes

Minutes of INA Business Meeting 10 June 2013 in Egmond aan Zee

Attendees: The meeting was hosted by Jordi Llorens and Christoph van Thriel with approximately 19 members in attendance.

Welcome – Jordi Llorens

Approval of minutes from INA Business Meeting held in San Francisco at the SOT meeting, March 2012.

- 1) President’s report – Jordi Llorens
- 2) Announcement of New Officers by Jordi Llorens
- 3) Secretary’s report - Sandra Allen reported that there are currently 245 full members and 31 student members – Appendix 1
- 4) Treasurer’s Report – Jan Lammers. The INA bank account remains healthy (~€55,000).
 - a. INA-12 financial report. A financial report has not been received from the organisers in China. However, there was no profit or loss to INA apart from the USD 10,000 seed money.
- 5) Web site update – Eugenio Vilanova. The domain neurotox.net is owned by INA and neurotox.org by Kevin Crofton.
- 6) Status of INA-14 meeting. Report by the INA-14 Local Organising Committee. The meeting was progressing well and it was expected that if all the promised financial support was received the meeting would break even from a financial perspective. The proceedings are to be published in a special issue of NeuroToxicology.
- 7) Status of INA-15 meeting. Report by the INA-15 Local Organising Committee. The meeting will be held in Montreal 27 June – 1 July 2015 in conjunction with NBTS. It was noted that it may also be possible for ICOH to be involved and Ed Levin was pursuing this. It was suggested that a Continuing Education Session for clinicians would be well received and J Reis offered to assist with some of the organizational aspects.

New Business

- 8) Discussion of INA-16 – from the floor. There was 1 proposal from ICOH for a joint meeting in Brazil. Ed Levin will also discuss with the NeuroToxicity Society. If the proposal does not develop further then it was suggested that Dusseldorf and/or Dortmund would be able to host.
- 9) IUTOX ballot for executive Committee Members and venue for ICT XV.
- 10) Any other new business?
 - a. Dr Henri Schroeder presented a proposal on behalf of Dr Rachid Soulimani for an INA sponsored meeting in 2014 in France “Early chronic exposure to low doses of persistent organic contaminants and food, health and environmental safety”. The proposal was supported and it was recommended that the meeting be held in September 2014 to avoid clashes with other important meetings.

- b. IUTOX votes. The members present were polled for their views on votes to be made at IUTOX meeting in July where Eugenio Vilanova was representing INA and would make our votes in person. The results were as follows:
- Host city: vote split - abstain
 - Officers:
 - President elect: Liliana Saldivar
 - Vice-president: Mary Gulumian
 - Secretary-general; Elaine Faustman
 - Treasurer: Heidi Foth
 - Directors: Tracey Zoetis, Nang Claude, Kendall Wallace Salmann Hussain, Lijie Fe.

11) The new president Dr Christoph van Thriel closed the meeting.

Appendix 1. Membership report

Active membership:

The INA currently has 245 full members and 31 student members.

Members hail from 34 countries and all continents except Antarctica.

Most are from N America and Europe (114 and 104).

9 new members in 2013: 8 full members, 1 student.

Statistics of membership from countries of origin are shown below.

Country	Total	Full	Student	Country	Total	Full	Student
Australia	1	1	0	Morocco	1	1	0
Brazil	1	1	0	Netherlands	14	9	5
Cameroon	1	0	1	Nigeria	4	2	2
Canada	6	6	0	Norway	5	5	0
Chile	1	1	0	P.R. China	6	6	0
Denmark	10	10	0	Portugal	4	4	0
Egypt	3	3	0	Russia	2	2	0
Finland	3	3	0	Saudi Arabia	1	1	0
France	10	10	0	Serbia	1	1	0
Germany	16	12	4	Singapore	1	1	0
Greece	1	1	0	Spain	15	13	2
Hungary	4	4	0	Sweden	9	8	1
India	8	4	4	Switzerland	4	4	0
Iraq	1	1	0	Thailand	7	7	0
Israel	1	1	0	UK	13	11	2
Italy	8	8	0	USA	108	100	8
Japan	5	3	2	Zimbabwe	1	1	0
				34	276	245	31