



CAAT-Europe ecopa actions

<http://www.remanet.net/>

ecopa 

Madrid 2011

Workshop ecopa





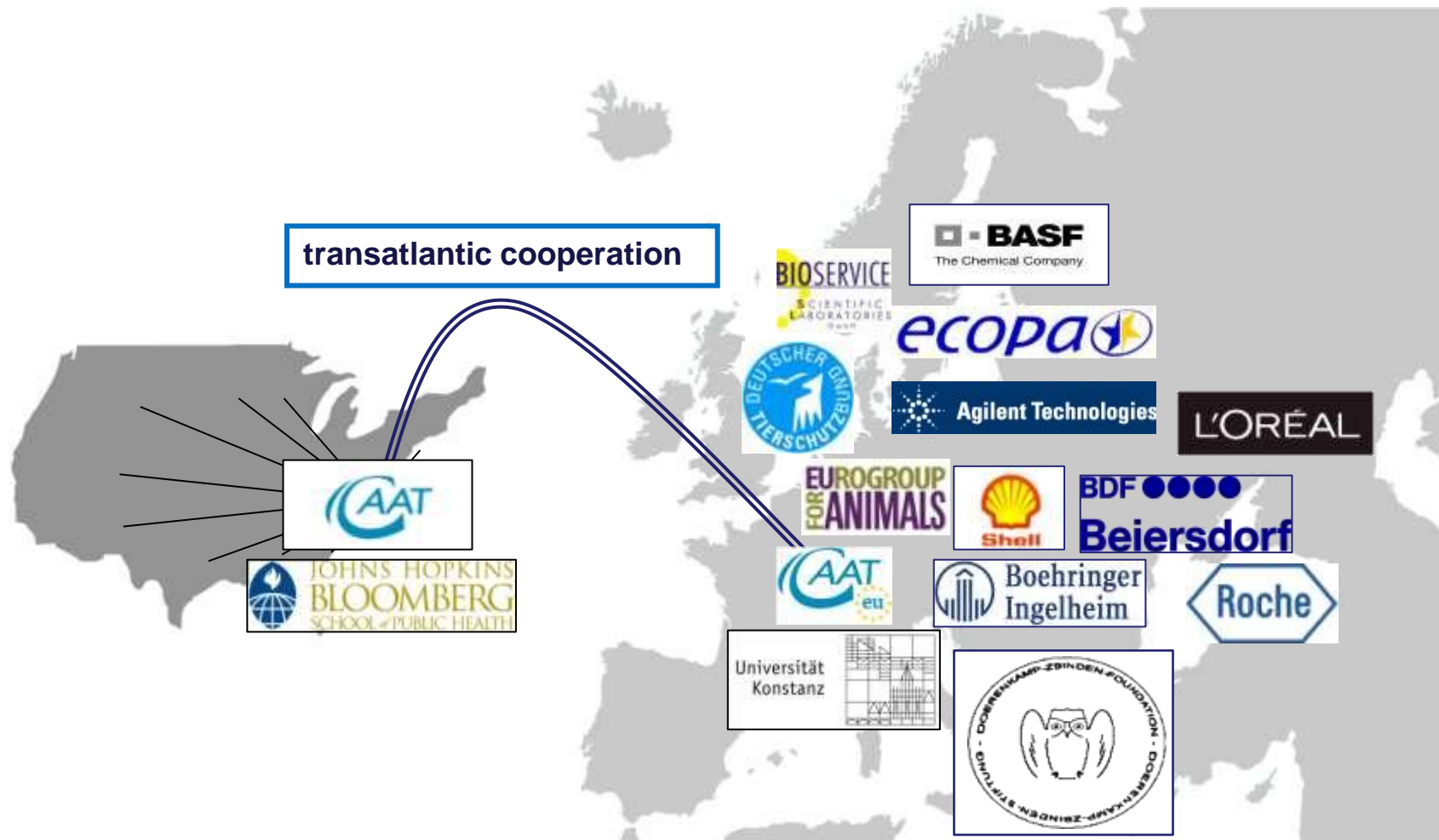
CAAT-Europe in 2011

- I. Workshops
- II. Infodays
- III. Meetings
- IV. Cooperations
- V. Publications
- VI. Future activities





Who we are...



Membership

Supporters / Associates

Agilent Technologies Inc.
 BASF – The Chemical Company
 Beiersdorf AG
 Bioservice
 Boehringer-Ingelheim Pharma
 Deutscher Tierschutzbund
 Doerenkamp-Zbinden
 Foundation
 ecopa
 Eurogroup for Animals/EWLA
 F. Hoffmann-La Roche Ltd.
 L'ORÉAL- RECHERCHE AVANCÉE
 Shell International B.V.

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CAAT-Europe Staff

Marcel Leist
 Thomas Hartung
 Mardas Daneshian
 Costanza Rovida
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CAAT Joint Board Meeting

CAAT Joint Advisory Board Retreat Summary

A collage of images related to the retreat. It includes a map of the Northeast United States (Pennsylvania, New Jersey, Connecticut) with a red dot marking the location of Tarrytown, New York. Below the map is a photograph of several chickens in a green field. To the left of the chickens is the CAAT logo and the Johns Hopkins Bloomberg School of Public Health logo. To the right of the chickens is the CAAT eu logo and the Universität Konstanz logo. The text 'Tarrytown, New York' and 'April 4-7, 2011' is centered below the chicken photo.

CAAT

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

Tarrytown, New York
April 4-7, 2011

CAAT eu

Universität Konstanz

The mission of CAAT-Europe

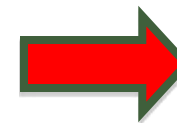
→ Further the field of **3Rs** and **tox21c**

- Strategic activities to promote **networking** and progress in the 3Rs field
- **Infodays** and **workshops**
- **Education** program
- Official communication platform
→ **ALTEX**
- Collaboration with the **transatlantic think tank for toxicology - t⁴**

t⁴ - The transatlantic think-tank of toxicology



- **Structured reviews** (evidence-based)
- **Conceptional paper**
- **Cost-benefit analyses**
- **Workshops** (reports)
- **Paradigm shift in toxicology**



ALTEX
AltWeb

Review and report series of t4 – the transatlantic think tank for toxicology

CAAT-Europe
Developmental Neurotoxicity
Embryonic stem cells
Food for thought on REACH
REACH
Directive 2010/63/EU
Nanotoxicology
Local lymph node assay
Review on the Adler Report
Nanotoxicology,
Repro and developmental tox in REACH
3Rs education
Marine biotoxins
Directive 2010/63/EU
Dog use in biomedical testing
Developmental toxicity
Systemic tox

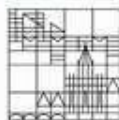
- Carcenogenicity
- Reproductive Toxicity
- Sensitization
- Toxicokinetix
- Repeat Dose

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Workshop Report

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European Workshops 2010 /2011

- **Teaching and education of 3R approaches**
 - > pilot course program, web repository
 - > stem cell training for industry
- **Marine biotoxins**
 - > pilot course program, web repository
- **With ecopa: Implementation of the new EU Directive 2010/63/EU: Opportunities for the 3Rs**
 - > suggested joint database / website workshop
- **Biomarkers in *in vitro* systems**
 - > strategy for in vitro based risk assessment

Summary of workshops ctd.

- **Critical evaluation on the use of dogs in biomedical research and toxicity testing**
- **Workshop on an assay battery for developmental neurotoxicity (DNT) testing**
- **Roadmap for systemic toxicity testing**

Implementation of the new EU Directive 2010/63/EU on the protection of animals used for scientific purposes: Opportunities for the 3Rs

First joint workshop with ecopa

31.01. – 02.02. 2011, Berlin, Germany

Outcome -> Consensus paper (in preparation)

Participants:

European Commission, ECVAM, UK Home Office, EPAA, HSI,

Member state perspective from Germany, Spain, Czech Republic,
Finland

Recommendations Workshop 2010/63/EU:

roadmap for each MS and jointly necessary

Art.1 include ITS, imaging technologies, pathway-based approaches
Create culture of 3Rs; academia now more clearly involved (train the trainer); So far only regulatory toxicology; historic reason for focus on reg tox. – now new instruments?)

Art.3 Extension to ITS, pathway-based approaches; continuum between development and validation at different sites and centralized peer-review needs definition

Art. 5 publication of negative data, mapping of 3Rs activity (bottom-up or top-down) & dissemination; (more than?) a database on what is available; new approaches to evaluate (validate) methods in basic research; loss of data / methods from FP5 & FP6 projects; consider pre-application for higher risk projects
dialogue with opinion leaders in a given area; problem: fast moving methods, thus databases difficult to keep up to date; key role of ethical review process (challenge but also trust into researcher)
don't forget International aspects
recombinant antibodies as opportunity
Toolbox (portal, central depository) of refinement aspects (humane endpoints, enrichment), artificial organs, imaging
Evidence-based medicine type of QA
ECVAM for Basic Research
Devaluation of the value of animal models
Link to Animal Welfare Action Plan objective of animal welfare center
Education: mobilize academia; mapping the use in under-grad training (ecopa?);
QA? how promote education alternatives (validate educational effect?), usefulness of chairs for alternatives?

Art. 15 severity concept is powerful tool for refinement; challenge to achieve harmonized for application especially of “severe”; new Swiss guideline could be helpful especially the specie-specific catalogues; 7-step-system in NL with retrospective learning; new: statistics on actual severity; list of banned experiments needed; problem that based on worst possible outcome (public perception); for transgenic animals problem of unexpected severity; differences between member states how transgenic animals classified; in need for animal welfare indicators? Example botox and shellfish toxin and attitude to regulate on basis of severity

Art. 18 tissue sharing example NL and Italy for monkeys, also EU projects and several countries for human tissues; possible workshop (ecopa) including mapping of experiences and actual needs for tissues; encourage on local level (animal welfare committees but also in project authorization)

Art. 23-24 education & training all people involved; modular approach, tailored to the needs of the trained individual; core module (natl. legislation, ethics, 3Rs) plus “buffet” of courses (credit system, QA); advisor for choice of courses; make visible available courses

Art. 26 Animal welfare body: Cooperation with Natl. committees important (to be established by MS); information access information and target for information; competence problem (?) but named person is ultimately responsible; independence and protection not clear; broader membership than minimum is advisable; FELASA recommendations; similarity to IACUC, but not meant to be control body (“culture of care”); important for refinement;

Art. 46 use for urging data release; database appears not feasible; leverage for abandoning control groups?

Planned CAAT-EU / ecopa follow-up workshop on websites / databases

Critical evaluation on the use of dogs in biomedical research and testing

In memoriam Hildegard Doerenkamp

21.06. – 23.06. 2011, Budapest, Hungary

- Outcome**
- > Refinement initiative of CAAT-Europe
 - > link to CAAT workshop on dogs
 - > Broad refinement initiative

Participants:

Universities (Netherlands, Hungary, Finland), F. Hofmann LaRoche, Pfizer Ltd., AstraZeneca, German animal welfare foundation, Doerenkamp-Zbinden Foundation, UFAW, FRAME, AAALAC, CAAT

Published online 28 June 2011 | *Nature* **474**, 551 (2011) |
doi:10.1038/474551a

News

Call to curb lab tests on dogs

naturenews

Canine remains the default option in outdated pharmaceutical toxicology.

Marian Turner

Workshop on an assay battery for developmental neurotoxicity (DNT) testing

04.10. – 06.10. 2011, Konstanz, Germany

Outcome: -> List of chemicals, which should be useful as training set to develop an in vitro test battery

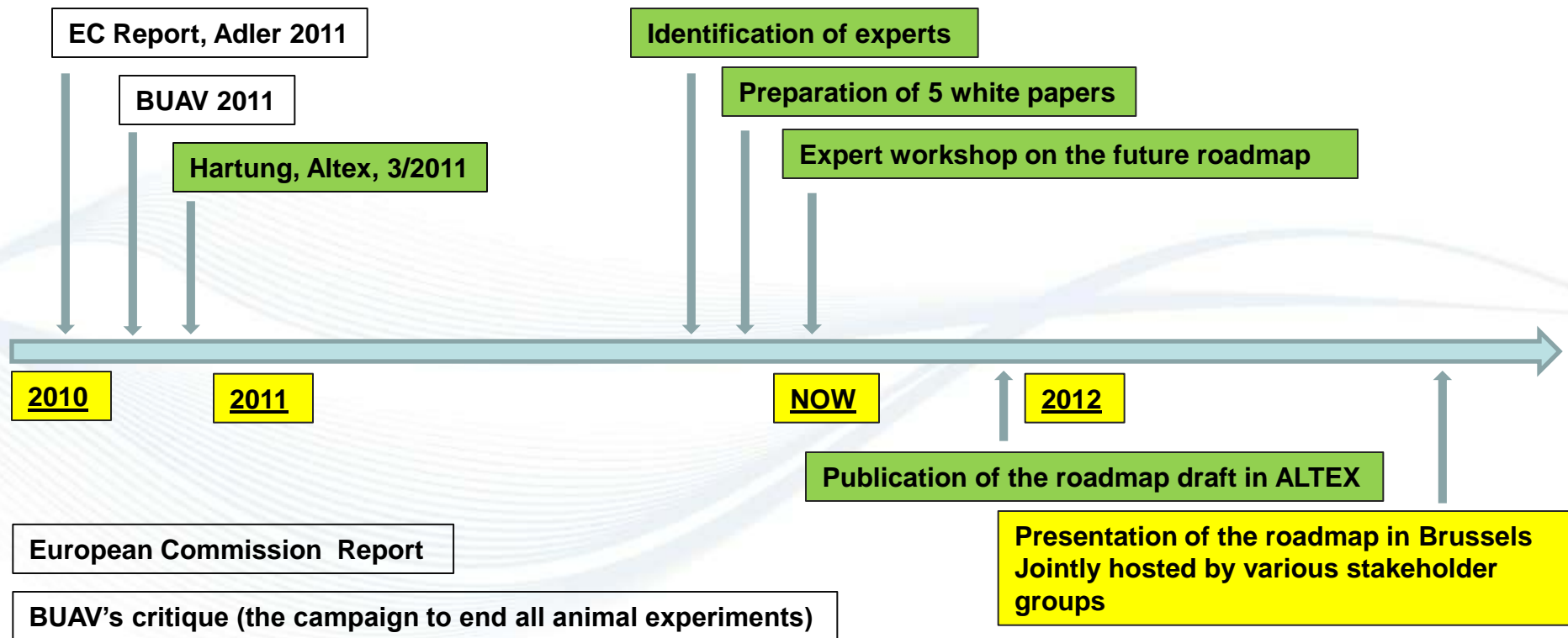
Participants:

EPA, ECVAM, RIFM (Netherlands National Institute for Public Health and the Environment)

Universities (Johns-Hopkins, Düsseldorf, Vanderbilt, Utrecht, UCDavies, Chicago)

CAAT-Europe, CAAT-US

Scientific roadmap for the future of animal-free systemic toxicity testing



Infodays

Infoday 2010

October, 28th in Konstanz, Germany



Infoday 2011

October, 13th in Konstanz, Germany

REACH, TSCA Reauthorization and Toxicology of the 21st Century

Information on status and the future of systemic toxicity testing for chemicals and cosmetics

→ speakers from academia, industry, government, animal welfare associations



Meetings

Neurotoxicology in occupational health, China

→ Review in Neurotoxicology (2011), in press

8th world congress on Alternatives, Canada

→ Several special sessions, Chairman ship, talks and posters

Joint Symposium with IVTIP, ESTIV on tissue models, Monaco

→ Evaluation and future strategy

Conference on 'Animal Alternatives', Ethiopia

→ Article in ALTEX

1st interMaster Conference on chemicals for REACH, Pavia

→ Getting ready for the 2013 deadline

Co-organizer for the Sens-it-iv end congress

→ The Sens-it-iv Tool Box and Scientific Spin-offs

International Neurotoxicology Association Meeting & International Symposium on Neurobehavioural Methods in occupational health

CAAT – special topic

- Session : Translating neurobehavioural endpoints into *in vitro* test assays
- Chair: Marcel Leist and Christoph van Thriel

Speakers:

- Christian Beste, Ruhr University, Germany
- Ambuja S. Bale, EPA, USA
- Pamela J. Lein, University of California, USA
- Marcel Leist, University of Konstanz, Germany
- Christoph v. Thriel, IfADo, Germany
- Remco Westerink, IRAS, Utrecht

→ Review in Neurotoxicology (2011), in press

8th world congress on alternatives in Montreal

CAAT-Activity

- TH
- Alternative in vitro assays in nanomaterial toxicology (**talk**)
 - 21st Century Toxicology with HTP consortium, 3Rs Center meeting, AltWeb, EBTox Steering (**special sessions**)
 - CAAT-US: 30th birthday (**organizer**)
- ML
- A stem cell based test battery to detect developmental neurotoxicants (**talk**)
 - Novel methodologies and their potential in vitro application for drug development and safety assessment (**talk, chair**)
- MD
- Regulatory and methodological shortcomings in assessment of marine biotoxins in fish and shellfish (**talk**)

– 8 scientific posters

1st interMaster Conference of Italian Master courses networks, Pavia, Italy

Toxicological characterisation aimed at the registration of chemical substances for REACH purposes:
getting ready for the 2013 deadline through the experience gained in 2010

Approved by:

- Italian Society of Toxicology
- Italian Society of Nanotoxicology
- IPAM (Italian Platform for Alternative Methods)
- National Council for Chemistry
- Inter-provincial Association of Chemists of Lombardy

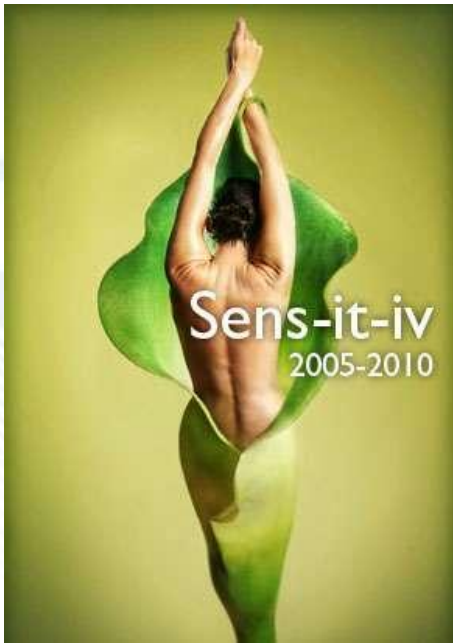
With the participation of all Italian Universities (8) that include a second level master course in a REACH subject

CAAT as Co-organizer for the Sens-it-iv end congress: The Sens-it-iv Tool Box and Scientific Spin-offs

Brussels 23-25 November 2011

Outcome:

t⁴ report with summary and conclusions from the Sens-it-iv project



Publications

Food for Thought ... on Mapping the Human Toxome

Thomas Hartung¹ and Mary McBride²

¹CAAT, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA, and CAAT-Europe, University of Konstanz, Germany; ²Agilent Technologies, Government Relations, Life Sciences and Chemical Analysis, Washington, DC, USA

ALTEX, 2011

CAAT:

~ 30 publications in 2010 and 2011
Several times mentioned in Nature

Nanotoxicology: "The End of the Beginning" – Signs on the Roadmap to a Strategy for Assuring the Safe Application and Use of Nanomaterials*

Ellen K. Silbergeld¹, Elizabeth Q. Contreras², Thomas Hartung³, Cordula Hirsch⁴, Helena Hogberg³, Ashish C. Jachak¹, William Jordan⁵, Robert Landstedel⁶, Jeffery Morris⁵, Anil Patri⁷, Joel G. Pounds⁸, Andrea de Vizcaya Ruiz⁹, Anna Shvedova¹⁰, Robert Tanguay¹¹, Norihisa Tatarazako¹², Erwin van Vliet³, Nigel J. Walker¹³, Mark Wiesner¹⁴, Neil Wilcox¹⁵, and Joanné Zurlo³

ALTEX, 2011



ALTEX 28, 2/11

Local Lymph Node Assay: How Testing Laboratories Apply OECD TG 429 for REACH Purposes

Costanza Rovida

CAAT-Europe, University of Konstanz, Germany



Invited manuscript: **The Local Lymph Node Assay (LLNA)**

Costanza Rovida (CAAT Europe),
Cindy Ryan, Serena Cinelli, David Basketter, Rebecca Dearman and
Ian Kimber

Submitted on October, 3 2011

How are Reproductive Toxicity and Developmental Toxicity addressed in REACH dossiers? - a Report by the Transatlantic Think Tank for Toxicology (t⁴)*

Costanza Rovida, Fabiola Longo and Thomas Hartung

Preliminary results from this paper have been published by Nature:

Published online 12 July 2011 | *Nature* **475**, 150-151 (2011) | doi:10.1038/475150a

News

Data gaps threaten chemical safety law

European companies are not providing robust information to regulators or alternatives to animal experiments.

[Natasha Gilbert](#)

Cooperation



CAAT-Europe functions:

- Organization of secretariat and homepage
- Communication of ecopa activities to the outside
- ecopa corner in ALTEX
- ecopa messenger



Most important upcoming Activities

Use of Metabolomics for safety assessment

- In cooperation with BASF/13.02.-15.02, Berlin
- 1 day Symposium, 1,5 days expert workshop

Roadmap to systemic toxicity (Brussels, March 2012)

Industrial quality standards for in vitro assays (SOT satellite meeting)

Pharma Industry Refinement Working Group

In preparation: Protein Drug Safety Working Group



EBT Collaboration

European branch kick-off:

17 June 2012

Stockholm

**Radisson Blu Royal Viking Hotel
(Satellite to EuroTox 2012)**