A TTC for PCPs?* *Mais, Oui!***

*Personal Care Products (cosmetics, perfumes, toiletries, personal cleansers, etc.)
** 'Mais, Oui': is french for 'But of course

***Drive Continues* to Replace Chronic Toxicity Tests With a Fabricated Threshold of Toxicologic Concern (TTC)**

***More Pro-Industry Bias Found:* EU Commision's Non-Food Scientific Advice Committees (SCCS, SCHER & SCENIHR)**

by Frida Ponce on May 10, 2008 (Flicker Creative Commons license)

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HELPING YOU BETTER COMMUNICATE OUR CHEMICAL RISKS

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Commissioned by Pesticide Action Network-Europe (PAN-E)

INTRODUCTION: **The TTC**

George Doyle/Thinkstock/DCL

One of the food and petrochemical (including pesticides, pharmaceuticals and personal care) industries' major efforts to protect their money-earning molecules from health & safety regulation, since 1967[1] has been the Threshold of Toxicologic Concern, the TTC. The TTC wears an aura of complex science, but its purpose is simply to eliminate the critical live mammal, chronic exposure toxicity test that is the heart of a risk assessment (RA) of chemicals.

A TTC achieves this desirable elimination by claiming to be a "threshold" ("safe") dose, below which it is claimed there will be no significant toxicity. A TTC is the 5th percentile (close to the most potent) chronic toxicity test result among hundreds of tested chemicals. A regulator using a TTC says that exposure below this dose will not cause a risk, despite that its toxicity is never tested (as in all RA, it is first divided by a factor meant to account for susceptibility differences—usually 100-fold).

Several TTCs have been created, each from a toxicity test dataset somewhat specific for a class of chemical structures. The largest TTC categories rely on an known correlations of structure and toxicity (for example, reactive molecules do damage the molecules of life). Using this incomplete "Structure-Activity Relation" (SAR) data, Cramer et al. successfully (if imprecisely) predicted the risk of hundreds of molecules from their structural components.[2] The TTC used this work to, for each of those three Cramer SAR classes, set as a TTC the 5th percentile (nearly most-potent result), finalizing it by dividing it by the usual 100-fold safety factor. The Cramer team was in the same food industry that created the TTC concept, indicating that the TTC and SAR are quite inseparable. Gradually, TTCs for other categories are appearing, e.g. for organophosphate/carbamate insecticides, which work by the same mechanism.

So long as the estimated exposure of the chemical's use is below the TTC, it allowed to be used without ever being tested for toxicity**.** ***The manufacturer thus avoids any risk that their chemical will test toxic at or below the TTC's daily dose***. Industry and many regulatory agencies have made huge efforts to substitute the TTC for chronic toxicity testing.

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This report tries to replicate the methods and format of a recent analysis of the links to industry of the EU Commission's food safety science advisors on the use of the TTC by Pesticide Action Network-Europe (PAN-E).[3] PAN-E found this wg of "scientists" was riddled with financial ties to the industry that would benefit from expansion of the TTC.

We document here a similar bias to objective science that occurs when the Commission's non-food regulatory agencies are captured by their for-profit industries. Industry can effectively "de-toxify" their many-making agents—here, by working to replace toxicity tests with the TTC.

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[1] Frawley JP 1967 'Scientific Knowledge & Common Sense as the basis for Food Packageing Regulatons. Food & Cosmetics Toxicology:5:293-308.

[2] Cramer GM, Ford RA, Hall RL 1978 Jun 'Estimation of toxic hazard--a decision tree approach' Food Cosmet Toxicol:16(3):255-76.

[3] http://www.pan-europe.info/Resources/Reports/PANE%20-%202011%20-%20A%20Toxic%20Mixture%20-%20Industry%20bias%20found%20in%20EFSA%20working%20group%20on%20risk%20assessment%20for%20toxic%20chemicals..pdf

OTHER, LONG-STANDING, FAILURES OF RISK ASSESSMENT ***ENABLE THE TTC***

***If* the toxicity tests our safety regulators require of industry tested reality, *then* applying a TTC assumption *might* be rational**. But our regulatory agencies become largely captured by the corporations they are meant to control, due to the later's resources and knowledge of their products.[4]

RAs are based on toxicity data generated by the very party to whom large revenues depend on it being found safe enough to market! An attempted reform (Good Laboratory Practices, GLP) made matters worse, and today it is no exaggeration to say that *not one* independent chronic toxicity result has been used in a RA that decides if and how the chemical is to be marketed; conversely, these tens of thousands of RAs use for their key study (the chronic toxicity finding) a GLP-compliant study from industry (this is only somewhat better in post-market 'review' RAs).

Classic toxicology (a discipline created by industry, beginning as and inseparable from pharmacology) is exclusively used in RA, propagated worldwide by the OECD. This is a system of rigid, utterly artificial toxicity test methods; that negates any need to perform fraud. Co-exposures are ignored. It only tests the effect of near-poisonous doses (despite being called chronic toxicity tests), not effects of doses we experience. The exquisite vulnerability of development is usually ignored, and they *always* kill the test animals before old age, so almost no disease develops! **This is the testing regime that produces the toxicity data from which a TTC is created.**

Moreover, the correlation between a chemical's strucure and its toxicity—necessary to create a TTC—is problematic. Generally SAR is unreliable, there's a large literature on its failures—and even expert modellers hired to validate the TTC find that the complexity of toxic modes of action can prevent structure from correlating with toxicity.[5] For example, that organo-phosphate & carbamate insecticides inhibit acetyl cholinesterase (their insecticidal mechanism and the basis of their new TTC) does not mean that is all they do—see for example the work of Ted Slotkin.

So in reality, the TTC's claim to be a safe daily dose of any chemical in a class (say, cosmetics) is easily falsified by curious (real) scientific inquiry. Once a company's chemical has been safely shepherded onto the market, independent academic scientists are curious about its effects; and their methods always (due to intellectual inquiry & the scientific method) investigate what the molecule does in reality. So both their tests and their results are certainly varied (one reason regulators don't use it), but in general **they *overwhelmingly* falsify the claimed safety of industry's self-interested testing, including the toxicity studies that a TTC is based on.**

Thus a TTC--aside from canceling actual toxicity tests of a chemical—also under-predicts chemical potencies. Yet these financially-independent toxicity studies are almost completely ignored in RA (including the TTC), in favor of the self-interested toxicity results from industry (thanks to unrealistic protocols being required in RA).
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[4] See e.g.: http://en.wikipedia.org/wiki/Regulatory_capture
[5] http://www.efsa.europa.eu/en/supporting/pub/159e.htm

A TTC FOR THE COSMETICS / PERSONAL CARE PRODUCT INDUSTRY

Pending Ban on Animal Testing Is Opportunity To Expand the TTC, But First an Exposure Data Gap Must Be Filled)

Environmental Defense, Canada

Cosmetics and other personal care products (PCP) cause some of our most intimate exposures to toxic chemicals; a lot of it is dermal--through the skin. In contrast, everything eaten goes to the liver after entering the blood, where chemicals undergo somewhat more metabolism and subsequent excretion than dermaly-absorbed chemicals. So no TTC (whose toxic potencies are almost all based on oral ingestion toxicity tests) would be valid when the exposure is mostly dermal, as for cosmetics/PCPs. For several years, parties have worked (see immediately below) to create TTCs based on chemical toxicities that were dermaly absorbed (using both experimental data and modeling of the absorbtion and excretion rates).

Second, the EU—pressured by industry via its animal-welfare front-groups—recently banned whole-animal toxicity tests for cosmetics/PCPs. What better rationale to raise the possibility of the TTC substitute?

Driven by these two motives, EU funders of scientific research (the FP7 round) have granted many millions of Euros to a cluster of scientific research projects to develop alternatives to the mammalian toxicity test, with the PCP industry as the key partner (both as co-funder and beneficiary of the research. The animal test ban looms!

One of this cluster is the **Cosmetics to Optimize Safety (CosmOS)** project, jointly funded by EU taxpayers and the EU Cosmetics Industry's association COLIPA[6]. Its key purpose is to generate the data to justify extrapolating the adsorption-to-excretion data of oral exposures, to the dermal exposures that predominate for cosmetics. Once the delivered internal dose from dermal exposures is can be predicted, the oral-exposure toxicity tests used to select a TTC can be used for dermal exposures, and a cosmetics TTC established.

Note that once again, the TTC proponents' claim--that toxicity tests will only be waived (and the TTC substituted) in limited instances--is contradicted.

The cosmetics industry is leading the charge to eliminate the mammalian toxicity tests (the only way to test human effects under controlled conditions). COSMOS and its FP7 research cluster are such efforts to replace the mammalian chronic toxicity test. The TTC is just one such effort; it could eventually even be based on in-vitro test results. **The cosmetics/PCP industry (and the chemical industry generally) are looking to integrate all such alternatives to live testing into a model called KNIME**[7]. ILSI is overseeing this work.

It is human to desire the welfare of animals. Overall welfare, including for laboratory animals, can only be achieved if toxicity testing is taken out of the hands of the party whose overriding interest is that their agent be declared safe enough to sell. Society can only acquire the definitive answers via live, mammalian tests. Only this will put an end to animal testing. Independent toxicity researchers agree that there is no substitute; they say that *in vitro/slico* methods will never predict what happens to a live mammal after exposure (also note how all data shows that rodent tests reliably predict human carcinogenicity (careful epidemiology)).[8] All industry is achieving with its science at odds with reality, is requiring further animal testing. Industry is using animal welfare in an effort to reduce the investigation into the risks of its revenue-raisers. The TTC fits this plan.
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[6] Currently changing its name to European Cosmetics Association or "Cosmetics Europe – The Personal Care Association".
[7] http://www.knime.org/
[8] DAVID P. RALL Jan 2000 LABORATORY ANIMAL TESTS AND HUMAN CANCER Drug Metabolism Review:32:2:119-128:119-28.

Previous & Pending Scientific Endorsements of a Cosmetics/PCP TTC

ILSI-EU, with its permanent wg on the TTC, has promoted the TTC to many agencies--most recently the European Food Safety Authority, EFSA; which has strongly endorsed expansion of TTC use on various classes of chemicals. Unbelievably, EFSA is even recommending its use on endocrine disrupting chemicals, whose very signature is that they are more potent at low than at high doses!

The EU Commission's non-food health & safety advice comes from the Scientific Committees on: Consumer Safety (SCCS); on Health and Environmental Risks (SCHER); and on Emerging and Newly Identified Health Risks (SCENIHR); administered by DG-SANCO, collectively the "3SCs".

As early as 2003, a predecessor to the 3SCs was informally promoting the TTC.[9] Then about five years ago, according to a communication we had with DG SANCO RA unit, they and the **Cosmetics** unit of DG ENTER asked the 3SCs to evaluate applying the TTC to cosmetics. This became a wg of the joint three SCs, the "3SC TTC wg". No doubt the cosmetics industry was worried about animal testing bans, and eventually the COSMOS research was launched (which assumes the industry will need the TTC).

The SANCO 3SC TTC wg issued a preliminary opinion in Dec. 2008,[10] but since then has slowed its work drastically, to coordinate its evaluation with other advisory bodies, such as EFSA's SC, which is about to publish its final opinion on EFSA's use of the TTC. Divided opinions may also have delayed them (see following).

The latest indication is that the 3SC wg will be more cautious than EFSA expansion of the TTC, but continue to recommend that Commision RA make expanded use of this substitute to toxicity tests.

SANCO & EFSA's SC TTC wgs are closely coordinating their recommendations on the TTC, indicating a possible big push to expand use of the TTC.

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[9] Bridges, J. (2003). Strategy for a future chemicals policy. The view of the Scientific Committee on Toxicology, Ecotoxicology and the Environment (CSTEE).

[10] http://ec.europa.eu/health/archive/ph_risk/committees/documents/sc_o_001.pdf

WHAT WE DID

Methods and Criteria Used to Analyze the 3SC TTC wg

Using PubMed--everything published in the life sciences--we looked at the careers of each wg member, to gauge their expertise in their field; including whether they published three or more primary research results (i.e., we excluded publications that were commentaries and qualitative reviews) in last in the last 5 years—indicating if they remained expert in their specialties.

We searched the papers in scientific journals indexed by ScienceDirect (which includes more of industry-favored journals, thus more papers about the TTC than PubMed returns) using the names of working group members and TTC as search terms. We looked at articles proposing, promoting or discussing the TTC, and checked which co-authors were involved. We also looked at their Declarations of [conflict] of interests (DoI) at the SANCO and EFSA website and looked at links to industry. Finally the internet was searched on ILSI-activities and relations of people from the TTC-working group with industry.

We defined financial bias on several grounds:

* the level of bias: did the wg member develop or promote TTC in the past?
* the level of industry relations: had the wg member formal links to or contracts with ILSI or other companies?
* the level of scientific activity: is the wg member an actively researching, thus involved in the latest science. The criterion here is if a person published two or more papers of original research per year (not commentary, opinion, informal reviews, statistical re-examination, etc) in the last 5 years.
* the level of industry-mindedness: did the person in question meet (regularly) with COLEPA or ILSI-on the TTC and similar (this is only used as confirmatory information).

RESULTS

It is interesting to see a split between independent and industry-conflicted advisors. The majority of the 3SC TTC wg was six quite independent scientists (not all currently performing primary research, however). But three had careers of collaboration with various commercial industries. The wg added three expert advisors—each with massive conflicts of interests--many with ties to the cosmetics industry. Thus half of this advisory gropup on the TTC was "industry friendly".

Perhaps a balance between public and private allegiances created a stalemate, contributing to the long delay in issuing an opinion. *It was not until after their Dec '08 preliminary opinion that they added a fourth member, a scientist with an intense record of advising to the pharmaceutical and other industries*. His client Merck KGaA is a critical member of COSMOS—it will test the cosmetics TTC against existing toxicity tests.
We recently learned that one of the independent scientists is no longer serving, and we do not know who if anyone replaced him (we keep the percent-of-influence figures, below, conservative by counting him). Thus this TTC wg attained a majority of "industry friendly" members, and it is due to rmake its final recommendations soon.

7 of 14 (**50**%) of members have or had working relations with ILSI or COLIPA (the cosmetics association);
8 of 14 (**57**%) have or had working relations with any industry overseen by EU health * safety regulators;
10 of 14 (**71**%) are not currently practicing research scientists;
5,5 of 14 (**39**%) have a record of promoting the TTC in place of actual toxicity testing.

Summary Table of 3SC TTC wg's Independence

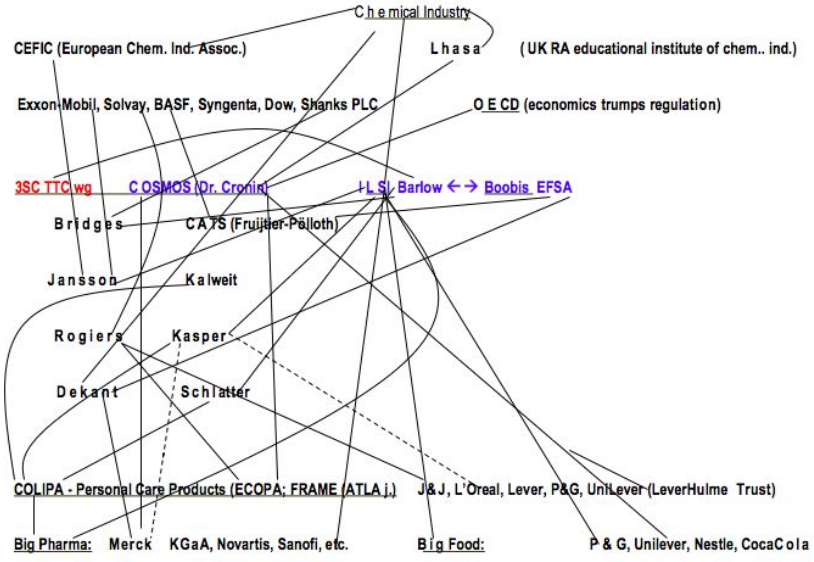
Red = corruption of science by private monied interests*; green = curiosity-driven (honest) researcher
(* in the limited case of "active researcher?", it may be due to retirement)

TTC 3SC wg: Member Advisor	COLIPA or ILSI Formal Relations?	COLIPA or ILSI Relations, via publications?	Any Industry Formal Relations?	Any Industry Relatons, via publications?	Active Researcher?	Develops or Promotes TTC (or writes on it)?
Bridges	Yes (ILSI)	Yes	Yes	Yes	No	Yes
Jansson	Yes	No	Yes	Yes	No	No
Rogiers	Yes	Yes	Yes	Yes	Yes	(writes on it)
Dekant	Yes	Yes	Yes	Yes	No	Yes
De Jong	No	No	No	No	Yes	No
Platzek	No	No	No	No	Yes	No
Rastogi	No	No	No	No	Yes	No
Sanner*	No	No	No	No	No	No
Van Engelen	No	No	No	No	No	No
Ladefoged	No	No	No	No	No	No
Fruijtier-Pölloth	Yes	Yes	Yes	Yes	No	Yes
Kalweit	Yes	Yes	Yes	Yes	No	No
Kasper	No	yes	Yes	Yes	No	Yes
Schlatter	Yes	Yes	Yes	Yes	No	Yes

*: recently communicated that he has left the wg

A graphic presentation of our results:

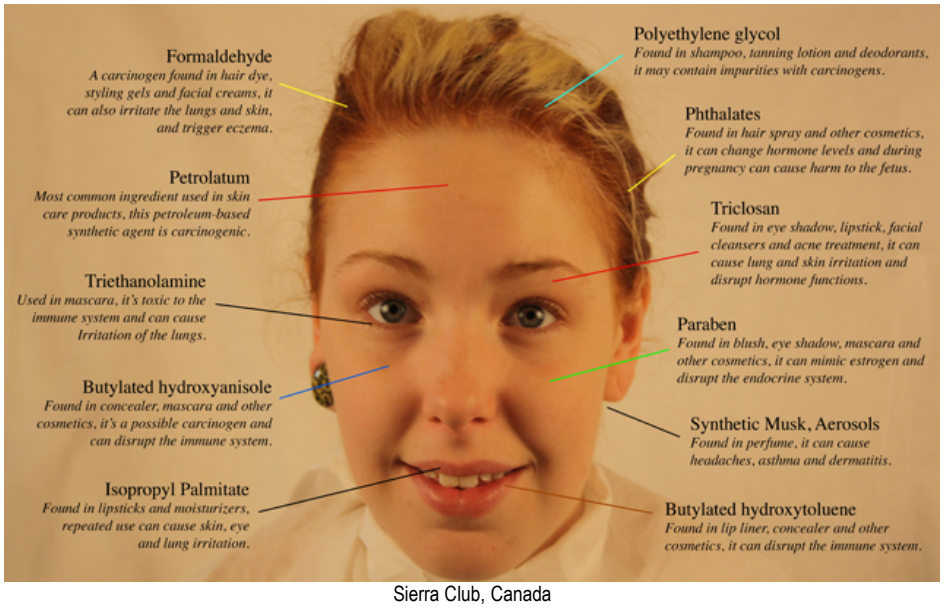
A Tough, Resilient Spider-Web of Connections:



Details of our search for industry connections and overall scientific competence are in the following tables of each wg member's career, with a citation for every link to COLIPA, IFSI and other industry that we found.

We discovered <u>four additional scientists</u> whom the wg thanked for their valuable contributions, so we briefly analyzed their independence. Once again, these additional experts are also massivelly conflicted

We also present both ILSI's and COSMOS' basic industry backers; and add a brief analysis of the <u>animal welfare advocate FRAME</u>, because their influential journal <u>ATLA</u> carried the publications of several members of the 3SC TTC wg (all this was added to the "spider-web of links above).



Sierra Club, Canada

IGNORED: DG SANCO REGULATIONS on INDEPENDENCE OF SCIENTIFIC ADVICE

The EU Commission claims to rely crucially upon reliable scientific knowledge[11] (emphasis added):

> "…2. ***Sound and timely scientific advice is an essential requirement for Commission proposals, decisions and policy*** relating to consumer safety, public health and the environment. The mission of the Committees and the Advisors of the Pool is to assist the Commission, and through the Commission the other European Institutions, with scientific advice in the fields of consumer safety, public health and the environment.
> …11. The scientific advice delivered by the Committees ***must not be influenced by any consideration other than the scientific assessment*** of the risks in question.
> 12. This principle implies ***in particular the independence from any external economic or political interests, but also from bias related to political, economic, social, philosophical, ethical, or any other non-scientific considerations***. [We note that economic interest, a powerful bias, is the only bias to objectivity that is controllable in practice].

Consequently, all serving on 3SC wgs (including outside experts named to the wg) operate under a continuing obligation to act independent of biasing interests, and to declare all interests (transparency)

Crucially, however, a declared interest of a 3SC wg member that conflicts with objective evaluation of the matter at hand is *per se* grounds for disqualifying the member from making such scientific considerations:

> 26. **Any Member, Advisor or External Expert who**….**may not be able to act independently, shall be excluded from the activities considered or may only be allowed to participate to the extent** and in a way compatible with the objective to preserve the process from any undue influence. In such a case, the Member, Advisor or Expert **may not act as Rapporteur or as Chair in relation to the specific matter and may not participate in decision making**. …Measures may include the physical withdrawal from the meeting for the point under discussion, or participation limited to the provision of factual information.

Nowhere do we see that DG SANCO's RA unit, the secretariat for the 3SCs, makes available any records of how the wgs implement this CoI procedures. No draft or final opinions, nor the 3SC's web pages appear to mention the conflicting interests in any wg's consideration of an issue, even though the wgs are required to record the specific interests that may conflict with the matter being dealt with.

Specifically for the 3SC TTC wg, there is no indication in their 2008 draft opinion or anywhere that the three wg members and four added experts, whom we find have significant conflicts of interests (out of the 13 total), were excluded from deliberations or votes in any way.

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[11] RULES OF PROCEDURE of the Scientific Committees, http://ec.europa.eu/health/scientific_committees/docs/rules_procedure_en.pdf These Rules of Procedure have been jointly adopted by the Scientific Committees on 18 December 2009, in conformity to Article 12 of Commission Decision 2008/721/EC of 5 September 2008.

CONCLUSIONS

The mission—bias, if you will--of our public health agencies is meant to be to promote health. Regardless of any bias, everyone should make decisions based on the most reliable knowledge mankind has, science. The results of our research into one advisory panel's financial conflicts E finds repeatedly that our regulatory agencies fail on both counts. Instead, powerful industry's private monetary interests are served.

Specifically, we again (after PAN-E's findings of the EFSA TTC wg) documented how use of the TTC (designed to avoid the monetary risk of a toxic finding) is being promoted by industry (led by ILSI) to regulators. Already the 3SCs were advising the EU Commission (in their 2008 preliminary report) the Commission that the TTC should substitute for toxicity tests. Unfortunately, since then, it appears that financial influences have shifted the balance of "the Commission's scientific advice" even further towards their private interests and away from public benefit.

We recommend **instead** that the Commission's scientific advisors, and its agencies, begin to perform RAs using realistic toxicity test methods, especially the crucial chronic toxicity test in live mammals, but performed only by financially independent scientists. Protocols such as those employed by the Ramazzini Institute, including not killing the test animals before most of any disease develops(!), should be used. Indeed, Ramazzini regularly finds toxicity where industry did not. So do thousands of scientists in academia. All their work, though it is far superior, is being wasted.

ILSI

from http://docs.exdat.com/docs/index-70471.html

A key partner in COSMOS is the **International Life Sciences Institute** (ILSI), a major research arm of the petrochemical and food industries (ILSI often protests that it and its scientists are independent, but always ends up admitting it is massively supported by corporation.[12]). For decades ILSI has been the TTCs core promoter. In the EU, by at least the late 1990's, ILSI-EU had formed an expert group to infuence the science regulatory opportunities of the TTC.[13] As early as 2003, a 3SCs scientist with links to ILSI (James Bridges, still serving on this cosmetics TTC wg) was saying that this predecessor to the 3SCs preliminarily supported the TTC.[14]

But one major reservation raised by several SCs was the TTC's inappropriateness to substitute for the toxicity of dermal exposures (see above). ILSI's signature is all over the genesis of COSMOS--likely they saw the test ban in the Cosmetics Directive as an opportunity to expand use of the TTC alternative to testing.

ILSI-EU has a Task Force on the TTC, which *inter alia* has set up two expert groups of industry scientists (members of the main TF and its groups here[15]), to put the cosmetics/ PCP TTC into use. Note how EFSA, JRC, USFDA, Health Canada and the WHO all are members or have permanent observers collaborating with industry/ILSI's TTC TF, or its working groups:

(Red denotes an ILSI connection to the 3SC TTC wg)

ILSI-EU TTC Task Force Collaborators Members – 2012

Dr. G Würtzen-Chair	**Consultant for Coca-Cola Eu**	DK
Dr.S Felter-Co-chair	**Procter & Gamble**	US
Mr. James Edwards	**DSM**	CH
Dr. P-J Ferret	**PierreFabreDermoCosmétique**	FR
Dr. Heli Hollnagel	**Dow Europe**	CH
Dr. Elena Lo Piparo	**Nestlé**	CH
Dr. Daniela Maurici*	**Euro. Food Safety Authority**	IT
Prof. em. A Renwick	**University of Southampton**	UK
Mr. Robert Safford	**Unilever**	UK
Dr. Jürgen Schnabel	**Givaudan International AG**	CH
Dr. T Stroheker	**Danone**	FR
Dr. A Tritscher*	**World Health Organization**	CH
Mr. M Ambrosio	**ILSI Europe**	BE
Dr. Stéphane Vidry	**ILSI Europe**	BE
Ms. Belinda Antonio	**ILSI Europe**	BE

* Observer

ILSI's Expert Group on the Application of the TTC Approach to Cosmetic Ingredients

Mr.RbtSafford-Chair	**Unilever**	UK
Prof. Alan Boobis	**Imperial College London**	UK
Dr. Susan Felter	**Procter & Gamble**	US
Dr. Heli Hollnagel	**Dow Europe**	CH
Dr. Kristi Jacobs	**US FDA**	US
Prof. Daniel Krewski	**University of Ottawa**	CA
Prof. em. A Renwick	**University of Southampton**	UK
Dr. Josef Schlatter	**Swiss FedOfficePublic Health**	CH
Dr. Andrew Worth	**EC – Joint Research Center**	IT
Prof. Chihae Yang	**Ohio State University**	US
Mr. M Ambrosio	**ILSI Europe**	BE
Dr. Stéphane Vidry	**ILSI Europe**	BE

ILSI Expert Group Evaluation of Oral-to-dermal Extrapolation

Dr. Gordon Barrett	**Health Canada**	CA
Dr. Scott Boyer	**AstraZeneca**	SE
Prof. Richard Guy	**University of Bath**	UK
Dr. Monteiro-Riviere	**North Carolina State Uni.**	US
Dr. James Plautz	**DSM**	CH
Dr. Clive Roper	**Charles River Laboratories**	UK
Dr. Helga Rothe	**Procter & Gamble**	DE
Dr. Diego Rua	**Food & Drug Administration**	US
Mr. Robert Safford	**Unilever**	UK
Dr. Miriam Verwei	**TNO**	NL
Prof. Faith Williams	**University of Newcastle**	UK
Dr. Chihae Yang	**Ohio State University**	US
Mr. M Ambrosio	**ILSI Europe**	BE
Dr. Stéphane Vidry	**ILSI Europe**	BE

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[12] Heilprin J., 'WHO to rely less on US research. Associated Press. 28 Jan 2006. Avail.: http://www.medkb.com/Uwe/ Forum.aspx/nutrition/5496/Money-Talks-in-Whispers [Accessed Feb. '12].

[13] Kroes R, Galli C, Munro I, et al. 2000 TTC for chemical substances found in the diet: a practical tool for assessing the need for toxicity testing. Food & Chemical Toxicol.:38:255-312.

[14] Bridges, J. (2003). Strategy for a future chemicals policy. The view of the Scientific Committee on Toxicology, Ecotoxicology and the Environment (CSTEE). This informal opinion appears to have become a white paper that promoted research on in vitro alternatives, including the TTC. ILSI cited it as available for the corporate lobbyist EUToC (no longer found there, or anywhere).

[15] http://www.ilsi.org/Europe/Pages/TF_ThresholdToxicological.aspx

FRAME / AtLA:

From Universities Federation for Animal welfare, UK

A few of the members and advisors on the 3SC TTC wg publish in a journal called Alternatives to Laboratory Animals (AtLA). It is published by the Fund for the Replacement of Animals in Medical Experiments (FRAME). FRAME is the UK's, and perhaps the EU's, leading advocate to stop toxicity testing on animals. Their ATLA is an influential journal, probably the lead one of a handful that publishes experiments on alternatives to animal toxicity testing. Though the journal fails to disclose its editorial board's affiliations, it belongs to FRAME, and so ATLA is a tool of the private interests of FRAME's corporate sustainers, below.[16]

Corporate members of FRAME

"FRAME is deeply grateful to all those companies taking out corporate membership, which helps to enable the continuation of our work There are five levels of corporate membership:

These are companies which donated an annual sum of £20,000 or more. These companies may collaborate with FRAME in specific or general research projects, or contribute to general funding.

British American Tobacco is a 5-star member.

These are companies which donated an annual sum of £10,000 to £20,000. These companies may collaborate with FRAME in specific or general research projects or contribute to general funding.

Asda Stores Ltd Avon Products Inc The Boots Company plc Procter & Gamble UK Ltd Reckitt Benckiser plc
J Sainsbury plc Tesco Stores Ltd

These are companies which donated an annual sum of £5,000-£10,000. …either for a defined purpose or for general funding.

Coty UK Ltd GlaxoSmithKline Ltd The Kennel Club

These are companies which donated an annual sum of £1,000 to £5,000. Such donations are of particular value in providing money for activities such as education and publicity, which do not involve research.

Charles River Laboratories Colgate Palmolive UK Ltd A & E Connock (Perfumery & Cosmetics) Ltd Covance Laboratories Ltd PZ Cussons (UK) Ltd Ecover (UK) Ltd Givaudan UK Ltd Harlan Laboratories Ltd Huntingdon Life Sciences Ltd Johnson & Johnson Ltd SC Johnson Ltd Neal's Yard Remedies Next plc Shire Pharmaceuticals Ltd Smith & Nephew Research Ltd Thor Personal Care SAS Unilever Vie At Home Ltd Waitrose Ltd"

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[16] http://www.frame.org.uk/page.php?pg_id=44

COSMOS BOX

COSMOS (**COSM**etics to **O**ptimize **S**afety) is run by **Dr. Mark Cronin** at Liverpool John Moores University School of Pharmacy & Chemistry. We did not review his publication history thoroughly, but obviously he is an active scientist doing primary research, though many of his publications are commentaries. Most of his co-authors are academic researchers, but he has published a few times with authors from biotechnology companies. His main work is on in vitro alternatives to animal tests, especially the role of structure-activity correlations. **Nevertheless**, the below highlighted (red) extract from his web page.[17] clearly shows his long-time work contact with the cosmetics/PCP industry.

"[SNIP]

Byrom Street, Liverpool, L3 3AF , UK + 44 151 231 2402 ; m.t.cronin@ljmu.ac.uk

...He has received grant funding and performed consultancies from diverse sources including UK government agencies (e.g. Defra), European Union (various framework programmes), the European Commission as well as chemical & personal product industries.

Research Interests: Main areas of research include the application of in silico models for toxicity and ADME effects in various sectors including industrial chemicals, pharmaceuticals, cosmetics and food additives. This includes the development of integrated testing strategies (ITS) for toxicological endpoints. Mark Cronin co-ordinates the EU / Colipa COSMOS project (http://www.cosmostox.eu/). An up todate publications list is available from: http://www.staff.livjm.ac.uk/phamcron/publications.htm

Teaching: Module leader for Research Methods and the Final Year Project on the Master of Pharmacy programme. Teaches pharmaceutical and physical chemistry, drug design, toxicology and use of computer-aided molecular design.

Collaborators: Various through the OSIRIS, COSMOS, OECD QSAR Toolbox and many others.

Publications: [link]

Further Information: Recent Grant Moneys Received & Consultancies

EU 6th & 7th Framework Programme Funding:

ReProTect Integrated Project 2004-2009

CAESAR Scientific Support Action 2006-2009

InSilicoTox Marie Curie Project 2006-2010

OSIRIS Integrated Project 2007-2011

eTox IMI Project 2009-2014

COSMOS Project 2010-2015

Other Funding

OECD QSAR Toolbox, European Chemicals Agency, Helsinki 2008-2012

Defra LINK project 2007-2010

Lhasa Ltd 2007-2010

Unilever Research 2008-2011

LeverHulme Academic Exchange 2004-2008

He is currently on the editorial boards of six international peer-reviewed journals, namely: SAR and QSAR in Environmental Research (1999-present); Pesticide Management Science (2001-present); Current Medicinal Chemistry (2006-present); Alternatives to Laboratory Animals (ATLA) (2008-present); International Journal of Molecular Sciences (Molecular Toxicology Section) (2009-present); Molecular Informatics (from 2010)

The applicant has acted on a number of national and international committees. These mainly relate to the promotion of predictive toxicology and reduction of animal testing as well as work with Learned Societies. During the past three years these can be summarised as follows:

Member of the Organisation of Economic Co-operation & Development (OECD) Working Group on (Quantitative) Structure-Activity Relationships ((Q)SARs), representative of the International Council for Animal Protection in OECD (ICAPO)

Member of various workshops organised by the European Commission including those by the European ECVAM Task Force on Endocrine Disruption and the ECB Workshop on the Role of Neural Networks in QSAR.

Member of the ILSI Europe Expert Group on "Chemical risk assessment in absence of adequate toxicological information"

Member of the International Steering Committee for the 12th, 13th and 14th International Workshop on QSAR in the Environmental Sciences held in 2006 (Lyon, France), 2008 (Syracuse, USA) and 2010 (Montreal, Canada) respectively."

[END OF SELECTION]

[17] http://www.ljmu.ac.uk/PBS/115913.htm

3SC TTC wg MEMBERS: DETAILED RESULTS

1. Name & Affiliation	**Prof. James Bridges (retired) toxicologist, University of Surrey - UK**  .mailto:bridges@surrey.ac.uk
2. Publications on (or mentioning) TTC	Paper on meeting on TTC in 2005, organized by EFSA & ILSI.[18]
3. Original Research papers in past 5 yrs.	None (retired 2003).
4. Career Background; Publications	Starting with analytical fluorescence biochemistry in the 1960's, his publication rate peaked in the late 1970's as he focused on the metabolism of toxic chemicals. From late 1980's he published little(!)--risk assessment methodologies, some toxicity experiments.
5. Links to Cosmetics, Other Industry	Paper casting doubt on animal testing, a major industry lobby topic.[19] One of his last papers was co-authored with UK Pharmaceutical industry[20]
6. Discovered Conflicts of Interests	ILSI Board Member, 2001-2006. Paid advice to waste disposal industry: Shanks plc, employee of Mass Tech Int'l
7. Inferred Sources of Income	Pension, government *per diums*, industry employment & consulting

1. Name & Affiliation	**Emeritus Prof. Bo Oscar Jansson–Stockholm University–SE**  **bo.jansson@itm.su.se**
2. Publications on (or mentioning) TTC	None.
3. Original Research papers in past 5 yrs.	1
4. Career Background; Publications	~20 published papers (in life sciences, claims ~200 papers, but, per his university web page, this includes posters, talks, etc.). Analytic chemist specializing in detection of persistent pollutants in animals/environment.
5. Links to Cosmetics, Other Industry	Key role (on Steering Cmtee)[21] of JRC's ExpoFacts Project, originally coordinated by ExxonMobil Biomedical Sciences and funded by CEFIC & ILSI.[22] Co-authored 'POPs & RA commentary-CEFIC, BASF, academics & government authors.[23]
6. Discovered Conflicts of Interests	Possibly no longer a member of either SANCO's or EFSA's scientific advisory committees, so no DoIs are available …yet SCHER vice-chair until very recently, possibly currently… (was on SCHER's predecessor cmtee, the SCTEE).
7. Inferred Sources of Income	Pension; university pay ad hoc (retired)

[18] S. Barlow , A.G. Renwick, J. Kleiner, J.W. Bridges, L. Busk, E. Dybing, L. Edler, G. Eisenbrand, J. Fink-Gremmels, A. Knaap, R. Kroes, D. Liem, D.J.G. Mu ller, S. Page, V. Rolland J. Schlatter, A. Tritscher, W. Tueting, G. Wurtzen, Risk assessment of substances that are both genotoxic and carcinogenic Report of an International Conference organized by EFSA and WHO with support of ILSI Europe, Food and Chemical Toxicology 44 (2006) 1636–1650.

[19] S.M Barlow, J.B Greig, J.W Bridges, A Carere, A.J.M Carpy, C.L Galli, J Kleiner, I Knudsen, H.B.W.M Koeter, L.S Levy, C Madsen, S Mayer, J.-F Narbonne, F Pfannkuch, M.G Prodanchuk, M.R Smith, P Steinberg, Hazard identification by methods of animal-based toxicology, Food and Chemical Toxicology, Volume 40, Issues 2-3, February-March 2002, Pages 145-91.

[20] Wood SA, Long JM, Simmonds RJ, Bridges JW, Stevenson D. Optimisation of the enantiomeric separation of 12 2-aminotetralin analogues using Chiral AGP high-performance liquid chromatog- raphy by simultaneous factorial design. J Pharm Biomed Anal. 1997 Oct;16(2):231-7

[21] http://web.jrc.ec.europa.eu/eis-chemrisks/doc/DefVal_1meeting.pdf and search for the single occurance of "Jansson".

[22] http://expofacts.jrc.ec.europa.eu/

[23] Harry W. Vallacka, Dick J. Bakkerb, Ingvar Brandtc, Eva Broström-Lundénd, Abraham Brouwere, Keith R. Bullf, Clair Goughg, Ramon Guardansh, Ivan Holoubeki, Bo Janssonj, Rainer Kochk, Johan Kuylenstiernaa,André Leclouxl, Donald Mackaym, Patrick McCutcheonn, Paolo Mocarellio, Rob D.F. Taalmanp Controlling persistent organic pollutants–what next? Environmental Toxicology and Pharmacology Volume 6, Issue 3, 1 November 1998, Pages 143–75.

1. Name & Affiliation	**Prof. Vera Rogiers** Head of Dpt. Of Toxicology, *Dermato-Cosmetology* & Pharmacognosy **Vrije Universiteit Brussel – BE** vrogiers@fafy.vub.ac.be 
2. Publications on (or mentioning) TTC	One commentary on RA for cosmetics at least mentions the TTC[24]
3. Original Research papers in past 5 yrs.	~40
4. Career Background; Publications	220 career publications, began on liver (metabolism) toxicity, moved into mechanisms of cancer and other disease (including cystic fibrosis), including gene expression & calcium signaling. Few toxicity papers.
5. Links to Cosmetics, Other Industry	Many published papers are on in vitro alternatives to toxicity tests, so she has worked with cosmetics industry—e.g. with ECOPA, a consortium of chemical industries (including cosmetics) and emotive animal welfare groups (behind which industry hides its agenda).
6. Discovered Conflicts of Interests	Chair of ECOPA-European Consensus Platform for Alternatives, funded in part by Johnson & Johnson and other corporations, especially cosmetics/PCP. Advisor to EPAA, the industry/EU partnership for alternatives to animal testing. Advisor to Solvay, the BE chemical multinationals.
7. Inferred Sources of Income	University. Industry consulting

In a PowerPoint presentation of obscure-origin/audience & created sometime after the wg's 2009 interim TTC report, this wg member (Dr. Rogiers) thanked the following for their contributions to their wg (no affiliations are provided):

U Bernauer A primary researcher with many commentaries on industry favored alternatives to RA. Often publishes with DE"s BfR (Gundert-Remy) and the Centre for Documentation and Evaluation of Alternatives to Animal Experiments (German acronym ZEBET), Even when pulishing primary research toxicity tests, often uses results to call for quicker ways to do RA—animal alternatives, etc.
Federal Institute for Risk Assessment, Thielallee 88-92, D-14195 Berlin mailto:Ulrike.Bernauer@bfr.bund.de

S Barlow Possibly the strongest driver for TTC use; as previously disclosed by PAN-E, she is not a primary researcher, rather her job is to pretend to be an objective scientist and so lobby regulators to adopt industry's RA methods, such as the TTC.

I Mangelsdorf A toxicologist with both primary research qualifications who nonetheless spends most of his papers talking about industry-sponsored RA methods; including several commentaries promoting the TTC (co-authored with its usual promoters). His employer is a government-industry hybrid research institute, the Fraunhofer Institute of Toxicology and Experimental Medicine, Drug Research and Clinical Inhalation, Hannover, mangelsdorf@ita.fraunhofer.de

H van de Sant Obscure—appears to work for animal welfare groups.

[24] Pauwels M, Rogiers V. Human health safety evaluation of cosmetics in the EU: a legally imposed challenge to science. Toxicol Appl Pharmacol. 2010 Mar 1;243(2):260-74.

Dr. Rogiers' .ppt also reveals the wg's **new member** (from SCHER standing cmtee.) since their 2008 interim report:

1. Name & Affiliation	**Prof. Wolfgang Dekant – DE Dpt. of Toxicology, U. Würzburg**  dekant@toxi.uni-wuerzburg.de
2. Publications on (or mentioning) TTC	A pair of commentaries in journal RTP; co-authored with BASF, explicitly promoting TTC[25]
3. Original Research papers in past 5 yrs.	29.
4. Career Background; Publications	Nearly 200 published papers, almost all on metabolites of toxic molecules—analytic detection methods and their mode of toxic action--many concern natural toxins, e.g. mold chemicals. Traditional, high dose toxicology. A few commentaries on alternatives to animal tests and other RA methods. On SANCO's SCHER, and EFSA advisory panel on Food additives, Flavorings & Food Contact Materials (unable to locate his EFSA DoI).
5. Links to Cosmetics, Other Industry	Much work on metabolism & excretion of automotive refrigerants & oxyfuels, reflecting his below COI's. With the German Merck (KGaA) (who are a key COSMOS partner, will validate the new cosmetics TTC with test chemicals) as co-author, found[26] that the *ueber-potent* estrogen bisPhenool-A is rapidly & entirely excreted in adult humans; contrary to far superior work done later (yet of course, this study is still relied on by regulators to keep bPA on the market).
6. Discovered Conflicts of Interests	Lists consulting for **~two dozen** for-profit companies, **but fails to name almost any of them** in his SANCO DoI, where he also discloses advising associations of auto makers.
7. Inferred Sources of Income	University professor; consults for industries, *per diums* from governments

[25] Stephanie Melching-Kollmuß, Wolfgang **Dekant**, Fritz Kalberlah Application of the "threshold of toxicological concern" to derive tolerable concentrations of "non-relevant metabolites" formed from plant protection products in ground and drinking water Regulatory Toxicology and Pharmacology, Vol 56, # 2, March 2010, 126-34.
Wolfgang **Dekant**, Stephanie Melching-Kollmuß, Fritz Kalberlah Toxicity assessment strategies, data requirements, and risk assessment approaches to derive health based guidance values for non-relevant metabolites of plant protection products Regulatory Toxicology & Pharmacology, Vol 56, # 2, March 2010, 135-42.

[26] Völkel W, Colnot T, Csanády GA, Filser JG, **Dekant** W. Metabolism and kinetics of bisphenol a in humans at low doses following oral administration. Chem Res Toxicol. 2002 Oct;15(10):1281-7.

1. Name & Affiliation	**Dr. Wim H. de Jong– National Institute for Public Health and the Environment – NL** mailto:W.de.Jong@rivm.nl Leads group evaluates safety of food, vaccines, medicines & pollutants
2. Publications on (or mentioning) TTC	None.
3. Original Research papers in past 5 yrs.	25
4. Career Background; Publications	100+ publications; editor for two journals. Trained as veterinarian, has expertise in immunology. Experiments on nano & medical device risks. Develops analytic methods, frequently finding toxicity.
5. Links to Cosmetics, Other Industry	None (advises ISO & CEN--EU standard-creating bodies, heavily dominated by industry, but public bodies..
6. Discovered Conflicts of Interests	None.
7. Inferred Sources of Income	Employed by national government.

1. Name & Affiliation	**Prof. Thomas Platzek - Bundesinstitut für Risikobewertung – DE thomas.platzek@bfr.bund.de**
2. Publications on (or mentioning) TTC	None
3. Original Research papers in past 5 yrs.	5.
4. Career Background; Publications	~30 published papers, co-authors academics and a few government scientists. Immunotoxicity of consumer product chemicals & by-products, especially dyes
5. Links to Cosmetics, Other Industry	None. Co-authored an in vitro experiment with German Institute for Textile Chemistry & Chemical Fibers.[27]
6. Discovered Conflicts of Interests	None.
7. Inferred Sources of Income	Government.

1. Name & Affiliation	**Dr. Suresh C. Rastogi - National Environmental Institute, DK scr@dmu.dk**
2. Publications on (or mentioning) TTC	None
3. Original Research papers in past 5 yrs.	4
4. Career Background; Publications	~ 70 publications, co-authors are academic & government scientists—contact dermatitis expert, so lots of work on personal care product chemicals, including creating analytic methods.
5. Links to Cosmetics, Other Industry	None.
6. Discovered Conflicts of Interests	None.
7. Inferred Sources of Income	Government

1. Name & Affiliation	**Prof. Tore Sanner - University of Oslo – NO Dpt. Environmental & Occupational Cancer, Institute for Cancer Research, Norwegian Radium Hospital. tore.sanner@kjemi.uio.no**
2. Publications on (or mentioning) TTC	TTC at least mentioned in one commentary.[28]
3. Original Research papers in past 5 yrs.	None.
4. Career Background; Publications	~150 published papers, academic & government scientists as co-authors. Until c. 10 years ago, published lots of cancer mechanism work involving smoke/smoking, radiation with the.syrian hamster Also on tobacco control and cancer RA issues. Recently, focused on alternatives to toxicity tests and to RA, such as giving mutagenic carcinogens a threshold dose under which they are assumed to be of zero risk. Frequently cited by the core industry scientists who are pushing for the TTC -- e.g.[29]
5. Links to Cosmetics, Other Industry	None.
6. Discovered Conflicts of Interests	None.
7. Inferred Sources of Income	University & hospital.

1. Name & Affiliation	**Dr. Jaqueline G. van Engelen – National Institute for Public Health & Environment- NL RIVM, SIR, Bilthoven jacqueline.van.engelen@rivm.nl**
2. Publications on (or mentioning) TTC	Two commentaries focus on the allowed waiving of toxicity tests nuder REACh (only if exposure is shown to be negligible) to argue the TTTC is just as safe.[30]
3. Original Research papers in past 5 yrs.	None.
4. Career Background; Publications	19 publications—only handful primary research—most comment RA methods, from public health perspective.
5. Links to Cosmetics, Other Industry	None.
6. Discovered Conflicts of Interests	None
7. Inferred Sources of Income	Government.

1. Name & Affiliation	**Dr. O. Ladefoged – Institute of Food Safety and Nutrition – DK National Food Institute, Technical University of Denmark (DTU) ol@DFVF.dk**
2. Publications on (or mentioning) TTC	None.
3. Original Research papers in past 5 yrs.	1.
4. Career Background; Publications	~50, mostly classic high-dose (even for endocrine disruptors) animal toxicity tests in industry-influenced classic toxicology journals—solvents, metals, began on drug toxicity studies. Only academic co-authors.
5. Links to Cosmetics, Other Industry	
6. Discovered Conflicts of Interests	None, but one of his last publications was a RA commentary in the industry journal Food Chem. Toxicology promoting probabilistic alternatives to actual toxicity tests of EDC pesticides, saying they are likely of no risk![31]
7. Inferred Sources of Income	Government/academia & per diums

27 Martina Meinke1, Mandana Abdollahnia1,Frank Gähr2, **Thomas Platzek3**, Wolfram Sterry1, Jürgen Lademann1 Migration and penetration of a fluorescent textile dye into the skin –in vivo versus in vitro methods Experimental Dermatology Volume 18, Issue 9, pages 789–792, September 2009.

[28] Dybing E, O'Brien J, Renwick AG, Sanner T. Risk assessment of dietary exposures to compounds that are genotoxic and carcinogenic--an overview.Toxicol Lett. 2008 Aug 15;180(2):110-7.

[29] Barlow S, Renwick AG, Kleiner J, Bridges JW, Busk L, Dybing E, Edler L, Eisenbrand G, Fink-Gremmels J, Knaap A, Kroes R, Liem D, Müller DJ, Page S, Rolland V, Schlatter J, Tritscher A, Tueting W, Würtzen G. Risk assessment of substances that are both genotoxic and carcinogenic report of an International Conference organized by EFSA and WHO with support of ILSI Europe. Food Chem Toxicol. 2006 Oct;44(10):1636-50.

[30] Vermeire T, van de Bovenkamp M, de Bruin YB, Delmaar C, **van Engelen J**, Escher S, Marquart H, Meijster T.Exposure-based waiving under REACH. Regul Toxicol Pharmacol. 2010 Dec;58(3):408-20.

Marquart H, Meijster T, Van de Bovenkamp M, Ter Burg W, Spaan S, **Van Engelen A** structured approach to Exposure Based Waiving of human health endpoints under REACH developed in the OSIRIS project. J. Regul Toxicol Pharmacol. 2011.

[31] Müller AK, Bosgra S, Boon PE, van der Voet H, Nielsen E, **Ladefoged** O. Probabilistic cumulative risk assessment of anti-androgenic pesticides in food. Food Chem Toxicol. 2009 Dec;47(12):2951-62.

EXPERTS On the WG

1. Name & Affiliation	**Dr. Claudia Fruijtier-Pölloth – CATS Consultants – DE** claudia@catsconsultants.com
2. Publications on (or mentioning) TTC	None.
3. Original Research papers in past 5 yrs.	None.
4. Career Background; Publications	Three published papers. Along with her husband the other prinicipal in CATS, they entered the revolving door from industry careers (she BASF; he five pharmaceutical companies) to advising government on how to regulate industry—i.e. they help an industry capture their regulator. EFSA and SANCO listed expert—subject to be called on for "independent" expert advice!
5. Links to Cosmetics, Other Industry	CATS serves inter alia the cosmetics industry; they have evaluated for clients the risks of over 50 cosmetic ingredients.[32] Thus we infer CATS is involved "up to their eyes" in the COSMOS TTC initiative.
6. Discovered Conflicts of Interests	Endless! One published commentary on RA is co-written with TTC fans as Boobis; also with ECETOC, ILSI, BASF, Syngenta, etc. authors.[33]
7. Inferred Sources of Income	Advises industry and government on toxicity issues

1. Name & Affiliation	**Dr. S. Kalweit - Bundesamt für Verbraucherschutz und Lebensmittelsicherheit – DE** s.kalweit@bgvv.de (1999!). Retired.
2. Publications on (or mentioning) TTC	None.
3. Original Research papers in past 5 yrs.	None.
4. Career Background; Publications	13 published papers, career—genotoxicity, assays on mutagenicity, and draize eye test.
5. Links to Cosmetics, Other Industry	The tests he specialized in were the most common protocols used by the cosmetics industry; so we infer he was asked for advice on this TTC committee. Coordinated toxicity test method development with COLIPA.[34]
6. Discovered Conflicts of Interests	Co-authors w/ cosmetic & pharmaceutical companies & associations--:L'Oreal, Merck AG.
7. Inferred Sources of Income	Pension, corporation consultancy fees

1. Name & Affiliation	**Dr. Peter Kasper – Scientific Director, Bundesinstituts für Arzneimittel und Medizinprodukte – DE P.Kasper@bfarm.de retired?**
2. Publications on (or mentioning) TTC	Two meeting reports and one research paper promote use of his genotoxicity data in the TTC; and the two meeting report co-authors (attendees) are ILSI, Proctor & Gamble, Dow; and Big Pharma, their toxicity consultants, and their regulators![35]
3. Original Research papers in past 5 yrs.	1.
4. Career Background; Publications	A few dozen primary research publications, career--genotoxicity.
5. Links to Cosmetics, Other Industry	Frequently co-authors with pharmaceutical industry—Novartis, Sanofi, etc. For example, he and other government agencies collaborated with Big Pharma authors to promote use of historical controls—a favorite industry way to detoxify dangerous toxicity results.[36]
6. Discovered Conflicts of Interests	Close relationship with Big Pharma throughout his career protecting the health of the Swiss people, but financial relationships are unknown.
7. Inferred Sources of Income	Pension? Consulting fees from pharmaceutical industry?

[32] http://www.catsconsultants.com/Previous%20projects.htm

[33] Carmichael N, Bausen M, Boobis AR, Cohen SM, Embry M, Fruijtier-Pölloth C, Greim H, Lewis R, Bette Meek ME, Mellor H, Vickers C, Doe J. Using mode of action information to improve regulatory decision-making: an ECETOC/ILSI RF/HESI workshop overview. Crit Rev Toxicol. 2011 Mar;41(3):175-86.

[34] Spielmann H, Balls M, Brand M, Döring B, Holzhütter HG, **Kalweit S**, Klecak G, Eplattenier HL, Liebsch M, Lovell WW, Maurer T, Moldenhauer F, Moore L, Pape WJ, Pfanenbecker U, Potthast J, De Silva O, Steiling W, Willshaw A. EEC/COLIPA project on in vitro phototoxicity testing: First results obtained with a Balb/c 3T3 cell phototoxicity assay. Toxicol In Vitro. 1994 Aug;8(4):793-6.

[35] Summary of major conclusions from the 4th IWGT, San Francisco, 9–10 September, 2005 Mutation Research/Genetic Toxicology and Environmental Mutagenesis, Volume 627, Issue 1, 3 February 2007, Pages 5-9

D.J. Kirkland, M. Hayashi, D. Jacobson-Kram, P. Kasper, J.T. MacGregor, L. Müller, Y. Uno Relevance and follow-up of positive results in in vitro genetic toxicity assays: An ILSI-HESI initiative Mutation Research/Genetic Toxicology and Environmental Mutagenesis, Volume 633, Issue 2, 4 October 2007, Pages 67-79

Véronique Thybaud, Marilyn Aardema, Daniel Casciano, Vicki Dellarco, Michelle R. Embry, B. Bhaskar Gollapudi, Makoto Hayashi, Michael P. Holsapple, David Jacobson-Kram, Peter Kasper, James T. MacGregor, Robert Rees Controlling of genotoxic impurities in pharmaceuticals: International harmonisation of regulatory requirements Toxicology Letters, Volume 205, Supplement, 28 August 2011, Page S7 P. Kasper

[36] Hayashi M, Dearfield K, Kasper P, Lovell D, Martus HJ, Thybaud V Compilation and use of genetic toxicity historical control data. Mutat Res. 2011 Aug 16;723(2):87-90.

1. Name & Affiliation	**Dr. Josef Rudolf. Schlatter- Federal Office of Public Health – CH** josef.schlatter@bag.admin.ch
2. Publications on (or mentioning) TTC	Kroes 2004, ILSI 1999, ILSI 2002[37] with Syngenta and Nestle, saying: "The concept is widely accepted by toxicologists", in total 7 publications promoting TTC.[38]
3. Original Research papers in past 5 yrs.	Three.
4. Career Background; Publications	About 40 – on food chemical toxicities, until c. 2000, when,,,
5. Links to Cosmetics, Other Industry	…he began publishing mostly on ways to deconstruct RA--various "safe dose" assumption methods, e.g. MoE, use of acute tox to avoid chronic toxicity tests, etc. Skeptic that toxic chemicals cause much cancer.[39] On MoE[40] with Nestle, Unilever, ILSI[41], re: "human relevance" (puts animal testing relevance for humans in doubt) industry lobby ECETOC.[42]
6. Discovered Conflicts of Interests	# ILSI-Europe expert group for TTC's application to cosmetics (part of their permanent TTC Task Force)—thus working COLIPA & that industry, also. # COLIPA/FP7 **COSMOS**: Scientific adviser for (declared this conflict to EFSA's TTC WG in their 11/'11 minutes, where **they decided it was insignificant**!. # ILSI: Member of Board of Trustees (non-remunerated) 2008 on. # ILSI: Member of the program strategy and stewardship committee. # ILSI: Scientific research on a range of public health and environmental issues, for the most part on generic issues # ILSI Europe Scientific Advisory Committee, Nutrition, food safety, natural toxins in food. # EUFIC (Food & Drink Industry): Scientific Advisory Board # FEMA (flavouring): consultancy
7. Inferred Sources of Income	Civil servant. Industry consultant.

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[37] E. Dybing, J. Doe, J. Groten, J. Kleiner, J. O'Brien, A.G. Renwick, J. Schlatter, P. Steinberg, A. Tritscher, R. Walker, M. Younes, Hazard characterisation of chemicals in food & diet: dose response, mechanisms & extrapolation issues,Food&Chem Toxicology 40 2002 237–82.

[38] Structure-based thresholds of toxicological concern (TTC): guidance for application to substances present at low levels in the diet Original Research Article
Food and Chemical Toxicology, Volume 42, Issue 1, January 2004, Pages 65-83
R Kroes, A.G Renwick, M Cheeseman, J Kleiner, I Mangelsdorf, A Piersma, B Schilter, J Schlatter, F van Schothorst, J.G Vos, G Würtzen
Safety evaluation of superabsorbent baby diapers Original Research Article
Regulatory Toxicology and Pharmacology, Volume 53, Issue 2, March 2009, Pages 81-89
Kistin Kosemund, Harald Schlatter, Jennifer L. Ochsenhirt, Edburga L. Krause, Daniel S. Marsman, Geetha N. Erasala
Approaches to the risk assessment of genotoxic carcinogens in food: A critical appraisal Original Research Article
Food and Chemical Toxicology, Volume 44, Issue 10, October 2006, Pages 1613-1635
J. O'Brien, A.G. Renwick, A. Constable, E. Dybing, D.J.G. Müller, J. Schlatter, W. Slob, W. Tueting, J. van Benthem, G.M. Williams,
Hazard characterisation of chemicals in food and diet: dose response, mechanisms and extrapolation issuesReview Article
Food and Chemical Toxicology, Volume 40, Issues 2–3, February–March 2002, Pages 237-282
E Dybing, J Doe, J Groten, J Kleiner, J O'Brien, A.G Renwick, J Schlatter, P Steinberg, A Tritscher, R Walker, M Younes
Threshold of toxicological concern for chemical substances present in the diet Original Research Article
Food and Chemical Toxicology, Volume 39, Issue 9, September 2001, Pages 893-905
Report of a workshop held on 5–6 October 1999 in Paris, FranceOrganised by the ILSI Europe Threshold of Toxicological Concern Task Force, S.M. Barlow, G. Kozianowski, G. Würtzen, J. Schlatter
Risk assessment of carcinogens in food Review Article
Toxicology and Applied Pharmacology, Volume 243, Issue 2, 1 March 2010, Pages 180-190
Susan Barlow, Josef Schlatter
Risk assessment of substances that are both genotoxic and carcinogenic: Report of an International Conference organized by EFSA and WHO with support of ILSI Europe Original Research Article
Food and Chemical Toxicology, Volume 44, Issue 10, October 2006, Pages 1636-1650
S. Barlow, A.G. Renwick, J. Kleiner, J.W. Bridges, L. Busk, E. Dybing, L. Edler, G. Eisenbrand, J. Fink-Gremmels, A. Knaap, R. Kroes, D. Liem, D.J.G. Müller, S. Page, V. Rolland, J. Schlatter, A. Tritscher, W. Tueting, G. Würtzen

[39] Lutz WK, Poetzsch J, Schlatter J, Schlatter C The real role of risk assessment in cancer risk management.. Trends Pharmacol Sci. 1991 Jun;12(6):214-7.

[40] Diane Benford, P. Michael Bolger, Philip Carthew, Myriam Coulet, Michael DiNovi, Jean-Charles Leb- lanc, Andrew G. Renwick, Woodrow Setzer, Josef Schlatter, Benjamin Smith, Wout Slob, Gary Williams, Tanja Wildemann, Application of the Margin of Exposure (MOE) approach to substances in food that are genotoxic and carcinogenic, Food and Chemical Toxicology 48 (2010) S2–S24.

[41] Susan Barlow, Josef Schlatter, Risk assessment of carcinogens in food, Toxicology and Applied Pharma- cology 243 (2010) 180–190.

[42] Alan R. Boobis, John E. Doe, Barbara Heinrich-Hirsch, M. E. (Bette) Meek, Sharon Munn, Mathuros Ruchirawat, Josef Schlatter, Carolyn Vickers, IPCS Framework for Analyzing the Relevance of a Noncancer Mode of Action for Humans, Crit Rev Toxicology,38:87–96, 2008.

A Tough, Resilient Spider-Web of Connections:

Chemical Industry

CEFIC (European Chem. Ind. Assoc.) **Lhasa (UK RA educational institute of chem. ind.)**

Exxon-Mobil, Solvay, BASF, Syngenta, Dow, Shanks PLC **OECD (economics trumps regulation)**

3SC TTC wg **ILSI Barlow ← → Boobis EFSA**

Bridges	**CATS (Fruijtier-Pölloth)**
Jansson	**Kalweit**
Rogiers	**Kasper**
Dekant	**Schlatter**

COSMOS (Dr. Cronin) COLIPA - Personal Care Products (ECOPA; FRAME (ATLA j.)

J&J, L'Oreal, Lever, P&G, UniLever (LeverHulme Trust)

Big Pharma: Merck KGaA, Novartis, Sanofi, etc. **Big Food: P&G, Unilever, Nestle, CocaCola**
