When science becomes fiction – the mystery of endocrine disruptors, toxic editors, lobbyists and multimillionaires

Comment to 'Do toxic editors trivialize hidden hazards?'

by Jan Hengstler

It takes one phone call to make an ordinary day, well quite extraordinary. On said day – the initially ordinary one – a colleague thought it wise to warn me of my new outlaw status at Labtimes. I was, unbeknownst to me, listed as a member of a band of 'toxic editors' who 'trivialize hidden hazards' because of our secret, 'under-the-table' payments from industry (3/2014, pp. 38-42, 'Do toxic editors trivialize hidden hazards?' by Jeremy Garwood). We had some laughs and made all the appropriate jokes related to my dubious honor, but, humor aside, I believe the public should be informed about the truth that led to a group of scientists being called out in such a public manner. I promise an exciting story with all the intricacies of a conspiracy novel – in it, we have a billionaire financier who funds a non-governmental organisation (NGO) office in Brussels that pays a freelance journalist to write an article about allegedly corrupt scientists (including myself). And, in a strange twist, selected passages of this commissioned article find their way verbatim into Labtimes by a wizard-like copy-and-paste mechanism.

The article in question introduces the reader to 17 evil editors of journals within the field of toxicology. According to Labtimes, 'some had received research funds from industry associations, others had served as paid industry consultants or advisors'. Coincidentally (or not), highlighted directly below this sentence are the names of four 'toxic editors', including my own. Before continuing with this story, I would like to make a few facts abundantly clear. I have never received money or favors from the chemical or pharmaceutical industry. I have also never served as a paid industry consultant, and have no undisclosed financial ties to industry. Furthermore, and to avoid any misunderstanding, it is not my opinion that cooperation projects funded by either the chemical or pharmaceutical industry are unethical by default. However, none of my projects, past or present, have been supported by these industries, rather, until now my research has been funded by research grants from the European Union, the German Federal Ministry of Education and Research (BMBF) and the German Research Foundation (DFG). For transparency, the research institution where I am employed (Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany) lists all funding sources on its public website (http://www.ifado.de/), allowing easy access for all, including journalists.

Besides my alleged, but non-existing, financial ties, Labtimes suggests yet another offence that categorizes me as a 'toxic editor': in one of my previous publications they identified two consultants and one former employee of a chemical company as coauthors (Hengstler et al., 2011). What a surprise that this publication was chosen as a basis for my placement onto this 'toxic editor' black list, as it represents a consensus paper of the Advisory Committee of the German Society of Toxicology (GT). Its background is clearly explained in the published conflict-of-interest section found on pages 265 and 286 of the article. The Advisory Committee is elected by the members of the German Society of Toxicology (the largest scientific toxicology organization in Europe with more than 1200 members) and consists of representatives from academia, industry and administration. The members of this committee present, discuss and justify the committee's activities to the other members of the society, for example at its yearly meeting. When diverse scientific viewpoints hamper decision-making on a particular subject (as explained on page 265 of the article), additional experts are called upon for their input. The writing of such a consensus paper is a truly democratic process, albeit a time and labor intensive one. Therefore, we were bemused to see that Labtimes uses co-authorship of a consensus paper of an elected scientific society advisory committee to contrive a conflict-of-interest.

A draft proposal and its scientific error

Let us now take a step back and ask what prompted Labtimes to so blatantly compromise the names of 17 scientists. The problem – and this was not clearly mentioned in the Labtimes article – is that members of the European Commission (EC) drafted a framework on chemicals legislation where they proposed to regulate endocrine disruptors in a manner similar to genotoxic carcinogens. We, the 'toxic editors', believed this to be a critical mistake, as it would counteract a balanced procedure that carefully regulates all hazardous chemicals.

It is well known that genotoxic carcinogens induce damage to our DNA. It is also known that a possible consequence of such damage is the initiation of a process that in the end may lead to cancer. Very small doses may induce the multistep process of carcinogenesis. For many genotoxic carcinogens, we do not know how many DNA adducts are required to cause cancer in humans. Critical doses may be very low and consequently, we do not know if safe levels even exist. Therefore, genotoxic carcinogens are regulated by a so-called 'a priori default assumption of no threshold', meaning that our exposure to genotoxic carcinogens should be reduced as much as technically possible, even if this costs billions of Euros. In practice, the situation remains unsatisfactory and we are still exposed to numerous critical genotoxic carcinogens in our everyday life.

But now back to the current EC draft on endocrine disruptors. A major blunder on the part of the EC was their plan to regulate endocrine disruptor chemicals by a 'no threshold assumption'. This approach is, in my opinion, simply wrong. Hormones bind specific receptors on the surface or within cells. This interaction influences downstream events, such as signal transduction networks that may be important for certain cell fate decisions, which ultimately determine the health of tissues and organisms. By definition, 'endocrine disruptors' interfere with the endocrine systems, e.g by mimicking or antagonizing a hormone, or by inhibiting or stimulating their production. However, it is well-established that hormones and endocrine disrupting chemicals interact with receptors by rules that can be described quantitatively. In other words, we can experimentally identify concentrations of endocrine disrupting chemicals that are low enough to no longer disturb hormone-receptor interactions. One approach would be to test endocrine disruptors in vivo using animal models, also considering the possible susceptibility at different stages in life, which could be addressed in two- or three-generation studies. These experimental strategies clearly show that threshold doses of endocrine disrupting chemicals exist, and importantly, below such thresholds cells or organisms are not compromised. This means that, in contrast to genotoxic carcinogens, safe exposure levels can be identified.

Dose response curves, including the mechanisms explaining non-monotonic curves, have been an integral part of basic toxicology courses for decades. Therefore, it is quite startling that Labtimes presents this concept as novel, even bordering on controversial. Non-monotonic curves may occur if a compound induces several molecular mechanisms, an observation that gained support with the advent of the mutagenicity test in the past century. Increasing concentrations of a mutagenic compound, as expected, increases the mutation rate. However, for some compounds, once a certain threshold was past, the mutation rate instead decreased – usually a consequence of cytotoxicity. Other well documented examples include trace elements, such as selenium. Too little in the diet results in health problems; too much can be toxic. Endocrine disruptors also induce several mechanisms, and therefore should not be considered as exceptions when their toxicities are discussed. If a compound induces a biological response at low doses, a weaker response at intermediate doses and stronger responses again at higher doses as suggested by the schedule on page 41 in the Labtimes article, this should become obvious by routine testing. The potential different shapes of the dose-response curves have nothing to do with the fact that endocrine disruptors show a threshold but genotoxic carcinogens do not. Therefore, pitting 'traditional toxicology' against the 'modern toxicology' is unwarranted.

Paracelsus's 'the dose makes the poison' is a general concept, and although almost cliché in the toxicology world, it is certainly valid regardless of the shape of the dose-response. A 'no-threshold assumption' for endocrine disruptors, as indented by the novel EU draft, is not only scientifically wrong, it is also detrimental, as we would have to invest enormously into reducing exposure levels to compounds for which harmless ranges can be identified. Furthermore, we would needlessly absorb resources that could be used to protect us from chemicals that present a more immediate danger. The

EU currently produces about 100,000 compounds in amounts that exceed one ton per year. For approximately 30,000 of these compounds, available toxicity data are insufficient for human risk evaluation. It is indeed important to study the toxicity of endocrine disruptors. However, they represent only a relatively small fraction of all potentially hazardous chemicals. A one-sided focus of research and legislation on these compounds would not serve the safety of the population. Numerous compounds compromise other important processes in our cells and organisms, e.g. inhibit membrane transporters, generate oxidative stress, disturb folding of proteins or interfere with signal transduction, which may lead to liver-, kidney-, neuro- or other forms of toxicity. What we need is a balanced strategy that includes the evaluation of all compounds to which we are exposed, and not unrealistically strict legislation for only a small subset of compounds, leaving out the majority of hazardous chemicals.

Back room bureaucrats and a whistle blower

In his exposé, Mr. Garwood for Labtimes writes with some reproach of the uproar and retaliation following the accidental leakage of the EC´s draft proposal (pp. 39-40). In my opinion, the response was justified, because of the apparent underhandedness of members of the EC who planned to draft their one-sided regulations in a back room in Brussels where only lobbyists and selected guests have access. As a common scientist I would never have had a chance to see the draft at a stage where scientific discussion was still possible. Therefore, I am grateful to the whistle blower who made this public. His/her action has avoided an unsatisfactory situation with little chance to discuss and correct obvious errors. Considering the ultra-rich and powerful lobbies and their possibilities to expose individuals in the media, I can fully understand that the whistle blower wishes to stay anonymous. It was also clear to us – the 18 editors of scientific journals – that there would be attempts to compromise our credibility. However, an attempt to simultaneously accuse almost all editors of scientific toxicological journals as biased lacks credibility, and everyone who reads our arguments will understand our motivation. Scientifically, the regulation drafted by the EC members was not acceptable and it is the duty of an upright scientist to express criticism and inform the public.

The players of the game

As a scientist, I have only limited insight into the political games played in the field of endocrine disruptors; this is not my job and my knowledge is based mostly on involuntary and rather unpleasant experiences. However, I am afraid that that Labtimes underestimates the complexity of the game. My firsthand experience arises from the reaction of lobby groups after publication of our review where we reported that current exposure levels of the general population to bisphenol A do not pose health hazards (Hengstler et al., 2011). It was not surprising that some members of the media tried to compromise me (as the corresponding author) by writing of my ‘financial ties to industry’, a fairy tale at best, since my funding from the industry was fantasies in the heads of the reporting journalists. However, I was surprised that such lies were initially only published in the USA, in numerous news magazines and blogs, almost on the same day with almost identical words. Only later, did a few European media find the story interesting. This conundrum was explained to my naïve self by a colleague more familiar with the complexities of politics in science. Bisphenol A, a basic compound for the production of plastic, is produced by more than a million tons per year in Europe. Some companies in the USA started to produce plastic based on compounds other than bisphenol A, but their products are more expensive. To sell their bisphenol A -free products they would of course profit from a situation where products based on bisphenol A are considered hazardous (independent of whether they pose a health risk or not). On the other hand, little is known about the toxicity of compounds replacing bisphenol A in such products – a problem that seems of surprisingly little interest to the media.

Links to Brussels, Zürich and beyond: who dictates the content of Labtimes?

As an editor you easily adopt strange habits. When reading a submitted manuscript, I routinely use a specific software to avoid publishing plagiarized texts in our journal. Sometimes for fun, I also use this software when reading other texts, and – oops! – the present article in Labtimes contains paragraphs that have simply been copied and pasted from another article. The list of 'toxic editors' in Labtimes 3/2014, page 41, was already published in the online magazine *Environmental Health News* (http://www.environmentalhealth news.org/ehs/news/2013/eu-conflict) and the text about myself is an ad verbatim copy and paste reproduction. Even more interesting, and not mentioned in the Labtimes article, is that one of the true authors of the text copied by Labtimes, freelance journalist *Stéphane Horel*, has undisclosed connections, and possibly financial ties, to a campaign agency named *Corporate Europe Observatory (CEO)*, an 'anti-lobby' lobbyist group in Brussels. Coincidentally, according to CEO's website, one of their aims is to 'expose corporate lobbying' and 'increase transparency' (http://corporateeurope.org/). Indeed, it is interesting to note that the idea of transparency only seems applicable to scientists and not to journalists on their own pay roll. Moreover, when looking into the actual funding sources of *Corporate Europe Observatory*, the advocated concept of transparency proves to be only skin deep. A main funding source, as attained from official EU records, is the *Isvara Foundation* which according to the meager information available on its official website (http://www.isvarafoundation.org/) is set up via 'personal donation' by an unnamed individual. Using a popular web-browser, the alledged identity of this individual is however only a few clicks away. Ayman Jallad is a Jordan-based billionaire who made his money by opening the middle-east market for products from the USA, particularly for machines from the American corporation Caterpillar. CEO is also financed by *RH Southern Trust* (http://rhsoutherntrust.org.uk/). Interestingly, a quick visit to their website reveals only one page that tells the reader "The trust funds are fully committed for the foreseeable future. Please do not apply for funding and waste your time and resources and ours. Thank you" and nothing else! Another of CEO's funding source is the *Adessium Foundation*, reportedly based on profits made by Dutch investment bankers before the last economic crisis.

The pieces of the jigsaw puzzle are slowly falling into place, and with them emerges quite a story. We have multi-millionaire businessmen hiding behind foundations with Swiss bank accounts together with bankers supporting lobbyists in Brussels who pay a freelance journalist to publish a black list containing names of European scientists, which makes its way onto the pages of Labtimes by copy-and-paste. As a scientist, I have now entered unknown territory and must leave it to the investigative journalists of Labtimes to put the pieces of this exciting puzzle together! Perhaps more easily answered is why does Labtimes uncritically and one-sidedly copy and paste a list of named scientific editors and reproduce false allegations. Why not simply call one of the 'toxic editors' to hear their side of the story and focus on the actual ongoing scientific debate – an interesting topic indeed?! The journalists should acknowledge that different stakeholders come in many shapes and forms and ask the real questions. Do certain large companies profit when consumers, particularly parents, buy more expensive products because they are labeled 'bisphenol A-free'? Are the replacements of bisphenol A really less hazardous and should the manufacturers of bisphenol A-free products be allowed to profit on the unjustified fear that has been impregnated into the minds of the public with one label and large campaigns? Who profits from ongoing campaigns hidden behind public trusts and NGOs? So many questions! Finding the answers would require careful research and a bit of courage; and it would guarantee powerful enemies. Exposing and blaming a group of scientists is so much easier.

The bone of contention and some self-advertisement

If it's one thing I have learned during my career, it's this: as a scientist you must learn to think positive – always use a situation for self-advertisement! Obviously, the bone of contention for becoming indexed on Labtimes' black list of 'toxic editors' was our review 'Critical evaluation of key evidence on the human health of exposure to bisphenol A' (Hengstler et al., 2011). While the reader of Labtimes atmospherically learns that this article must be very, very evil, its content remains completely untouched. What is this paper about? The goal of the Advisory Committee of the German Society of Toxicology was to summarize human biomonitoring studies on the endocrine disrupting chemical bisphenol A, and to then compare exposure of the general population to doses where we would expect endocrine disrupting effects. We learned that bisphenol A exposure of the general

population is much too low to cause toxic effects. The article represents a careful and comprehensive analysis - please read it! Finally, despite the lobbying and media campaigns, I will continue to enjoy my scientific work and publish the results as they are.

Hengstler JG, Foth H, Gebel T, Kramer PJ, Lilienblum W, Schweinfurth H, Völkel W, Wollin KM, Gundert-Remy U. Critical evaluation of key evidence on the human health hazards of exposure to bisphenol A. Crit Rev Toxicol. 2011 Apr;41(4):263-91.