RECORDS MANAGEMENT SECTION

The University of Edinburgh
Old College
South Bridge
Edinburgh EH8 9YL

Direct Dial 0131 651 4099
Switchboard 0131 650 1000

Email recordsmanagement@ed.ac.uk

17 August 2018

File ref: T3/26/445

Mr Vincent Harmsen

Sent by email: request-495644-2eeedeca@whatdotheyknow.com

Dear Mr Harmsen

Your information request

Thank you for your three emails of 4 July 2018 requesting information about correspondence sent or received by a named member of staff. This letter responds to your request for correspondence between the member of staff and six other named individuals and four named organisations between 1 January 2016 and 1 July 2016.

We apologise again for the delay in responding to your request. As previously explained, we are experiencing a high volume of information requests at this time and a number of staff absences.

Access to information

As you note in your requests, the correspondence relates to 'endocrine disrupting chemicals' or 'endocrine active chemicals'. Information about these chemicals and the regulation of them is environmental information as described in the Environmental Information (Scotland) Regulations 2004 (EIRs). Therefore we are responding to your request in line with EIRs rather than freedom of information legislation. In technical terms this means that the information you requested is exempt under section 39(2) of the Freedom of Information (Scotland) Act 2002 (FOISA). This exemption is subject to the public interest test.

The University acknowledges the public interest in openness and transparency, particularly in relation to the environmental. However, as the public has a statutory right to access environmental information under EIRs, the University considers the public interest in withholding this information under FOISA outweighs the public interest in disclosing it under FOISA.

Correspondence with organisations

You asked for correspondence between Professor Richard Sharpe and the following four named organisations in between 1 January 2016 and 1 July 2016:

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336

- European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC)
- European Risk Forum (ERF)
- International Life Sciences Institute (ILSI)
- Health and Environmental Sciences Institute (HESI)

The University has searched its records and it does not hold any information in relation to this part of your request.

Correspondence with individuals

You asked for correspondence between Professor Richard Sharpe and the following six named individuals between 1 January 2016 and 1 July 2016:

- Alan Boobis
- Colin Berry
- Pat Heslop-Harrison
- Daniel Dietrich
- Wolfgang Dekant
- Helmut Greim

The University does hold information in relation to this part of your request and I enclose some of this information.

You will notice that parts of the documents have been redacted. The redactions have been made either because the correspondence contains individuals' personal information or because disclosure would harm the interests of the individuals. I have also removed any obvious duplicate information that I noticed as I processed the request.

Personal information

Under the Data Protection law, disclosure of personal information must not breach any of the data protection principles in Article 5(1) of the General Data Protection Regulation (GDPR). The individuals had no expectation that their correspondence would be disclosed. Therefore in some cases, disclosing individuals' personal information, including their views and opinions, would breach the principles. The Environmental Information (Scotland) Regulations 2004 does not require us to provide this sort of information as it is exempt under Regulation 11(2).

Third party interests

In some cases I cannot provide information because doing so would, or be likely to, cause substantial prejudice to the interests of the individuals who provided the information voluntarily to the University. The individuals were under no legal obligation to supply this information, and they have not consented to disclosure. The Environmental Information (Scotland) Regulations 2004 do not require us to provide this sort of information as it is exempt under Regulation 10(5)(f).

This exemption is subject to the public interest test. There is clear public interest in the transparent operation of universities, particularly with regard to the role of academic staff in informing public policy. We are therefore pleased to disclose some of the information you have requested. However, there is also public interest in ensuring that academic staff working collaboratively together across different universities can have open and constructive pre-meeting discussions. The public interest would not be served if academic staff felt inhibited in doing so for fear that this type of information would be disclosed against their wishes and contrary to their interests. Therefore the University considers that the public interest in withholding some of the information outweighs the public interest in releasing it.

You stated that the individuals were part of a delegation of scientists that met with the EU Commissioner for Public Health, Vytenis Andriukaitis, in 2016 to discuss the regulation of 'endocrine active chemicals'. You explained that the aim of your request is to create transparency and reconstruct public policy. I therefore also enclose a paper by the seven academics who are the focus of your request. The paper states their views on the subject matter and the same views were communicated to the EU Commissioner. Discussions about the drafting of the paper and draft versions are included within the attached correspondence. The paper is publicly available at https://lra.le.ac.uk/bitstream/2381/38673/2/DietrichHeslopHarrisonEtAlRisk.pdf.

Right to review

If you are dissatisfied with this response, you may ask the University to conduct a review of this decision by contacting the University's Records Management Section (www.ed.ac.uk/records-management/about/contact) in writing (e.g. by letter or email) or in some other recorded form (e.g. audio or video tape). You should describe the original request, explain your grounds for dissatisfaction, and include an address for correspondence. You have 40 working days from receipt of this letter to submit a review request. When the review process has been completed, if you are still dissatisfied, you may appeal to the Scottish Information Commissioner using the guidance at www.itspublicknowledge.info/Appeal. If you do not have access to the Internet, please let me know and I will provide a copy of the relevant web pages.

Privacy notice

The University of Edinburgh's privacy notice, which describes how we use the information you have supplied about yourself and your request, is available on-line at Privacy Notice.

Yours sincerely

Ann-Marie Noble
Information Compliance Manager

Enclosure:

1. Paper – “Allowing pseudoscience into EU risk assessment processes is eroding public trust in science experts and in science as a whole: The bigger picture. Chemico-Biological Interactions”
2. Correspondence

If you require this letter in an alternative format, such as large print or a coloured background, please contact the Records Management Section on 0131 651 4099 or email recordsmanagement@ed.ac.uk

326. **Dietrich DR, Dekant W, Greim H, Heslop-Harrison P, Berry C, Boobis A, Hengstler JG, Sharpe R. 2016.**Editorial: Allowing pseudoscience into EU risk assessment processes is eroding public trust in science experts and in science as a whole: The bigger picture. *Chemico-Biological Interactions* **257:** 1-3. 21 July 2016. http://dx.doi.org/10.1016/j.cbi.2016.07.023

Allowing pseudoscience into EU risk assessment processes is eroding public trust in science experts and in science as a whole: The bigger picture

Daniel R. Dietrich*, Wolfgang Dekant Helmut Greim Pat Heslop-Harrison Sir Colin Berry, Alan Boobis, Jan Hengstler and Richard Sharpe

doi:10.1016/j.cbi.2016.07.023

Imagine we are beamed back into the 12th century and are staying overnight at a country tavern. We by our clothes met with both curiosity and hostility from the tavern regulars. In the middle of the night we are roughly wakened by the owner and some of his men and directly accused of having stolen from one of the regulars after first poisoning him. Despite our protests and the lack of any reasonable proof we are accused of being thieves and murderers and are subjected to trial by ordeal to prove our innocence.

The trial takes the form of having our hands and feet tied and being thrown into the river; if we sink and drown we are obviously guilty, however if we float God has recognized our innocence and lets us live (*judicium Dei*). To a scientist, it seems likely we would drown.

Thankfully, over the past 800 years the development of the judicial system has brought us to the point where an accused is considered innocent until proven guilty. Whether the context is Criminal, where a "beyond reasonable doubt" standard of proof is required, or Civil, where the "balance of probability" is the standard, the burden of proof lies with the accusing party, but in either case is based on objective evidence.

If we were in the tavern now, it would be necessary for the accuser (or his legal representative) to prove, beyond reasonable doubt in this case, that we had poisoned the man and stolen the goods from him. In practice, the onus of the demonstration of proof on the accuser is not restricted to criminal cases but applies to many legal procedures in democracies.

Unfortunately Europe, in the application of its legislation relating to chemicals, is in danger of falling back into the medieval approach. The most recent example is the advocacy group- [1], media- and NGO- [2] driven move to have glyphosate banned, despite solid evidence and multiple expert assessments [3], [4] and [5] that this herbicide is without risk to consumers and is the herbicide with the least negative environmental and health impact. The "public" is being misled by pseudoscientists to believe that the compound is highly dangerous to humans and the environment, a claim that runs counter to the evidence and to expert (critical) assessment of that evidence. The media are rife with quotes from poorly informed and often scientifically less well-informed politicians and others who had analysed their water, urine, beer, and vegetables and reported trace amounts of glyphosate, four-thousand-fold below potentially harmful levels for humans [6]. Under this onslaught of misinformation, decision-makers may prefer to disregard evidence-based data that contradict a precautionary viewpoint.

In a similarly misleading vein, there have been seemingly endless discussions about "endocrine disrupters" and their postulated human health effects, based on association studies. For these to be causal, they require us to accept that extremely low-level exposures cause effects in humans, whereas most of the experimental data indicate such exposures are without effect. Most recently, the debate on "endocrine disruptors" has shifted focus to the concept that doses of these compounds below their 'no-observed-effect level' (in animal and in vitro studies) can cause adverse effects (so-called non-monotonic dose-response curves) [7], even though the evidence that endocrine systems can be perturbed in this way just does not exist; indeed, there is ample human data on abnormally low hormone exposures that tell us this is not how such systems work. However, this detailed evidence is being ignored and the most prominent proponents of endocrine disruption-mediated human health effects are now using this to argue that hazard identification alone is necessary for regulatory purposes [7]. However, hazard characterization, including potency evaluation, and exposure assessment are the principles on which the protection of humans from adverse effects of environmental chemicals is undertaken, and has proved to be very effective. This is also the consensus approach recommended for endocrine disrupters [8]. This is a logical path that demands detailed evidence gathering and weighing of the science that then forms the basis of the information on which the legal process is based. Do we want to throw this trusted and tried process away?

Relying on hazard identification alone relieves the "accusing party" of the burden of proof (i.e. obtaining the evidence) and allows for endless new allegations of potential effects on human health, for which evidence is not required – it is simply assumed to be present. We don't think that any of us would like our doctors to use similar approaches for looking after our health; no, doctors want evidence of what is wrong so that they can target it specifically to restore normal health. The consequences of doing otherwise can be fatal [9]. What about the wider implications of a hazard-based approach? Will we ban cars or aeroplanes because they are clearly hazardous, or oxygen and water because they are hazardous to human health? In this regard, the putative hazard has now changed; now endocrine disrupters are being advocated as a prime cause for obesity and type II diabetes [10]. How credible is this? We know that obesity and type II diabetes can often be corrected by reducing appetite, food intake and additional exercise, difficult though this may be, but what evidence is there that reducing exposure to so-called endocrine-disrupting 'obesogens' can reduce the incidence of obesity and type II diabetes? There is no such evidence, yet we are asked to believe that 'obesogens' are an important human health risk and because of this should be the major focus of future research and regulation efforts in this area [11]. Like medieval justice, the accusing (scaremongering) party never faces the consequences of their accusations or allegations. On the contrary, the accusing party will benefit from the uncertainty introduced. However, any damages incurred, whether these be to human health, through unintended consequences, society or the economy [12], are common good and not the responsibility of the accusing party.

These trends are testimony to the apparent movement to overturn the use of verifiable facts and evidence-based risk assessment in regulation and politics. Further, they undermine the concept of burden of proof, central to our judicial systems, developed over the past centuries. Indeed, arguably, undue emphasis on hazard identification alone has already found its way into some EU chemicals legislation, ignoring more informative weight of evidence and risk assessment approaches, based on sound science, that have served society well over the years. Indeed, it is not merely chemical risk assessment that is currently at stake, it is science as a whole. Reports of the lack of reproducibility of published scientific findings [13] and public

disagreement among scientists (and pseudoscientists) on the dangers of compounds, despite good evidence to the contrary, erodes public trust in scientists, and science as a whole – few without scientific training realize that science progresses by the detection of, and subsequent elimination of, errors. This is why acting on findings in isolation, all too common an occurrence today, is an unsound strategy. Perhaps equally important, failure of decision makers to recognise this, leads to unnecessarily restrictive and potentially damaging regulation.

Arguments such as those we voice above are now routinely attacked, sometimes with blatant disregard for the facts and scientific evidence provided, on the basis that 'this is what the chemical industry wants, so these authors must be speaking on behalf of that industry' or worse 'these scientist must be paid by industry, thus are corrupt and therefore trivialize hazards' [14], [15] and [16]. This is not the case! But such unwarranted accusations of conflicts of interest in the absence of robust scientific evidence to support their assertions [17] and [18], have become the mode du jour in such disputes [19]. In some cases, this has resulted in conflict of interest policies that could lead to an overall lack of scientific balance among the group of experts considered not to be thus conflicted. A number of NGO's have an interest in maintaining public concerns about specific issues, and indeed may rely on such concerns for charitable donations. Hence, there is a strong motivation to disregard data that contradicts a precautionary point of view. Regrettably, some scientists appear to put the need to obtain research funding above the objective appraisal of the evidence. Unlike potential financial bias, these possible conflicts of interest [19] are rarely considered in such debates. But these attitudes can distort opinions provided to organisations such as EFSA, WHO, WHO/IARC, EPA and others. The consequence is that scientific argument and weight of evidence that might disagree with the initial allegation or accusation, can be undermined. This process damages the credibility of governmental organizations and the well-developed processes that are the very foundations of our society and our well-being. Simply following the discussion on the alleged effects of MMR vaccine on autism provides ample evidence of this [20].

For sure, the chemical industry has every interest in protecting its products and profits, and will lobby to this effect. However, to ensure longevity of their products and to avoid litigation, industry is as interested in an evidence-based approach to risk assessment as we are, and collecting the evidence is a huge and expensive task that industry has to undertake, as is mandated by the regulating authorities, to justify the safety of its products. Is it sensible to say "No" to such evidence and instead to assume that if a chemical is hazardous it should be banned, irrespective of how low the concentrations are that we, the public, are exposed to? In essence, we would be saying that an evidence-based approach is not as good as a presumptive approach based on no evidence. This is to throw away scientific principles and good practice and to replace it with something akin to witchcraft.

It is time to end the influence of pseudoscience and pseudoscientists, including some self-appointed public advocacy groups, on European legislation. We advocate this not because of what the chemical industry may want or not want, but because it is the most credible, scientifically-sound and societally-beneficial solution, utilising well-defined and transparent processes of evidence gathering, weighing and risk assessment that should be at the core of decisions that support all legal procedures. This system is what has been developed, tried and tested in Europe over the years and is demonstrably protective of human health. Thus this surely should have been the aim of the European Commission in its decision on the criteria for EDCs in the regulation of biocides and pesticides [21].

References

[1] A.T.W.I Action, Protect Our Health, Stop Monsanto (2016)

[2] P.A.N. Europe Environmental NGOs Press Charges Against Monsanto German government institute and European Food Safety Authority (2016)

[3] J. FAO/WHO Pesticide residues in food 2016 J. FAO/WHO (Ed.), Special Session of the Joint FAO/WHO Meeting on Pesticide Residues, JMPR FAO/WHO (2016), p. 123

[4] B.f. Risikobewertung The BfR Has Finalised its Draft Report for the Re-evaluation of Glyphosate BfR, Berlin (2015)

[5] E.F.S. Authority Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate EFSA J., 13 (2015), pp. 4302–4408

[6] B.f. Risikobewertung Glyphosate in Urine – Concentrations Are Far below the Range Indicating a Potential Health Hazard Opinion No. 014/2013Berlin (2013)

[7] E. News Society Leaders Help Inform International EDC Regulations (2016)

[8] R. Solecki, A. Kortenkamp, Å. Bergman, I. Chahoud, G.H. Degen, D.R. Dietrich, H. Greim, H. Håkansson, U. Hass, T. Husoy, M. Jacobs, S. Jobling, A. Mantovani, P. Marx-Stoelting, A. Piersma, R. Slama, R. Stahlmann, M. van den Berg, R.T. Zoeller, A.R. Boobis Scientific principles for the identification of endocrine disrupting chemicals – a consensus statement Environ. Health Perspect. (2016) (in press)

[9] P. Posadzki, A. Alotaibi, E. Ernst Adverse effects of homeopathy: a systematic review of published case reports and case series. Int. J. Clin. Pract., 66 (2012), pp. 1178–1188

[10] J. Legler, T. Fletcher, E. Govarts, M. Porta, B. Blumberg, J.J. Heindel, L. Trasande Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union J. Clin. Endocrinol. Metab., 100 (2015), pp. 1278–1288

[11] J.J. Heindel et al. Parma consensus statement on metabolic disruptors Environ. Health, 14 (2015), p. 54 http://dx.doi.org/10.1186/s12940-015-0042-7

[12] D.R. Dietrich, W. Dekant, H. Greim, P. Heslop-Harrison, C. Berry, A. Boobis, J. Hengstler, R.M. Sharpe Don't mar legislation with pseudoscience. Nature, 535 (2016), p. 355

[13] M. Baker 1,500 scientists lift the lid on reproducibility. Nature, 533 (2016), pp. 452–454

[14] J. Garwood Do toxic editors trivialise hidden hazards? Lab. Times, 3 (2014), pp. 39–42

[15] S. Horel A Toxic Affair: Season Finale Corporate Europe Observatory (2016)

[16] S. Horel, B. Bienkowsi Special Report: Scientists Critical of EU Chemical Policy Have Industry Ties (2013) Environmental Health News

[17] R. Slama, J.P. Bourguignon, B. Demeneix, R. Ivell, G. Panzica, A. Kortenkamp, T. Zoeller Scientific issues relevant to setting regulatory criteria to identify endocrine disrupting substances in the European Union Environ. Health Perspect. (2016) http://dx.doi.org/10.1289/EHP217

[18] P. Grandjean, D. Ozonoff Transparency and translation of science in a modern world Environ. Health, 12 (2013), p. 70

[19] D.R. Dietrich, J.G. Hengstler Conflict of interest statements: current dilemma and a possible way forward Arch. Toxicol. (2016) http://dx.doi.org/10.1007/s00204-016-1783-y

[20] P. Hobson-West 'Trusting blindly can be the biggest risk of all': organised resistance to childhood vaccination in the UK Sociol. Health Illn., 29 (2007), pp. 198–215

[21] E. Commission Press Release 15.06.2016: Commission Presents Scientific Criteria to Identify Endocrine Disruptors in the Pesticides and Biocides Areas European Commission, Bruxelles (2016)

*Corresponding author.

Daniel R. Dietrich Human and Environmental Toxicology, University of Konstanz, 78457 Konstanz, Germany

Wolfgang Dekant Department of Toxicology, University of Wuerzburg, Versbacher Str. 9, 97078 Wuerzburg, Germany

Helmut Greim Technical University of Munich, Hohenbachernstr. 15-17, 85354 Freising-Weihenstephan, Germany

Pat Heslop-Harrison Department of Genetics, University Road, University of Leicester, LE1 7RH, United Kingdom

Sir Colin Berry Queen Mary – Pathology, Queen Mary, London, London E1 4NS, United Kingdom

Alan Boobis Department of Medicine, Hammersmith Campus, Imperial College London, London W12 0NN, United Kingdom

Jan Hengstler Department of Toxicology, IfADo, Ardeystrasse 67, 44139 Dortmund, Germany

Richard Sharpe MRC Centre for Reproductive Health, 47 Little France Crescent, University of Edinburgh, Edinburgh EH16 4TJ United Kingdom

Available online 21 July 2016

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Friday, 1 July 2016 at 08:53
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, [redacted] Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>, [redacted] 'Helmut Greim' [redacted], Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>,"Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>
Subject: Re: GMO

Me also

Richard

From: <Boobis>, Alan R <x.xxxxxx@xxxxxxxx.xx.xx >
Date: Friday, 1 July 2016 08:19
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, [redacted] Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >, [redacted] 'Helmut Greim' [redacted], Colin Berry [redacted], "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, Information Services <x.xxxxxx@xx.xx.xx >
Subject: RE: GMO

Dan

I have signed the petition. Very pleased that this is possible.

Best wishes,

Alan

From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx]
Sent: 01 July 2016 08:14
To: [redacted]

[redacted] Wolfgang Dekant <[redacted]>; [redacted] 'Helmut Greim' [redacted]; Colin Berry [redacted]; Heslop-Harrison, Pat (Prof.) <[redacted]>; SHARPE Richard <[redacted]>; Boobis, Alan R <[redacted]>

Subject: FW: GMO

Dear colleagues

[redacted]

Best

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: [redacted]
http://www.umwelttoxikologie.uni-konstanz.de

Von: [redacted]
Datum: Freitag, 1. Juli 2016 02:58
An: Daniel Dietrich <[redacted]>
Betreff: GMO

Daniel:

[redacted]

[redacted]

[redacted]

From: SHARPE Richard <r.sharpe@ed.ac.uk>
Date: Monday, 20 June 2016 at 08:38
To: Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>, Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, Colin Berry <colin@sircolinberry.co.uk>
Cc: Pat Heslop-Harrison <phh4@leicester.ac.uk>, Alan R Boobis <a.boobis@imperial.ac.uk>, [redacted] Helmut Greim [redacted]
Subject: Re: Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science

Not me, I was aiming to send a reminder this week.
Richard

From: Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>
Date: Monday, 20 June 2016 08:21
To: Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, Colin Berry <colin@sircolinberry.co.uk>
Cc: Pat Heslop-Harrison <phh4@leicester.ac.uk>, Alan R Boobis <a.boobis@imperial.ac.uk>, SHARPE Richard <r.sharpe@ed.ac.uk>, [redacted] Helmut Greim [redacted]
Subject: Re: Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science

Dear all, [redacted]

wd

Am 17.06.16 um 08:34 schrieb Daniel Dietrich:

[redacted]

[redacted]

Thanks
Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz

Universitätsstrasse. 10
D-78457 Konstanz, Germany

Telephone: [redacted]

Secretary)
Portable-Phone: [redacted]
Fax:
email: Daniel.Dietrich@uni-konstanz.de
http://www.umwelttoxikologie.uni-konstanz.de

Von: Colin Berry <colin@sircolinberry.co.uk>
Datum: Freitag, 17. Juni 2016 08:18
An: Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>, Pat Heslop-Harrison <phh4@leicester.ac.uk>, Alan R Boobis <a.boobis@imperial.ac.uk>, SHARPE Richard <r.sharpe@ed.ac.uk>, [redacted], Helmut Greim [redacted]
Betreff: RE: Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science

NO, we were not. In the Nature/Science editorial system there is a breath-taking scrupulousness about balance and anything which looks like a polemic is shunned. That is way I was always against attributing motives etc.
If we want to be aggressive about it (I don't argue with that , our "opponents" are) we should look at a different level of publication – like New Scientist, say.

Colin

From: Daniel Dietrich [mailto:daniel.Dietrich@uni-konstanz.de]
Sent: Thursday, June 16, 2016 8:25 PM
To: Colin Berry; Wolfgang Dekant; Pat Heslop-Harrison; Alan R Boobis; SHARPE Richard; [redacted]; Helmut Greim
Subject: Fwd: Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science

[redacted]

Best
Dan

Von meinem iPhone gesendet

Anfang der weitergeleiteten E-Mail:

> **Von:** [redacted]
> **Datum:** 16. Juni 2016 20:50:52 MESZ
> **An:** 'Daniel Dietrich' <Daniel.Dietrich@uni-konstanz.de>
> **Kopie:** [redacted]
> **Betreff: RE: Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science**
>
> [redacted]
>
> [redacted]
>
> [redacted]
>
> [redacted]
>
> ---
>
> **From:** Daniel Dietrich [mailto:Daniel.Dietrich@uni-konstanz.de]
> **Sent:** Wednesday, June 15, 2016 9:00 AM
> **To:** [redacted]
> **Cc:** [redacted]
> **Subject:** Press release by EC commission on endocrine disrupter Criteria and a Policy Forum manuscript for submission to Science
> **Importance:** High

Dear [redacted]

[redacted]

Sincerely

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

--

Prof. Dr. Wolfgang Dekant
Department of Toxicology, University of Wuerzburg
Versb[redacted]7078 Wuerzburg, Germany
Tel. [redacted]
Fax:
Mobil: [redacted]

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Thursday, 16 June 2016 at 10:41
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Subject: Re: EDC announcement

Hi Dan

Coi attached.

Good luck

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Wednesday, 15 June 2016 14:14
To: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Cc: Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>, [redacted] "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Greim, Helmut" [redacted], "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>
Subject: Re: EDC announcement

[redacted]

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: SHARPE Richard <x.xxxxxx@xx.xx.xx >
Datum: Mittwoch, 15. Juni 2016 14:52
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx >, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, [redacted], Colin Berry [redacted]
Betreff: Re: EDC announcement

Thanks Dan, that's more or less what I concluded, but I always find such pronouncements to be so obtuse (because of trying to please and appease all), that I'm never sure that I get the correct message. What did ring through was the emphasis throughout that scientific method and scientific evidence would be the drivers, which sounds very Andriukaitis-infuenced (so maybe we had some effect).

Dan, what did you mean by your last sentence?

BW

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Wednesday, 15 June 2016 13:45
To: SHARPE Richard <x.xxxxxx@xx.xx.xx >, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx >, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, [redacted] Colin Berry [redacted]
Subject: Re: EDC announcement

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: SHARPE Richard <x.xxxxxx@xx.xx.xx >
Datum: Mittwoch, 15. Juni 2016 14:34
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx >, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxx.xx.xx >, [redacted], Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>
Betreff: Re: EDC announcement

I need some of you more used to EC-language to interpret this for me, as it reads a bit self-contradictorily (to me) - i.e. everyones a winner!

http://europa.eu/rapid/press-release_IP-16-2152_en.htm
The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.
The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.

Science /AAAS Authorship Form and Statement of Conflicts of Interest

Author Name: Richard Sharpe

Manuscript# _____

Title Allowing pseudoscience into EU risk assessment processes is eroding public trust in science experts and in science as a whole

Each author must complete the following form prior to acceptance of their paper:

I. Authorship:

The authorship policies of *Science* follow those recommended by the report "On Being a Scientist", 3rd Edition, published by the US National Academy of Sciences (http://www.nap.edu/catalog/12192.html). In particular, we note that "just providing laboratory space for a project or furnishing a sample used in the research is not sufficient to be included as an author, although such contributions... may be recognized in a separate acknowledgement section."

In order to meet our requirements for authorship of a paper, you must have participated significantly in the reported research or writing of the paper. Please affirm that you meet these criteria by indicating your contribution to all of the following descriptions (circle from 0% responsible to 100% responsible): I…

Authorship Activity	Level of participation
Participated in the design and/or interpretation of the reported experiments or results.	0 20 40 60 80 100%
Participated in the acquisition and/or analysis of data. State Which data: _____	0 20 40 60 80 100%
Participated in drafting and/or revising the manuscript.	0 20 40 60 80 100%
Was primarily responsible for a particular, specialized role in the research, e.g. statistical analysis, crystallography, preparation of cell lines; please briefly state which: _____	0 20 40 60 80 100%
Provided administrative, technical or supervisory support.	0 20 40 60 80 100%

The senior author from each lab or group must answer this question: I have personally checked all the original data that was generated by my lab or group:

✓ Yes ____Not applicable; I am not the senior author or lab head.

If yes, these data are presented in these figures and tables (including the Supporting Online Material):

_____.

I have or will review the revised manuscript and approve of its resubmission to Science for publication.

✓ Yes ____No

If my university or institution has a separate publication license that applies to me (as at e.g.,Harvard, MIT, Open University) I have applied for a waiver. This does not apply to waivers for the U.S. or other government employees (click NA)

✓ Yes ____ There are no publication policies or restrictions limiting my ability to grant exclusive publication rights to AAAS or not applicable as I am employed by the U.S. or other governments.

II. Data sharing:

I affirm that all data necessary for a reader of Science to understand and evaluate the conclusions of the paper will be archived in an approved database and made available to any reader.

____Yes ____No

III. Materials sharing:

After publication, all reasonable requests for materials and data must be fulfilled. I will abide by this responsibility:

✓ Yes

Science must be informed of any restrictions on sharing of materials [Materials Transfer Agreements (MTA's) or patents, for example] applying to materials used in the reported research.

✓ No, there are no MTA's

____Yes—information on MTA's is described below.

IV. Conflict of Interest:

Science has a primary responsibility to its readers and to the public to provide in its pages clear and unbiased scientific results and analyses. We think that our readers should be informed of additional relationships of our authors that could pose a conflict of interest. Thus, for readers to evaluate the data and opinions presented in Science, they must be informed of financial and other interests of our authors that may be at odds with unbiased presentation of data or analysis.

Therefore, *Science* believes that manuscripts (Brevia, Essays, Perspectives, Policy Forums, Reports, Research Articles, Reviews, and Viewpoints) should be accompanied by clear disclosures from all authors of their affiliations, funding sources, or financial holdings that might raise questions about possible sources of bias. Disclosure is accomplished in three ways:

First, by a complete listing of the current institutional affiliations of the authors.

This list must include academic as well as corporate and other industrial affiliations. As the editors deem appropriate, items in this list will be included in the author affiliations printed in the manuscript. Please indicate below:

✓ All my affiliations are listed on the title page of the paper.

Additional affiliations not on the title page are:

Second, through the acknowledgment of all financial contributions to the work being reported, including contributions "in kind." All funding sources will be listed in the published manuscript. Please indicate below:

✓ All my funding sources for this study are listed in the acknowledgement section of the paper.
____ Additional funding sources not noted in the manuscript are:

Third, through the execution of a statement disclosing to the Editors all financial holdings, professional affiliations, advisory positions, board memberships, patent holdings and the like that might bear a relationship to the subject matter of the contribution. The Editors will determine whether the material disclosed to them should be published as part of the article.

The following are declarable relationships: **Financial**: Significant financial interest (equity holdings or stock options) in any corporate entity dealing with the material or the subject matter of this contribution. Please disclose the entity and the nature and amount of the holding:

✓ None

____I have a financial relationship, as described below.

Management/Advisory affiliations: Within the last 3 years, status as an officer, a member of the Board, or a member of an Advisory Committee of any entity engaged in activity related to the subject matter of this contribution. Please disclose the nature of these relationships and the financial arrangements.

_____None

✓ I have a management/advisory relationship, as described below:

*Current: Member of Royal Society of Chemistry Expert Panel on development of a study design to address potential responses and adverse effects at very low dose exposure to endocrine disrupting chemicals

*2013-2015 Member of the European Commission Scientific committee on emerging and newly identified health risks (SCENIHR): use of phthalates in medical devices

Paid Consulting: Within the last 3 years, receipt of consulting fees, honoraria, speaking fees, or expert testimony fees from entities that have a financial interest in the results and materials of this study. Please enumerate.

_____None

✓ I have a consulting relationship, as described below:

2011-2013: Member of an external expert Science Advisory Panel for BASF on azole compounds and their endocrine disrupting properties (consultancy fees)

Patents: A planned, pending, or awarded patent on this work by any of the authors or their institutions. Please explain.

✓ None

____I or my institution has a patent related to this work, as described below

Declaration:I declare that I have read Science's full Conflict of Interest Policy and have disclosed all declarable relationships as defined therein, if any.

This form was submitted on 16th June 2016

Signature 

Name Richard Sharpe

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Wednesday, 15 June 2016 at 14:19
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Subject: Re: EDC announcement

Dan I sent my COI yesterday, but here it is again.
Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Wednesday, 15 June 2016 14:14
To: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Cc: Colin Berry [redacted], "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Greim, Helmut" [redacted], "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>
Subject: Re: EDC announcement

[redacted]

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Datum: Mittwoch, 15. Juni 2016 14:52
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted]

[redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted], Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
Betreff: Re: EDC announcement

Thanks Dan, that's more or less what I concluded, but I always find such pronouncements to be so obtuse (because of trying to please and appease all), that I'm never sure that I get the correct message. What did ring through was the emphasis throughout that scientific method and scientific evidence would be the drivers, which sounds very Andriukaitis-infuenced (so maybe we had some effect).

Dan, what did you mean by your last sentence?

BW

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Wednesday, 15 June 2016 13:45
To: SHARPE Richard <x.xxxxxx@xx.xx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted], Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
Subject: Re: EDC announcement

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Datum: Mittwoch, 15. Juni 2016 14:34
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted]

[redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, [redacted], Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>

Betreff: Re: EDC announcement

I need some of you more used to EC-language to interpret this for me, as it reads a bit self-contradictorily (to me) - i.e. everyones a winner!

http://europa.eu/rapid/press-release_IP-16-2152_en.htm

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.
The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005336.

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Wednesday, 15 June 2016 at 14:12
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted] Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
Subject: Re: EDC announcement

I guess that many different things can be read into the wording, and ultimately it will all depend on what actions result. The battlefield will clearly be on the pesticides/biocides and what derogations are allowed and what will determine these key decision-points.
In that regard it seems that not much has changed, although the wording may indicate that derogation may involve more of an uphill battle than beforehand?
I am told by a journalist that environmental groups are 'already calling foul on the plan', but presumably that's because there is still a theoretical escape door.

Richard

From: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
Date: Wednesday, 15 June 2016 13:52
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, SHARPE Richard <x.xxxxxx@xx.xx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted], Colin Berry [redacted]
Subject: Re: EDC announcement

I am not so sure that this is good news. More detail can be found at http://ec.europa.eu/health/endocrine_disruptors/docs/com_2016_350_en.pdf and it is not encouraging.

Best wishes,

Alan

[redacted]

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Tuesday, 14 June 2016 at 11:44
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted] Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>
Subject: Re: Perspectives / Correspondence for The LAncet

Hi Dan

My COI form also attached.
Thanks for your lead and hard work on this.

BW

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Monday, 13 June 2016 16:13
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, SHARPE Richard <x.xxxxxx@xx.xx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted], Colin Berry [redacted]
Subject: Re: Perspectives / Correspondence for The LAncet

All

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz

Universitätsstrasse. 10
D-78457 Konstanz, Germany

Telephone: [redacted]

Portable-Phone: [redacted]
Fax:

email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
Datum: Montag, 13. Juni 2016 16:55
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, SHARPE Richard <x.xxxxxx@xx.xx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted] Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
Betreff: Re: Perspectives / Correspondence for The LAncet

Dan

In the interests of full disclosure, I now try to be comprehensive in such declarations. Please see attached.

Best wishes,

Alan

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Sent: 13 June 2016 15:35
To: Greim, Helmut; Wolfgang Dekant; Boobis, Alan R; SHARPE Richard; Heslop-Harrison, Pat (Prof.); [redacted]; Colin Berry
Subject: FW: Perspectives / Correspondence for The LAncet

Dear all

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT

Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz

Universitätsstrasse. 10
D-78457 Konstanz, Germany

Telephone:

Portable-Phone:
Fax:
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von:
Datum: Montag, 13. Juni 2016 15:11
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Betreff: RE: Perspectives / Correspondence for The LAncet

Dear Prof. Dietrich,

From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx]
Sent: 13 June 2016 10:04
To:
Subject: Perspectives / Correspondence for The LAncet
Importance: High

[redacted]

Dan Dietrich

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz

Universitätsstrasse. 10
D-78457 Konstanz, Germany

Telephone: [redacted]

Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Saturday, 11 June 2016 at 22:19
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
Cc: Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>,"Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, [redacted]
Subject: Re: in case you've not seen

I'm not suggesting this for inclusion/modification of the editorial/opinion piece, but I wondered tonight whether we ought not at some stage to pose to journalists the relative financial impediments that could result from industry getting it wrong with one of their products (e.g. Because of EDC activity) as opposed to the green/NGO bodies getting it wrong with their support for widespread banning (or of a specific compound). You don't need me to tell you the relative sums. I know we touch on this in our editorial, but it is indirect and very much 'not in your face'. In terms of trying to get across the relative differences in accountability/cost, it makes no difference to NGOs if they're wrong but industry would pay a huge price. So the relative importance of 'getting it right' is completely different.

I shirk from voicing such arguments because it makes you sound like a spokesperson for industry, but if our editorial does result in the sorts of attacks that we might predict, it would be one argument to wield in front of a good scientific journalist – ask them to ask the NGOs how they would make themselves accountable. Indeed, are they accountable in any way other than to their like-minded supporters? I don't think they are, yet they gets lots of money form EC.

I'd be interested to hear your experience in such issues and whether this is a weapon to fight with or one that can only self-harm.

BW

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Saturday, 11 June 2016 19:00
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >
Cc: Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx >, Information Services <x.xxxxxx@xx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, [redacted]
Subject: Re: in case you've not seen

[redacted]

[redacted]
Dan

Von meinem iPhone gesendet

Am 11.06.2016 um 18:55 schrieb "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>:

> Dan
>
> I suggest '....attacked, sometimes with clear ...'
>
> Best wishes,
>
> Alan
>
> Sent from my iPad
>
> On 11 Jun 2016, at 15:46, Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de> wrote:
>
> [redacted]
> Dan
>
> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
> Professor of Human and Environmental Toxicology,
> Faculty of Biology, University of Konstanz
> P.O. Box 622
> Universitätsstrasse 10
> D-78457 Konstanz, Germany
>
> Telephone: [redacted]
> Portable-Phone: [redacted]
> Fax: [redacted]
> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
> http://www.umwelttoxikologie.uni-konstanz.de
>
> ---
>
> **Von:** "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
> **Datum:** Samstag, 11. Juni 2016 16:21
> **An:** Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>
> **Cc:** Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, "Greim, Helmut" [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>, SHARPE Richard

<x.xxxxxx@xx.xx.xx >, "Heslop-Harrison, Pat (Prof.)"
<xxxx@xxxxxxxxx.xx.xx >, [redacted]
Betreff: Re: in case you've not seen

I agree we should not attribute motive. However in several articles in the press there has been 'clear disregard' for the evidence, as documented in a number of emails with the journalists in question. This is more than just a crusade on their part but a wilful misrepresentation of information provided in advance of publication.

But we should mix up the views of scientists with whom we disagree from those of journalists sympathetic to these views.

Best wishes,

Alan

Sent from my iPad

On 11 Jun 2016, at 14:58, Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx> wrote:

> Let's not have "malicious" we are expressing opinions about the motives of others again. What about "with apparent disregard for the scientific evidence, which has been carefully considered by those jealous of their scientific reputation". Or something like that
> Colin
>
> ---
>
> **From:** Daniel Dietrich [mailto:Daniel.Dietrich@uni-konstanz.de]
> **Sent:** Saturday, June 11, 2016 2:05 PM
> **To:** Greim, Helmut; Wolfgang Dekant
> **Cc:** Boobis, Alan R; SHARPE Richard; Colin Berry; Heslop-Harrison, Pat (Prof.); [redacted]
> **Subject:** Re: in case you've not seen
>
> Dear ALL
>
> [redacted]
>
> Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT

Professor of Human and Environmental Toxicology, Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Am 11.06.2016 12:16 schrieb "Greim, Helmut" unter [redacted]

> [redacted]
> Helmut
>
> Am 11.06.2016 09:48, schrieb Wolfgang Dekant:
>
> > Dear all, [redacted]
> > wd
> > Am 10.06.16 um 16:03 schrieb Boobis, Alan R:
> >
> > > Richard
> > > I share your feelings on this.
> > > Even more frustrating is that I responded in detail on a number of
> > > these issues to [redacted] and [redacted] then went ahead

published
contradictory interpretations anyway. An example is the claim that
what we presented to the Commissioner contradicted the Berlin
consensus, yet it was exactly what was in para 24 of that document,
as agreed by all present.
Best wishes,
Alan
Sent from my iPad
On 10 Jun 2016, at 09:45, SHARPE Richard <x.xxxxxx@xx.xx.xx > wrote:

> Dear fellow grizzleds
> It seems increasingly to me, that the 'other camp' if I can call
> them that, not only speak a different language to any that I
> understand, but cannot possibly countenance the idea that
> different scientists may justifiably have different views, without
> this being explained by a devilish conspiracy (unless there's
> something that you other guys are not telling me!!). It seems to
> me that one side is dealing with science the other with science
> fiction, and [redacted] is clearly an enthusiast of the fiction
> side. Remarkable but utterly depressing to see science made to
> look so foolish and stupid.
> Richard
> From: <Boobis>, Alan R <x.xxxxxx@xxxxxxxx.xx.xx >
> Date: Friday, 10 June 2016 13:21
> To: Information Services <x.xxxxxx@xx.xx.xx >, "Greim, Helmut"
> [redacted], Daniel Dietrich
> <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
> Cc: Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>, "Heslop-Harrison, Pat
> (Prof.)" <xxxx@xxxxxxxxx.xx.xx>, Wolfgang Dekant
> <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >, [redacted]
> [redacted]

> > > Subject: Re: in case you've not seen
> > > And for more detail se

http://corporateeurope.org/sites/default/files/attachments/ceo-edc_addendum-june-5.pdf

> > > [1]
> > > Best wishes,
> > > Alan
> > > ---
> > > FROM: SHARPE Richard <x.xxxxxx@xx.xx.xx >
> > > SENT: 10 June 2016 12:35
> > > TO: Greim, Helmut; Daniel Dietrich
> > > CC: Colin Berry; Boobis, Alan R; Heslop-Harrison,
> > > Pat (Prof.);
> > > Wolfgang Dekant; [redacted]
> > > SUBJECT: Re: in case you've not seen

https://www.theparliamentmagazine.eu/articles/news/endocrine-disruptors-com

> > > mission-breach-eu-law-says-parliament
> > > --
> > > The University of Edinburgh is a charitable body,
> > > registered in
> > > Scotland, with registration number SC005336.

--
Prof. Dr. Wolfgang Dekant
Department of Toxicology
University of Wuerzburg
Versbacher Str. 9
97078 Wuerzburg
Tel.: [redacted]
Fax: [redacted]
Links:
---
[1]
http://corporateeurope.org/sites/default/files/attachments/ceo-edc_addendum-june-5.pdf

[redacted]

From: SHARPE Richard <r.sharpe@ed.ac.uk>
Date: Friday, 10 June 2016 at 09:54
To: Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, Colin Berry <colin@sircolinberry.co.uk>, "Boobis, Alan R" <a.boobis@imperial.ac.uk>, "Greim, Helmut" [redacted]
Cc: "Heslop-Harrison, Pat (Prof.)" <phh4@leicester.ac.uk>, Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>, [redacted]
Subject: Re: Last version before we submit

Couple of minor typographical changes but otherwise good to go in my opinion. I think Alan's changes have been a big help.

Best wishes

Richard

From: Daniel Dietrich [redacted]
Date: Friday, 10 June 2016 08:25
To: Colin Berry <colin@sircolinberry.co.uk>, "Boobis, Alan R" <a.boobis@imperial.ac.uk>, "Greim, Helmut" [redacted]
Cc: Information Services <R.Sharpe@ed.ac.uk>, "Heslop-Harrison, Pat (Prof.)" <phh4@leicester.ac.uk>, Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>, [redacted]
Subject: Last version before we submit

Dear ALL

[redacted]

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
Datum: Freitag, 10. Juni 2016 06:25
An: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx >, "Greim, Helmut" [redacted], Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Cc: SHARPE Richard <x.xxxxxx@xx.xx.xx >, "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx >, Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >, [redacted]
Betreff: RE: Editorial on risk and regulation comments

I like Alans bit on conflicts and I agree about salt, as I said before .I don't think it adds much and will be picked on by some.
Colin

From: Boobis, Alan R [mailto:x.xxxxxx@xxxxxxxx.xx.xx]
Sent: Thursday, June 9, 2016 10:07 PM
To: Greim, Helmut; Daniel Dietrich
Cc: SHARPE Richard; Colin Berry; Heslop-Harrison, Pat (Prof.); Wolfgang Dekant; [redacted]
Subject: Re: Editorial on risk and regulation comments

Dan

Building on what has gone before, I am providing some suggestions for the text. In particular, I have expanded slightly the section on conflict of interest.

Best wishes,

Alan

From: Greim, Helmut [redacted]

Sent: 09 June 2016 13:23
To: Daniel Dietrich
Cc: Boobis, Alan R; SHARPE Richard; Colin Berry; Heslop-Harrison, Pat (Prof.); Wolfgang Dekant; [redacted]
Subject: Re: Editorial on risk and regulation comments

Dear all,

[redacted]

Helmut

Am 09.06.2016 13:57, schrieb Daniel Dietrich:
> Dear Alan (and others)
> [redacted]
> Dan
> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
> Professor of Human and Environmental Toxicology,
> Faculty of Biology, University of Konstanz
>
> Universitätsstrasse. 10
> D-78457 Konstanz, Germany
>
> Telephone: [redacted]
> [redacted]
> Portable-Phone: [redacted]
> Fax: [redacted]
> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
> http://www.umwelttoxikologie.uni-konstanz.de
>
>
>
>
>
>
>
> Am 09.06.16 13:16 schrieb "Boobis, Alan R" unter
> <x.xxxxxx@xxxxxxxx.xx.xx >:
>
>> Dan
>>

>> I am [redacted] but will send comments by end of tomorrow at
>> latest.
>>
>> Best wishes,
>>
>> Alan
>>
>> Sent from my iPad
>>
>>> On 9 Jun 2016, at 07:13, Daniel Dietrich
>>> <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx> wrote:
>>>
>>> Hi Richard
>>> [redacted]
>>> Best
>>> Dan
>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>> Professor of Human and Environmental Toxicology,
>>> Faculty of Biology, University of Konstanz
>>>
>>> Universitätsstrasse. 10
>>> D-78457 Konstanz, Germany
>>>
>>> Telephone: [redacted]
>>> [redacted]
>>> Portable-Phone: [redacted]
>>> Fax: [redacted]
>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>
>>>
>>>
>>>
>>>
>>>
>>>
>>> Am 09.06.16 13:06 schrieb "SHARPE Richard" unter <x.xxxxxx@xx.xx.xx >:
>>>
>>>> Hi Dan and Co
>>>>
>>>> I have to admit that there were a few things in the editorial draft
>>>> that
>>>> came around that I would not like to sign my name to.
>>>> I think it was just too dogmatic and dismissive, especially on the
>>>> ED
>>>> side, and I do not think this would serve us well. I know that Dan
>>>> wants

>>>> a hard-hitting editorial,
>>>> but what we don't want to do is to fall into the same traps that the
>>>> ED
>>>> brigade have fallen into (i.e. Being dismissive of evidence, even if
>>>> the
>>>> evidence is inconclusive).
>>>>
>>>> So I've considerably rewritten various parts, not all of which may
>>>> sit
>>>> well with one or more of you. And of course this is just another
>>>> bone
>>>> for
>>>> you all to chew upon.
>>>> I'm unsure of the wisdom of being upfront re the chemical industry
>>>> as
>>>> I've tried to do, but if you think it is wise then I'm sure it can
>>>> be
>>>> written better than I have done.
>>>>
>>>> Anyway, I'm out of the loop for a few days now, so you have plenty
>>>> of
>>>> time to chew this to pieces.
>>>>
>>>> Best wishes
>>>>
>>>> Richard
>>>>
>>>> PS: I used the latest version that Dan sent around.
>>>>
>>>>
>>>>
>>>> On 08/06/2016 14:39, "Daniel Dietrich"
>>>> <Daniel.Dietrich@uni-konstanz.de>
>>>> wrote:
>>>>
[redacted]
>>>>> Dan
>>>>>
>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>>>
>>>>> Professor of Human and Environmental Toxicology, Faculty of
>>>>> Biology,
>>>>> University of Konstanz
>>>>> P.O. Box 622
>>>>> Universitätsstrasse 10
>>>>> D-78457 Konstanz, Germany
>>>>>
>>>>> Telephone: [redacted]
>>>>>

>>>>> Portable-Phone: [redacted]
>>>>> Fax: [redacted]
>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>> Am 08.06.2016 15:18 schrieb "Colin Berry" unter
>>>>> <xxxxx@xxxxxxxxxxxx.xx.xx>:
>>>>>
>>>>>> Daniel,
>>>>>> Another go
>>>>>> I don't go for " accusation"- it's really the" arousal of
>>>>>> suspicion"
>>>>>> and
>>>>>> I think it appears pejorative as it is now. We want to argue for
>>>>>> science,
>>>>>> not opinion
>>>>>> For the same reason, I do not care for "denunciation" later on
>>>>>> which
>>>>>> is
>>>>>> why I used colour - what is happening is a malign influence on
>>>>>> the
>>>>>> quality of debate.
>>>>>> Regards
>>>>>> Colin.
>>>>>>
>>>>>> -----Original Message-----
>>>>>> From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx]
>>>>>> Sent: Wednesday, June 8, 2016 11:02 AM
>>>>>> To: Heslop-Harrison, Pat (Prof.); Wolfgang Dekant; Colin Berry;
>>>>>> SHARPE
>>>>>> Richard; 'Boobis, Alan R'; Greim, Helmut; [redacted]
>>>>>> Subject: Re: Editorial on risk and regulation comments
>>>>>>
>>>>>> Dear Colin, Wolfgang, Pat, Helmut, Jan, Alan and Richard [redacted]
[redacted]
[redacted]
[redacted]
[redacted]
[redacted]
[redacted]
[redacted]
[redacted] Dan
>>>>>>
[redacted]
[redacted]

[redacted]
[redacted] Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>>>>
>>>>>> Professor of Human and Environmental Toxicology, Faculty of
>>>>>> Biology,
>>>>>> University of Konstanz P.O. Box 622 Universitätsstrasse 10
>>>>>> D-78457 Konstanz, Germany
>>>>>>
>>>>>> Telephone: [redacted]
>>>>>> [redacted],
>>>>>> Secretary)
>>>>>> Portable-Phone: [redacted]
>>>>>> Fax: [redacted]
>>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>>
>>>>>>
>>>>>>
>>>>>>
>>>>>>
>>>>>>
>>>>>>
>>>>>> Am 08.06.2016 09:28 schrieb "Heslop-Harrison, Pat (Prof.)" unter
>>>>>> <xxxx@xxxxxxxxx.xx.xx >:
>>>>>>
>>>>>>> Dear All,
>>>>>>>
[redacted]
>>>>>>>
[redacted]

[redacted]

>>>>>>>
>>>>>>> Pat.
>>>>>>>
>>>>>>> Pat Heslop-Harrison.
>>>>>>>
>>>>>>> Professor J.S. (Pat) Heslop-Harrison
>>>>>>> Department of Genetics
>>>>>>> University of Leicester
>>>>>>> Leicester LE1 7RH UK
>>>>>>>
>>>>>>> E-mail: xxxx@xx.xx.xx [redacted]
>>>>>>>
>>>>>>> Annals of Botany blog: www.AoBBlog.com
>>>>>>> Websites: www.molcyt.com [redacted] Chief Editor,
>>>>>>> Annals of

>>>>>>> Botany: www.annbot.com
>>>>>>>
>>>>>>> Phone: [redacted]
>>>>>>> Mobile phone: [redacted]
>>>>>>> FAX: [redacted]
>>>>>>>
>>>>>>> _____
>>>>>>> From: Wolfgang Dekant [xxxxxx@xxxx.xxxxxxxxxxxxx.xx]
>>>>>>> Sent: 08 June 2016 08:00
>>>>>>> To: Colin Berry; Daniel Dietrich; Heslop-Harrison, Pat (Prof.);
>>>>>>> SHARPE
>>>>>>> Richard; 'Boobis, Alan R'; Greim, Helmut; Jan Hengstler
>>>>>>> Subject: Re: Commissioner Andriukaitis statement on glyphosate
>>>>>>>
>>>>>>> Hi, [redacted]
>>>>>>>
>>>>>>>
>>>>>>> wd
>>>>>>>
>>>>>>>
>>>>>>> wd
>>>>>>>
>>>>>>>
>>>>>>>> Am 08.06.16 um 08:37 schrieb Colin Berry:
>>>>>>>> Dear Dnaiel,
>>>>>>>> I hope you do not mind my having a go at this - I enjoyed
>>>>>>>> the
>>>>>>>> tavern idea.
>>>>>>>> There are a number of changes that are trivial but which I
>>>>>>>> hope increase the pithiness of the commentary . For example , I
>>>>>>>> have
>>>>>>>> replaced "lack of any" evidence with "no" and so on - in a
>>>>>>>> tavern
>>>>>>>> (pub) they are usually "regulars" rather than locals in the
>>>>>>>> vernacular. "Medially" does not mean of the media but towards
>>>>>>>> the
>>>>>>>> middle.
>>>>>>>> But some more important bits. I have commented on standards
>>>>>>>> of
>>>>>>>> proof. Criminal standards are not usually invoked in regulation
>>>>>>>> -
>>>>>>>> you
>>>>>>>> don't have to like Godell's mathematics or be a Popperian to
>>>>>>>> know
>>>>>>>> that
>>>>>>>> something in science may be true or false, despite the evidence
>>>>>>>> in

>>>>>>>> its
>>>>>>>> favour so far. Introducing the "balance of probabilities"
>>>>>>>> concept
>>>>>>>> ,
>>>>>>>> as in civil law, means you must consider the weight of evidence
>>>>>>>> -
>>>>>>>> that
>>>>>>>> is what we want. The judicial system have not improved only
>>>>>>>> because of
>>>>>>>> science so I modified this.
>>>>>>>>   Is there a better example than salt - or do we need this
>>>>>>>> bit?
>>>>>>>>   I am concerned , as I have said before, about attributing
>>>>>>>> motives to others, even if we believe the accusations to be
>>>>>>>> true.
>>>>>>>> SO I
>>>>>>>> would not go on about Monsanto or glyphosate. If you feel it
>>>>>>>> needs
>>>>>>>> ot
>>>>>>>> be in , can I work on it a bit?
>>>>>>>>   Celeste Condit wrote very well on who is the "public" and
>>>>>>>> who
>>>>>>>> appoints themselves to speak for them; I wil hunt our t some
>>>>>>>> refs
>>>>>>>> which might be useful.
>>>>>>>> Again, apologies for treading on toes - this is meant to help.
>>>>>>>> Best wishes
>>>>>>>> Colin
>>>>>>>>
>>>>>>>> Ps Not all public advocacy groups are bad.
>>>>>>>>
>>>>>>>> -----Original Message-----
>>>>>>>> From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx]
>>>>>>>> Sent: Tuesday, June 7, 2016 6:28 PM
>>>>>>>> To: Heslop-Harrison, Pat (Prof.); Colin Berry; SHARPE Richard;
>>>>>>>> 'Boobis, Alan R'; Greim, Helmut; Wolfgang Dekant; [redacted]
>>>>>>>> Subject: Re: Commissioner Andriukaitis statement on glyphosate
>>>>>>>> Importance: High
>>>>>>>>
>>>>>>>> Dear all
[redacted]
>>>>>>>> Dan
>>>>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>>>>>>
>>>>>>>> Professor of Human and Environmental Toxicology, Faculty of
>>>>>>>> Biology,
>>>>>>>> University of Konstanz P.O. Box 622 Universitätsstrasse 10
>>>>>>>> D-78457 Konstanz, Germany
>>>>>>>>

>>>>>>>> Telephone: [redacted]
>>>>>>>> [redacted]
>>>>>>>> Secretary)
>>>>>>>> Portable-Phone: [redacted]
>>>>>>>> Fax: [redacted]
>>>>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>>>>
>>>>>>>>
>>>>>>>>
>>>>>>>>
>>>>>>>>
>>>>>>>>
>>>>>>>>
>>>>>>>> Am 05.06.2016 22:42 schrieb "Heslop-Harrison, Pat (Prof.)" unter
>>>>>>>> <xxxx@xxxxxxxxx.xx.xx >:
>>>>>>>>
>>>>>>>> Dear All,
>>>>>>>>
[redacted]
>>>>>>>>
>>>>>>>> Best wishes,
>>>>>>>>
>>>>>>>> Pat.
>>>>>>>>
>>>>>>>> Professor J.S. (Pat) Heslop-Harrison Department of Genetics
>>>>>>>> University of Leicester Leicester LE1 7RH UK
>>>>>>>>
>>>>>>>> E-mail: xxxx@xx.xx.xx [redacted]
>>>>>>>>
>>>>>>>> Annals of Botany blog: www.AoBBlog.com
>>>>>>>> Websites: www.molcyt.com [redacted]') Chief Editor,
>>>>>>>> Annals
>>>>>>>> of
>>>>>>>> Botany: www.annbot.com
>>>>>>>>
>>>>>>>> Phone: [redacted]

>>>>>>>>> Mobile phone: [redacted]
>>>>>>>>> FAX: [redacted]
>>>>>>>
>>>>>>> --
>>>>>>> Prof. Dr. Wolfgang Dekant
>>>>>>> Department of Toxicology, University of Wuerzburg Versbacher Str.
>>>>>>> 9,
>>>>>>> 97078 Wuerzburg, Germany Tel. [redacted]
>>>>>>> Fax: [redacted]
>>>>>>> Mobil: [redacted]
>>>> --
>>>> The University of Edinburgh is a charitable body, registered in
>>>> Scotland, with registration number SC005336.
>>>
>>>

Editorial:
Allowing pseudoscience into EU risk assessment processes is eroding public trust in science experts and in science as a whole

Daniel R. Dietrich, Wolfgang Dekant, Helmut Greim, Pat Henslop-Harrison, Colin Berry, Alan Boobis, Jan Hengstler and Richard Sharpe.

Imagine we are beamed back into the 12th century and are staying overnight at a country tavern. Based on our clothes we are easily identified as foreigners and are confronted not only with curiosity but also hostility from the tavern regulars. In the middle of the night we are roughly wakened by the owner and some of his men and directly accused of having stolen from one of the regulars after first poisoning him. Despite our protests and the lack of any reasonable proof we are accused of being thieves and murderers and are subjected to trial by ordeal to prove our innocence.

The trial takes the form of having our hands and feet tied and being thrown into the river; if we sink and drown we are obviously guilty, however if we float God has recognized our innocence and let us live *(judicium Dei)*. To a scientist, it seems likely we would drown.

Thankfully, over the past 800 years the development of the judicial system has brought us to the point where an accused is considered innocent until proven guilty. Whether the context is Criminal, where a "beyond reasonable doubt" standard of proof is required, or Civil, where the "balance of probability" is the standard, the burden of proof lies with the accusing party.

With us, in the tavern it would be necessary for the accuser (or his legal representative) to prove, beyond reasonable doubt in this case, that we had poisoned the man and stolen the goods from him. In practice, the onus of the demonstration of proof on the accuser is not restricted to criminal cases but applies to many legal procedures in democracies.

Unfortunately Europe, in the application of its legislation relating to chemicals, is in danger of falling back into the medieval approach. The most recent example is the advocacy group- {Action, 2016 #45}, media- and NGO- {Europe, 2016 #46} driven move to have glyphosate banned, despite solid evidence and multiple expert assessments {FAO/WHO, 2016 #40;Risikobewertung, 2015 #41;Authority, 2015 #42} that this herbicide is without risk to consumers and is the herbicide with the least negative environmental and health impact. The "public" is being misled by pseudoscientists to believe that the compound is highly dangerous to humans and the environment, a claim that runs counter to the evidence and to expert (critical) assessment of that evidence. The media are rife with quotes from poorly informed and often scientifically less well-informed politicians and others who had analysed their water, urine, beer, and vegetables and found trace amounts of glyphosate {Risikobewertung, 2013 #47}, several orders of magnitude below those that would be associated with any harm.

In a similarly misleading vein, there have been seemingly endless discussions about "endocrine disrupters" and their postulated human health effects, based on association studies. For these to be causal, they require us to accept that extremely low-level exposures cause effects in humans, whereas most of the experimental data indicate such exposures are without effect. Most recently, the debate on "endocrine disruptors" has shifted focus to the concept that doses of these compounds below their 'no-observed-effect level' (in animal and in vitro studies) can cause adverse effects (so-called non-monotonic dose-

response curves) {News, 2016 #44}, even though the evidence that endocrine systems can be perturbed in this way just does not exist; indeed, there is ample human data on abnormally low hormone exposures that tell us this is not how such systems work. However, this detailed evidence is being ignored and the most prominent proponents of endocrine disruption-mediated human health effects are now using this to argue that hazard identification alone is necessary for regulatory purposes {News, 2016 #44}. However, hazard characterization, including potency evaluation, and exposure assessment are the principles on which the protection of humans from adverse environmental chemical effects is undertaken, and has proved to be very effective. This is also the approach recommended for endocrine disrupters {Solecki, 2016 #54}. This is a logical path that demands detailed evidence gathering and weighing of the science that then forms the basis of the information on which the legal process is based. Do we want to throw this trusted and tried process away?

Relying on hazard identification alone relieves the "accusing party" of the burden of proof (i.e. obtaining the evidence) and allows for endless new allegations of potential effects on human health, for which evidence is not required – it is simply assumed. We don't think that any of us would like our doctors to use similar approaches for looking after our health; no, doctors want evidence of what is wrong so that they can target it specifically to restore normal health. What about the wider implications of a hazard-based approach? Will we ban cars because they are clearly hazardous, or sugar because it can be hazardous to human health? In this regard, the putative hazard has now changed; now endocrine disrupters are being advocated as a prime cause for obesity and type II diabetes {Legler, 2015 #15}. How credible is this? We know that obesity and type II diabetes can often be corrected by reducing appetite, food intake and additional exercise, difficult though this may be, but what evidence is there that reducing exposure to so-called endocrine-disrupting 'obesogens' can reduce the incidence~~s~~ of obesity and type II diabetes? There is no such evidence, yet we are asked to accept that 'obesogens' are an important human health risk. Like medieval justice, the accusing party never faces the consequences of their accusations or allegations. Any damages incurred, whether these be to human health through unintended consequences, society or the economy, are common good and not the responsibility of the accusing party.

These trends are testimony to the apparent movement to overturn the use of evidence-based risk assessment in regulation. Further, they undermine the concept of burden of proof, central to our judicial systems, developed over the past centuries. Indeed, arguably, undue emphasis on hazard identification alone has already found its way~~,~~ into some EU chemicals legislation, ignoring more informative weight of evidence and risk assessment approaches, based on sound science, that have served society well over the years. Indeed, it is not merely chemical risk assessment that is currently at stake, it is science as a whole. Reports of the lack of reproducibility of published scientific findings {Baker, 2016 #51} and public disagreement among scientists (and pseudoscientists) on the dangers of compounds, despite good evidence to the contrary, erodes public trust in science and scientist as a whole – few without scientific training realize that science progresses by the detection of, and subsequent elimination of, errors. Perhaps equally important, failure of decision makers to recognise this leads to unnecessarily restrictive and potentially damaging regulation.

Arguments such as those we voice above are now routinely attacked on the basis that 'this is what the chemical industry wants, so these authors must be speaking on behalf

of that industry' {Garwood, 2014 #7;Horel, 2016 #52;Horel, 2013 #5}; {Garwood, 2014 #7;Horel, 2016 #52;Horel, 2013 #5}. This is not the case. But such unwarranted accusations of conflicts of interest in the absence of robust scientific evidence to support their assertions {Slama, 2016 #48;Grandjean, 2013 #6}, have become the mode du jour in such disputes. In some cases, this has resulted in conflict of interest policies that could lead to an overall lack of scientific balance among the group of experts considered not to be thus conflicted. A number of NGO's have an interest in maintaining public concerns about specific issues, and indeed may rely on such concerns for charitable donations. Hence, there is a strong motivation to disregard data that contradicts a precautionary point of view. Regrettably, some scientists appear to put the need to obtain research funding above the objective appraisal of the evidence. Unlike potential financial bias, these possible conflicts of interest {Dietrich, 2016 #53} are rarely considered in such debates. But these attitudes can distort opinions provided to organisations such as EFSA, WHO, EPA and others. The consequence is that scientific argument and weight of evidence brought forth that might disagree with the initial allegation or accusation can be undermined. This process damages the credibility of governmental organizations and the well-developed processes that are the very foundations of our society and our well-being. For sure, the chemical industry has every interest in protecting its products and profits, and will lobby to this effect. To ensure longevity of their products and to avoid litigation, industry is as interested in an evidence-based approach to risk assessment as we are, and collecting the evidence is a huge and expensive task that industry has to undertake to justify the safety of its products. Is it sensible to say No to such evidence and instead to assume that if a chemical is hazardous it should be banned, irrespective of how much we, the public, are exposed to? In essence, we would be saying that an evidence-based approach is not as good as a presumptive approach based on no evidence. This is to throw away scientific principles and good practice and to replace it with something akin to witchcraft.

It is time to end the influence of pseudoscience and pseudoscientists, including some self-appointed public advocacy groups, on European legislation. We advocate this not because of what the chemical industry may want or not want, but because it is the most credible, scientifically-sound and societally-beneficial solution, utilising well-defined and transparent processes of evidence gathering, weighing and risk assessment that should be at the core of decisions that support all legal procedures. This is what has been developed, tried and tested in Europe over the years and is demonstrably protective of human health.

References:

Editorial:
Allowing pseudoscience into EU risk assessment processes will erode public trust in science experts and in science as a whole

Daniel R. Dietrich, Wolfgang Dekant, Helmut Greim, Pat Henslop-Harrison, Colin Berry, Alan Boobis, Jan Hengstler and Richard Sharpe.

Imagine we are beamed back into the 12th century and are staying overnight at a country tavern. Based on our clothes we are easily identified as foreigners and are confronted with curiosity but also hostility from the tavern regulars. In the middle of the night we are roughly wakened by the owner and some of his men and directly accused of having stolen from one of the regulars after first poisoning him. Despite our protests and the lack of any reasonable proof we are accused of being thieves and murderers and are subjected to trial by ordeal to prove our innocence.

The trial takes the form of having our hands and feet tied and being thrown into the river; if we sink and drown we are obviously guilty, however if we float God has recognized our innocence and let us live *(judicium Dei)*. To a scientist, it seems likely we would drown.

Thankfully, over the past 800 years the development of the judicial system has brought us to the point where an accused is considered innocent until proven guilty. Whether the context is Criminal, where a "beyond reasonable doubt" standard of proof is required, or Civil, where the "balance of probability" is the standard, the burden of proof lies with the accusing party.

With us, in the tavern it would be necessary for the accuser (or his legal representative) to prove, beyond reasonable doubt in this case, that we had poisoned the man and stolen the goods from him. In practice, the onus of the demonstration of proof on the accuser is not restricted to criminal cases but applies to many legal procedures in democracies.

Unfortunately Europe in the application of its legislation relating to chemicals has fallen back into the medieval approach. The most recent example is the advocacy group, media and NGO driven banning of glyphosate, despite solid evidence and multiple expert assessments (BfR, EFSA, WHO/FAO JMPR) that this herbicide is not carcinogenic and is the herbicide with the least negative environmental and health impact. The "public" is mislead by pseudoscientists to believe that the compound – off patent and made by at least 50 companies – is highly dangerous to humans and the environment~~—~~, a claim that runs counter to the evidence and to expert (critical) assessment of that evidence~~Such claims can only be based on inability to comprehend the scientific data that inform discussion of the issues~~. The media are rife with quotes from poorly informed and often scientifically less well-informed politicians who had analysed their water, urine, beer, and vegetables and found unimaginably small concentrations of glyphosate, ~~unfortunately~~ often measured by inappropriate methodology and ~~thus~~ not verifiable. Actually, even simple sodium chloride, ~~know as table salt,~~ which is more toxic than glyphosate, can be found in all of the previous samples at much higher concentrations.

In a similarly misleading vein, there has been seemingly endless discussions about "endocrine disrupters", and their ~~have focused reports on~~ ~~presumed~~ postulated human health effects, based on association studies. If these are cause-effect observations, they require us to accept that extremely low level exposures cause effects in humans, whereas most of the experimental data says such exposures are without effect. ~~Examining these~~

Formatted: Highlight

Commented [Office1]: I wonder about this and whether it really adds anything to this debate, given that we do need salt in our diet but we dont need glyphosate. So its not really a debate clincher.

~~presumptions with care makes clear that none withstand any form of scientific scrutiny. All currently available evidence points toward low human exposure to man made~~Most recently, the debate on "endocrine disruptors" has shifted focus to the concept that doses of these compounds below the 'no-effect level' (in animal and in vitro studies) can cause adverse effects (so-called non-monotonic dose-response curves), even though the evidence that endocrine systems can be perturbed in this way is just not there; indeed, there is plenty of human data on abnormally low hormone exposures that tell us this is not how such systems work. ~~and there is no evidence for adverse health effects.~~ However, ~~a number of natural compounds with hormonal activities (phytoestrogens in plants, certain mycotoxins) have been identified as potential health issues (cite EFSA on zearalenone, Dan Doegres comments on soy milk~~). ~~It is not surprising that~~this detailed evidence is being ignored and the most prominent proponents of endocrine disruption mediated human health effects are ~~interested~~ now using this issue to justify ~~in~~ hazard identification as being sufficient for regulatory purposes. Until now, ~~, i.e. the "accusation" part, but not in the~~ hazard characterization ~~nor the~~and potency evaluation or risk assessment~~;~~ have been the principles on which regulation and protection of humans from adverse environmental chemical effects has been undertaken, and has proved to be very effective. ~~the~~ This is a logical path that demands detailed ~~essential~~ evidence gathering and weighing of the science that ~~should~~ then forms the basis of the information on which the legal process is based. Do we want to throw this trusted and tried process away?

Relying on hazard identification alone relieves the "accusing party" of the burden of proof (ie obtaining the evidence) and allows for endless new ~~accusations and~~ allegations, for which evidence is not required – it is simply assumed. I don't think that any of us would like our doctors to use similar approaches for looking after our health; no, doctors want evidence of what is wrong so that they can target it specifically to restore normal health. What about the wider implications of a hazard-based approach? Will we ban cars because they are clearly hazardous, or sugar because it can be hazardous to human health? ~~Science may, by using careful analysis, disprove that "endocrine disrupters" reduce male fertility in humans; this is however largely ignored while the original accusations are kept alive in the media and press releases. Moreove~~In this regard~~r~~, the putative hazard ~~is then~~has now changed; now endocrine disrupters are being advocated as a ~~the~~ prime cause for obesity and type II diabetes. ~~The public will not be aware that sugar is an endocrine disrupter and will not have an informed view of its association with obesity and the onset of type II diabetes in the young.~~How credible is this? We know that obesity and type II diabetes can be corrected by reducing appetite and food intake, difficult though this may be, but what evidence is there that reducing exposure to so-called endocrine-disrupting 'obesogens' can achieve this? There is no such evidence, yet we are asked to accept that obesogens are an important human health risk. Like medieval justice, the accusing party never faces the consequences of their accusations or allegations. Any damages incurred, whether these be social or economic, are not the responsibility of the accusing party.

These trends are testimony to the apparent movement to overturn legislation relying on evidence based risk assessment. Further, they undermine the development of our judicial systems of the past centuries. Indeed, undue emphasis on hazard identification has already found its way~~,~~ into some EU chemicals legislation, ignoring the well tested weight of evidence and risk assessment approaches developed through robust and reproducible science. Indeed, it is not merely the chemical risk assessment that is currently at stake, it is

Commented [Office2]:

science as a whole. Reports of the lack of reproducibility of published science and public disagreement of well informed scientists (and pseudoscientists) on the dangers of compounds, erodes public trust in science and scientist as a whole – few without scientific training realize that science progresses by the detection of, and subsequent elimination of, errors.

Arguments such as those we voice above are now routinely attacked on the basis that 'this is what the chemical industry wants, so these authors must be speaking on behalf of that industry'; this is not the case. ~~Thought terminating clichés, s~~Such ~~as~~ accusations of conflicts of interest in lieu of providing scientific evidence, that can be discussed in a learned manner, has become very much the fashion in some of the publications on endocrine disrupters and pesticides. These are seldom uniformly considered – many NGO's have an interest in maintaining concerns in the absence of data or by the disregard of data that contradicts a point of view. These attitudes can even begin to ~~colour~~ distort the view of the expertise provided to EFSA, OECD, BfR and others and are apparently intended to undermine any scientific argument brought forth that might disagree with the initial allegation or accusation. This process undermines the credibility of governmental organizations and the well-developed processes that are the very foundations of our society and our well-being. For sure, the chemical industry has every interest in protecting its products and profits, and will lobby to this effect. But do people really think that industry do not care if their products are harmful to humans? Considering the litigenous world in which we live, such a blasé attitude would be a quick road to ruin for any company. We believe that industry are as interested in an evidence-based approach to risk assessment as we are, and collecting the evidence is a huge and expensive task that industry has to undertake to justify the safety of their products. Is it sensible to say No to such evidence and instead to assume that if a chemical is hazardous it should be banned, irrespective of how much we, the public, are exposed to? In essence, we would be saying that an evidence-based approach is not as good as a presumptive approach based on no evidence. This is to throw away scientific principles and good practice and to replace it with something akin to witchcraft.

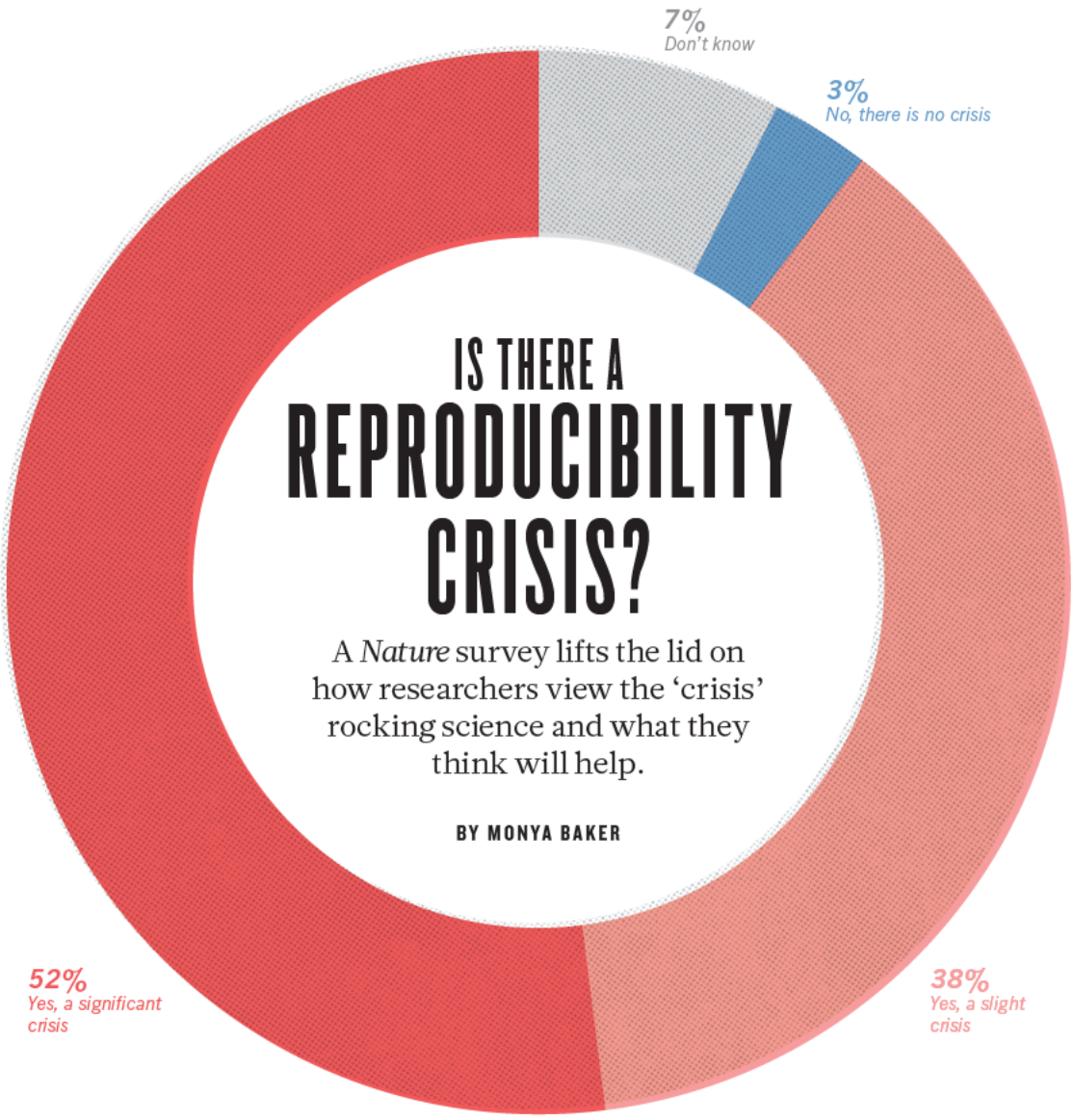
It is time to end the influence of pseudoscience and pseudoscientists, including some self-appointed public advocacy groups, on European legislation. We advocate this not because of what the chemical industry may want or not want, but because it is utilising ~~. We should return to~~ the sound science of well-defined and transparent processes of evidence gathering, weighing and risk assessment that should be at the core of the information that supports all legal procedures. This is what has been developed, tried and tested in Europe and is demonstrably protective of human health.

Commented [DD3]: Would „defame" or „denounce" be a stronger or better term?

[redacted]

Date: Thu, 26 May 2016 12:22:27 +0100
Subject: Re: reproducibility.....or not
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>,
"Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>,
"'Boobis, Alan R'" <x.xxxxxx@xxxxxxxx.xx.xx>,
"Greim, Helmut" [redacted],
Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>,
[redacted]
Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxx.xx>,
[redacted]

>I’m sure we can all identify with this.



IS THERE A REPRODUCIBILITY CRISIS?

A *Nature* survey lifts the lid on how researchers view the 'crisis' rocking science and what they think will help.

BY MONYA BAKER

More than 70% of researchers have tried and failed to reproduce another scientist's experiments, and more than half have failed to reproduce their own experiments. Those are some of the telling figures that emerged from *Nature*'s survey of 1,576 researchers who took a brief online questionnaire on reproducibility in research.

The data reveal sometimes-contradictory attitudes towards reproducibility. Although 52% of those surveyed agree that there is a significant 'crisis' of reproducibility, less than 31% think that failure to reproduce published results means that the result is probably wrong, and most say that they still trust the published literature.

Data on how much of the scientific literature is reproducible are rare and generally bleak. The best-known analyses, from psychology[1] and cancer biology[2], found rates of around 40% and 10%, respectively. Our survey respondents were more optimistic: 73% said that they think that at least half of the papers in their field can be trusted, with physicists and chemists generally showing the most confidence.

The results capture a confusing snapshot of attitudes around these issues, says Arturo Casadevall, a microbiologist at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. "At the current time there is no consensus on what reproducibility is or should be." But just recognizing that is a step forward, he says. "The next step may be identifying what is the problem and to get a consensus."

Failing to reproduce results is a rite of passage, says Marcus Munafo, a biological psychologist at the University of Bristol, UK, who has a long-standing interest in scientific reproducibility. When he was a student, he says, "I tried to replicate what looked simple from the literature, and wasn't able to. Then I had a crisis of confidence, and then I learned that my experience wasn't uncommon."

The challenge is not to eliminate problems with reproducibility in published work. Being at the cutting edge of science means that sometimes results will not be robust, says Munafo. "We want to be discovering new things but not generating too many false leads."

THE SCALE OF REPRODUCIBILITY

But sorting discoveries from false leads can be discomfiting. Although the vast majority of researchers in our survey had failed to reproduce an experiment, less than 20% of respondents said that they had ever been contacted by another researcher unable to reproduce their work (see 'A 'crisis' in numbers'). Our results are strikingly similar to another online survey of nearly 900 members of the American Society for Cell Biology (see go.nature.com/kbzs2b). That may be because such conversations are difficult. If experimenters reach out to the original researchers for help, they risk appearing incompetent or accusatory, or revealing too much about their own projects.

A minority of respondents reported ever having tried to publish

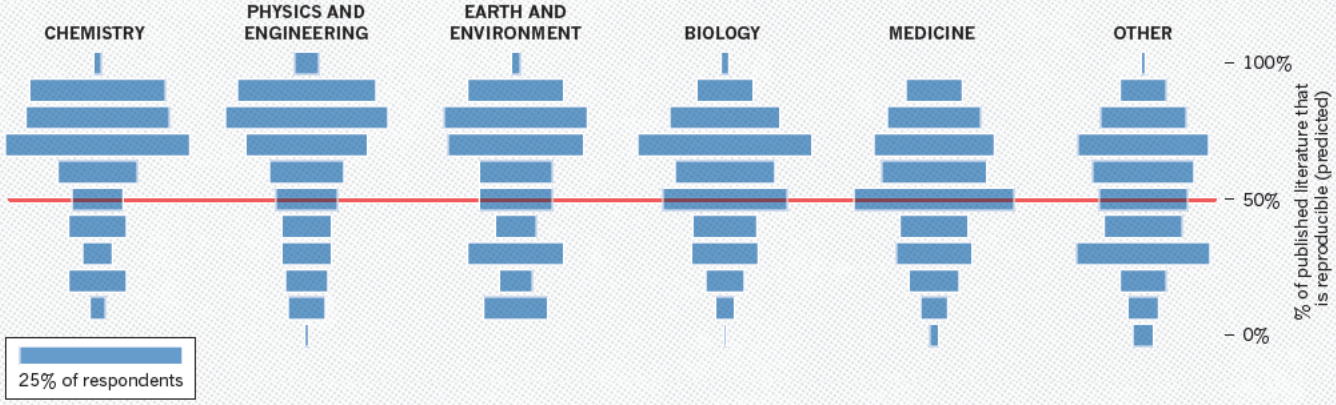
© 2016 Macmillan Publishers Limited. All rights reserved.

A 'CRISIS' IN NUMBERS

Nature surveyed 1,576 scientists online to get their thoughts on reproducibility in their field and in science in general. See **go.nature.com/2vjr4y** for more charts and access to the full data.

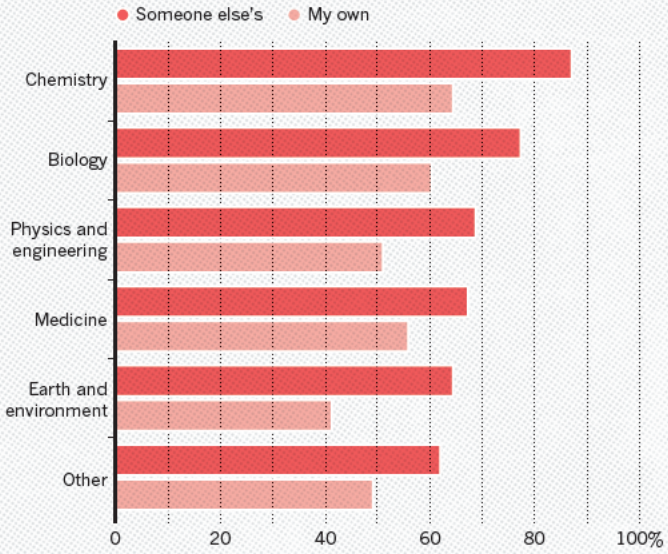
HOW MUCH PUBLISHED WORK IN YOUR FIELD IS REPRODUCIBLE?

Physicists and chemists were most confident in the literature.



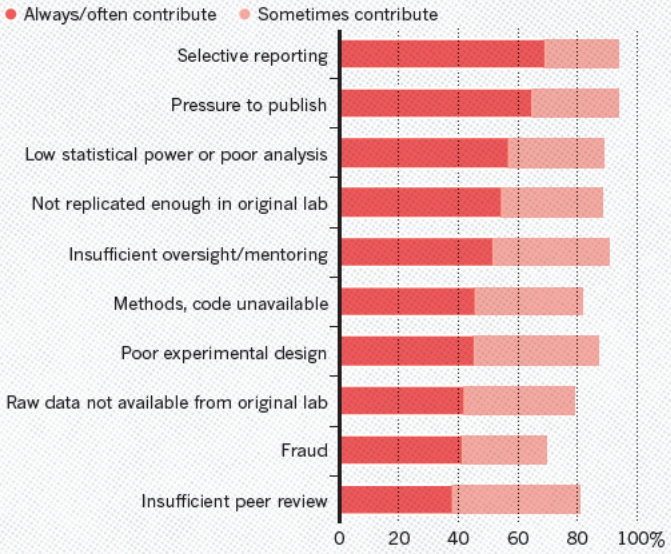
HAVE YOU FAILED TO REPRODUCE AN EXPERIMENT?

Most scientists have experienced failure to reproduce results.



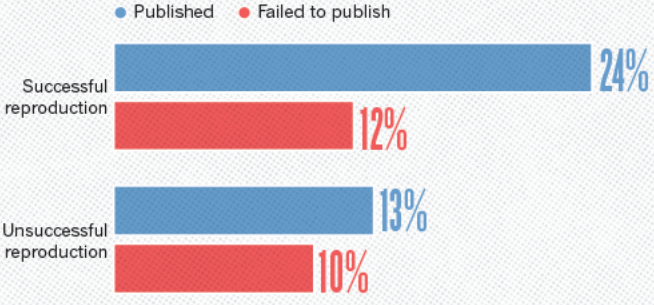
WHAT FACTORS CONTRIBUTE TO IRREPRODUCIBLE RESEARCH?

Many top-rated factors relate to intense competition and time pressure.



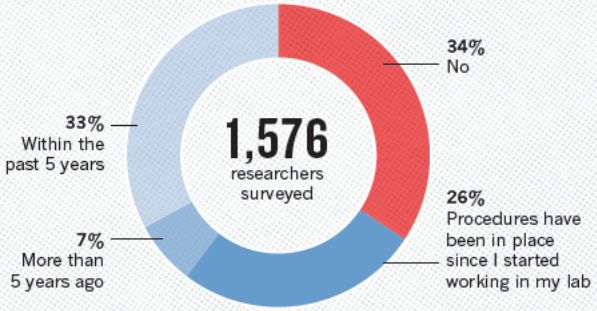
HAVE YOU EVER TRIED TO PUBLISH A REPRODUCTION ATTEMPT?

Although only a small proportion of respondents tried to publish replication attempts, many had their papers accepted.



HAVE YOU ESTABLISHED PROCEDURES FOR REPRODUCIBILITY?

Among the most popular strategies was having different lab members redo experiments.



Number of respondents from each discipline:
Biology **703**, Chemistry **106**, Earth and environmental **95**, Medicine **203**, Physics and engineering **236**, Other **233**

© 2016 Macmillan Publishers Limited. All rights reserved.

a replication study. When work does not reproduce, researchers often assume there is a perfectly valid (and probably boring) reason. What's more, incentives to publish positive replications are low and journals can be reluctant to publish negative findings. In fact, several respondents who had published a failed replication said that editors and reviewers demanded that they play down comparisons with the original study.

Nevertheless, 24% said that they had been able to publish a successful replication and 13% had published a failed replication. Acceptance was more common than persistent rejection: only 12% reported being unable to publish successful attempts to reproduce others' work; 10% reported being unable to publish unsuccessful attempts.

Survey respondent Abraham Al-Ahmad at the Texas Tech University Health Sciences Center in Amarillo expected a "cold and dry rejection" when he submitted a manuscript explaining why a stem-cell technique had stopped working in his hands. He was pleasantly surprised when the paper was accepted[3]. The reason, he thinks, is because it offered a workaround for the problem.

Others place the ability to publish replication attempts down to a combination of luck, persistence and editors' inclinations. Survey respondent Michael Adams, a drug-development consultant, says that work showing severe flaws in an animal model of diabetes has been rejected six times, in part because it does not reveal a new drug target. By contrast, he says, work refuting the efficacy of a compound to treat Chagas disease was quickly accepted[4].

"REPRODUCIBILITY IS LIKE BRUSHING YOUR TEETH. ONCE YOU LEARN IT, IT BECOMES A HABIT."

THE CORRECTIVE MEASURES

One-third of respondents said that their labs had taken concrete steps to improve reproducibility within the past five years. Rates ranged from a high of 41% in medicine to a low of 24% in physics and engineering. Free-text responses suggested that redoing the work or asking someone else within a lab to repeat the work is the most common practice. Also common are efforts to beef up the documentation and standardization of experimental methods.

Any of these can be a major undertaking. A biochemistry graduate student in the United Kingdom, who asked not to be named, says that efforts to reproduce work for her lab's projects doubles the time and materials used — in addition to the time taken to troubleshoot when some things invariably don't work. Although replication does boost confidence in results, she says, the costs mean that she performs checks only for innovative projects or unexpected results.

Consolidating methods is a project unto itself, says Laura Shankman, a postdoc studying smooth muscle cells at the University of Virginia, Charlottesville. After several postdocs and graduate students left her lab within a short time, remaining members had trouble getting consistent results in their experiments. The lab decided to take some time off from new questions to repeat published work, and this revealed that lab protocols had gradually diverged. She thinks that the lab saved money overall by getting synchronized instead of troubleshooting failed experiments piecemeal, but that it was a long-term investment.

Irakli Loladze, a mathematical biologist at Bryan College of Health Sciences in Lincoln, Nebraska, estimates that efforts to ensure reproducibility can increase the time spent on a project by 30%, even for his theoretical work. He checks that all steps from raw data to the final figure can be retraced. But those tasks quickly become just part of the job. "Reproducibility is like brushing your teeth," he says. "It is good for you, but it takes time and effort. Once you learn it, it becomes a habit."

One of the best-publicized approaches to boosting reproducibility is pre-registration, where scientists submit hypotheses and plans for data analysis to a third party before performing experiments, to prevent cherry-picking statistically significant results later. Fewer than a dozen people mentioned this strategy. One who did was Hanne Watkins, a graduate student studying moral decision-making at the University of Melbourne in Australia. Going back to her original questions after collecting data, she says, kept her from going down a rabbit hole. And the process, although time consuming, was no more arduous than getting ethical approval or formatting survey questions. "If it's built in right from the start," she says, "it's just part of the routine of doing a study."

THE CAUSE

The survey asked scientists what led to problems in reproducibility. More than 60% of respondents said that each of two factors — pressure to publish and selective reporting — always or often contributed. More than half pointed to insufficient replication in the lab, poor oversight or low statistical power. A smaller proportion pointed to obstacles such as variability in reagents or the use of specialized techniques that are difficult to repeat.

But all these factors are exacerbated by common forces, says Judith Kimble, a developmental biologist at the University of Wisconsin–Madison: competition for grants and positions, and a growing burden of bureaucracy that takes away from time spent doing and designing research. "Everyone is stretched thinner these days," she says. And the cost extends beyond any particular research project. If graduate students train in labs where senior members have little time for their juniors, they may go on to establish their own labs without having a model of how training and mentoring should work. "They will go off and make it worse," Kimble says.

WHAT CAN BE DONE?

Respondents were asked to rate 11 different approaches to improving reproducibility in science, and all got ringing endorsements. Nearly 90% — more than 1,000 people — ticked "More robust experimental design" "better statistics" and "better mentorship". Those ranked higher than the option of providing incentives (such as funding or credit towards tenure) for reproducibility-enhancing practices. But even the lowest-ranked item — journal checklists — won a whopping 69% endorsement.

The survey — which was e-mailed to *Nature* readers and advertised on affiliated websites and social-media outlets as being 'about reproducibility' — probably selected for respondents who are more receptive to and aware of concerns about reproducibility. Nevertheless, the results suggest that journals, funders and research institutions that advance policies to address the issue would probably find cooperation, says John Ioannidis, who studies scientific robustness at Stanford University in California. "People would probably welcome such initiatives." About 80% of respondents thought that funders and publishers should do more to improve reproducibility.

"It's healthy that people are aware of the issues and open to a range of straightforward ways to improve them," says Munafo. And given that these ideas are being widely discussed, even in mainstream media, tackling the initiative now may be crucial. "If we don't act on this, then the moment will pass, and people will get tired of being told that they need to do something." SEE EDITORIAL P.437

Monya Baker *writes and edits for* Nature *from San Francisco.*
Dan Penny *aided in creation and analysis of the survey.*

1. Open Science Collaboration *Science* http://dx.doi.org/10.1126/science.aac4716 (2015).
2. Begley, C. G. & Ellis, L. M. *Nature* **483,** 531–533 (2012).
3. Patel, R. & Alahmad, A. J. *Fluids Barriers CNS* **13,** 6 (2016).
4. da Silva, C. F. *et al. Antimicrob. Agents Chemother.* **57,** 5307–5314 (2013).

© 2016 Macmillan Publishers Limited. All rights reserved.

[redacted]

Date: Wed, 18 May 2016 20:05:01 +0100
Subject: Re: meeting with Commissioner May 3
From: SHARPE Richard <R.Sharpe@ed.ac.uk>
To: "Greim, Helmut" [redacted]
Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>
CC: Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>,
"Boobis, Alan R" <a.boobis@imperial.ac.uk>,
"Heslop-Harrison, Pat (Prof.)" <phh4@leicester.ac.uk>,
Colin Berry [redacted]

When real, as opposed to scientific, politics at this level intrudes into
the 'debate' then it looks very much a battle that cannot be won.
All we can do is fight the scientific battle, if we are allowed to!
On the positive side, it certainly makes you need a beer!

Richard

On 18/05/2016 19:44, "Greim, Helmut" [redacted]
wrote:

[redacted]

>Regards
>Helmut
>
>Am 18.05.2016 18:49, schrieb Daniel Dietrich:
>> [redacted]
>> Dan
>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>
>> Professor of Human and Environmental Toxicology, Faculty of Biology,
>> University of Konstanz
>> P.O. Box 622
>> Universitätsstrasse 10
>> D-78457 Konstanz, Germany
>>
>> Telephone: [redacted]
>>
>> Portable-Phone: [redacted]
>> Fax: [redacted]

>> email: Daniel.Dietrich@uni-konstanz.de
>> http://www.umwelttoxikologie.uni-konstanz.de
>>
>>
>>
>>
>>
>>
>>
>> Am 18.05.2016 16:13 schrieb "Wolfgang Dekant" unter
>> <dekant@toxi.uni-wuerzburg.de>:
>>

[redacted]

>>>
>>> w
>>>
>>> Am 18.05.16 um 13:42 schrieb Daniel Dietrich:

[redacted]

>>>> Dan
>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>>
>>>> Professor of Human and Environmental Toxicology, Faculty of Biology,
>>>> University of Konstanz
>>>> P.O. Box 622
>>>> Universitätsstrasse 10
>>>> D-78457 Konstanz, Germany
>>>>

>>>> Telephone: [redacted]
>>>>
>>>> Secretary)
>>>> Portable-Phone: [redacted]
>>>> Fax: [redacted]
>>>> email: Daniel.Dietrich@uni-konstanz.de
>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>
>>>>
>>>>
>>>>
>>>>
>>>>
>>>>
>>>> Am 18.05.2016 13:03 schrieb "SHARPE Richard" unter
>>>> <r.sharpe@ed.ac.uk>:
>>>>
>>>>> I just finished a conversation with a [redacted]
>>>>> about our meeting with the commissioner etc; [redacted]
>>>>>
>>>>> [redacted] and we had a fairly
>>>>> wide-ranging
>>>>> conversation, during which [redacted]
>>>>> [redacted]
>>>>> about
>>>>> every interaction I have had with industry (which is not much, but
>>>>> [redacted]. It became clear [redacted] we are all
>>>>> tainted
>>>>> by industry, which is why what we said to the commissioner (i.e. Is
>>>>> in
>>>>> our
>>>>> press release) is exactly what industry would say. There we have it.
>>>>> [redacted] well do you not think that this is a good thing that
>>>>> industry's position is in line with the scientific evidence, [redacted]
>>>>> any idea that the conflicts on the
>>>>> other
>>>>> side
>>>>> are as bad or worse than any that I or you guys may have. [redacted]
>>>>> asbestos etc as evidence of how industry does not stick to the
>>>>> evidence
>>>>> and I asked [redacted] to give me some recent examples - [redacted]
>>>>> neocotinoids, glyphosate and endocrine disruptors!
>>>>>
>>>>> I spent a good 30 minutes once I realised [redacted] in
>>>>> trying
>>>>> to convince [redacted] that my position has only ever been driven and
>>>>> motivated
>>>>> by one thing - the available scientific evidence and that all that
>>>>> was
>>>>> presented at the meeting with the commissioner was what the evidence
>>>>> shows, not what industry thinks or wants. I also told [redacted] how I

>>>>> speak
>>>>> to
>>>>> both sides (industry and NGOs such as ChemTrust) as to speak to one
>>>>> only
>>>>> is to lay oneself open to influence and [redacted] I said that the EDC brigade only speak to each other
>>>>> and
>>>>> will
>>>>> not countenance any data that does not fit with their view. I
>>>>> specifically
>>>>> asked [redacted] 'So, do you think that scientific experts should not speak
>>>>> to
>>>>> industry - that we should withhold our information and expertise?',
>>>>> and
>>>>> [redacted] So there
>>>>> we
>>>>> have it - we will be attacked and pilloried on such grounds.
>>>>>
>>>>> I think that when this comes back to bite us, we should ask
>>>>> journalists
>>>>> the question that I asked [redacted]. And suggest that they ask their
>>>>> reading
>>>>> public the same question, couched slightly differently such as ' Do
>>>>> you
>>>>> think we would be safer if the chemical/other industry regularly
>>>>> spoke
>>>>> to
>>>>> independent scientific experts or would we be safer if these experts
>>>>> refused to speak to industry to advise them?'Because, in essence
>>>>> that
>>>>> is
>>>>> what this journalist is implying.
>>>>>
>>>>> It's a sad day for science when it is not the evidence that calls
>>>>> the
>>>>> tune
>>>>> but conspiracy theorists speaking on behalf of believers.
>>>>>
>>>>> Sorry to be the bringer of bad news.
>>>>>
>>>>> Richard
>>>>>
>>>>>
>>>>> --
>>>>> The University of Edinburgh is a charitable body, registered in
>>>>> Scotland, with registration number SC005336.
>>>>>
>>>
>>> --
>>> Prof. Dr. Wolfgang Dekant
>>> Department of Toxicology, University of Wuerzburg
>>> Versbacher Str. 9, 97078 Wuerzburg, Germany
>>> Tel. [redacted]
>>> Fax: [redacted]
>>> Mobil: [redacted]
>>>

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Monday, 16 May 2016 at 19:06
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, Wolfgang Dekant <xxxxxx@xxxx.xxx-wuerzburg.de>, Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>Alan R Boobis <x.xxxxxx@xxxxxxxx.xx.xx>, Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx>
Subject: FW: Homeopaths and arsenic-Joe Schwarcz's the Right Chemistry

From: [redacted]
Date: Monday, 16 May 2016 17:56
To: [redacted]
Subject: Homeopaths and arsenic-Joe Schwarcz's the Right Chemistry

The Right Chemistry: Adult colouring books beat homeopathy any day

 JOE SCHWARCZ, SPECIAL TO THE MONTREAL GAZETTE
Published on: May 14, 2016 | Last Updated: May 14, 2016 9:58 AM EDT

During a recent talk on the relationship between the body and the mind, I mentioned the newest anxiety-relieving craze, colouring books. Aimed at adults, these feature intricate patterns, making it quite a challenge to stay inside the lines. The contention is that focusing on the special patterns distracts the mind from anxiety and stress. Evidence is sketchy, but millions of colouring books are flying off the shelves, topping best-seller lists. That in itself says something

After my talk, I was approached by a woman who claimed she had something better than colouring books to relieve anxiety, and slipped a vial full of pills into my hand. She didn't seem like a clandestine drug pusher, so I thought I would look down and find some pills of lorezapam or maybe St. John's Wort. Such was not the case. The label on the vial read "Arsenicum album 30C."

No, she was not trying to poison me. These were homeopathic arsenic pills based on the curious notion that a substance that in large doses causes certain symptoms can, in homeopathic potency, repel the same symptoms. Since arsenic poisoning is associated with anxiety and restlessness, a person suffering such symptoms should find relief in a homeopathic dose of arsenic. In the bizarre world of homeopathy, potency increases with greater dilution, and a dose of 30C is said to be extremely potent. Such a pill is made by sequentially diluting a solution of arsenic 100-fold 30 times and then impregnating a sugar pill with a drop of the resulting solution. At a dilution of 30C, not only is there no trace of arsenic left, there isn't even a water molecule that has ever encountered any of the original arsenic.

Homeopathy is a scientifically bankrupt practice that was invented more than 200 years ago by German physician Samuel Hahnemann, who was disenchanted with bloodletting and purging, common medical procedures at the time. He was a good man who searched for kinder and gentler treatments, and homeopathy fit that rubric. Since knowledge of molecules was almost non-existent at the time, Hahnemann could not have realized that his diluted solutions contained nothing. Actually, the truth is that they did contain something. A hefty dose of placebo!

Now here is the kicker to this story. Hahnemann was quite accomplished in chemistry and actually developed the first chemical test for arsenic. In 1787, he found that arsenic in an unknown sample was converted to an insoluble yellow precipitate of arsenic trisulfide on treatment with hydrogen sulfide gas. When in 1832 John Bodle in England was accused of poisoning his grandfather by putting arsenic in his coffee, John Marsh, a chemist at the Royal Arsenal, was asked to test a sample of the coffee. While he was able to detect arsenic in the coffee using Hahnemann's test, the experiment could not be reproduced to the satisfaction of the jury and Bodle was acquitted. Knowing that he could not be tried for the same crime again, he later admitted to killing his grandfather.

The confession infuriated Marsh and motivated him to develop a better test for arsenic. By 1836, he had discovered that treating a sample of body fluid or tissue with zinc and an acid converted any arsenic to arsine gas, AsH_3, which could then be passed through a flame to yield metallic arsenic and water. The arsenic would then form a silvery-black deposit on a cold ceramic bowl held in the jet of the flame and the amount of arsenic in the original sample could be determined by comparing the intensity of the deposit with that produced with known amounts of arsenic.

The Marsh test received a great deal of publicity in 1840 when Marie LaFarge in France was accused of murdering her husband by putting arsenic into his food. LaFarge was known to have bought arsenic from a local chemist, which she claimed was to kill rats that had infested the house. A maid swore that she has seen her mistress pour a white powder into her husband's drink and LaFarge had also sent a cake to her husband, who was travelling on business just prior to his becoming ill. The dead husband's family suspected that LaFarge had poisoned him and somehow got hold of remnants of food to which she had supposedly added arsenic. The Marsh test revealed the presence of arsenic in the food and in a sample of egg nog, but when the victim's body was

exhumed, the investigating chemist was unable to detect arsenic.

To help prove LaFarge's innocence by corroborating the results of the investigation of the exhumed body, the defence enlisted Mathieu Orfila, a chemist acknowledged to be an authority on the Marsh test. Much to the defence's chagrin, Orfila showed that the test had been carried out incorrectly and used the Marsh test to conclusively prove the presence of arsenic in Mr. LaFarge's exhumed body. Marie LaFarge was found guilty and sentenced to life in prison. The controversial case captured the imagination of the public and was closely followed through newspaper accounts, making LeFarge into a celebrity. It would also go down in the annals of history as the first case in which a conviction was secured based on direct forensic toxicological evidence. Because of Orfila's role in the case, he is often deemed to be the "founder of the science of toxicology." The Marsh test became the subject of everyday conversations and even became a popular demonstration at fairgrounds and in public lectures. This had an interesting spinoff. Poisonings by arsenic decreased significantly. The existence of a reliable test served as a deterrent.

As far as claims about relieving anxiety with homeopathic arsenic go, well, they cause me anxiety. I think I'll flush those homeopathic tablets down the drain (no worry about arsenic pollution here) and buy a colouring book.

[redacted]
Joe Schwarcz is director of McGill University's Office for Science & Society (mcgill.ca/oss). He hosts The Dr. Joe Show on CJAD Radio 800 AM every Sunday from 3 to 4 p.m.

[redacted]

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Tuesday, 10 May 2016 at 10:19
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, Wolfgang Dekant <xxxxxx@xxxx.xxx-wuerzburg.de>, Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>Alan R Boobis <x.xxxxxx@xxxxxxxx.xx.xx>, Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx>, Helmut Greim [redacted]
Subject: Re: Brussels expenses

[redacted]

Cheers

Richard

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Saturday, 7 May 2016 at 12:27
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>, Alan R Boobis <x.xxxxxx@xxxxxxxx.xx.xx>, Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx>, Helmut Greim [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxx-wuerzburg.de>
Subject: Re: US Oak Foundation funding on ED

Just a couple of comments/additions, though not sure how helpful they are.

1. I presume the Boston public health grant will have gone to [redacted] So not all are as crazy and uncaring of scientific principles as others, speaking of which…..
2. [redacted] So no wonder these folk feel empowered, they're being given credibility at the highest possible level.

Rant over

Richard

From: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>
Date: Saturday, 7 May 2016 00:57
To: Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>, Alan R Boobis <x.xxxxxx@xxxxxxxx.xx.xx >, Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx >, Information Services <x.xxxxxx@xx.xx.xx >, Helmut Greim [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxx-wuerzburg.de>
Subject: Fwd: US Oak Foundation funding on ED

[redacted]

Dan
Von meinem iPhone gesendet

Anfang der weitergeleiteten E-Mail:

Von: [redacted]
Datum: 4. Mai 2016 18:14:13 MESZ
An: "[redacted]" <[redacted]>
Betreff: US Oak Foundation funding on ED

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]jpg>

[redacted]

From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
Date: Saturday, 7 May 2016 at 11:49
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>, Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>, Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>,Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx>, Helmut Greim [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>
Subject: Re: US Oak Foundation funding on ED

I agree with all of the changes (improvements) made but I think the very last 3 words can now be deleted as they're redundant.

Best

Richard

From: <Boobis>, Alan R <x.xxxxxx@xxxxxxxx.xx.xx >
Date: Saturday, 7 May 2016 10:11
To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, Information Services <x.xxxxxx@xx.xx.xx >, Colin Berry [redacted], Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx >, Helmut Greim [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >
Subject: RE: US Oak Foundation funding on ED

Dan et al

I think this strikes a reasonable balance between making the point whilst not being overly confrontational. I have only minor suggestions to this version.

I suspect that there will be time (and need) for a more aggressive piece when the response is published!

Best wishes,

Alan

From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx]
Sent: 07 May 2016 09:11
To: SHARPE Richard <x.xxxxxx@xx.xx.xx >; Colin Berry [redacted]; Boobis, Alan R <x.xxxxxx@xxxxxxxx.xx.xx >; Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx >; Helmut Greim [redacted]; Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx >
Subject: Re: US Oak Foundation funding on ED
Importance: High

Dear Richard, [redacted]

[redacted]

[redacted]

[redacted]

Dan

Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
Professor of Human and Environmental Toxicology,
Faculty of Biology, University of Konstanz
P.O. Box 622
Universitätsstrasse 10
D-78457 Konstanz, Germany

Telephone: [redacted]
Portable-Phone: [redacted]
Fax: [redacted]
email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
http://www.umwelttoxikologie.uni-konstanz.de

Von: SHARPE Richard <x.xxxxxx@xx.xx.xx >
Datum: Samstag, 7. Mai 2016 08:40
An: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>, Colin Berry <xxxxx@xxxxxxxxxxxx.xx.xx>, Alan R Boobis <x.xxxxxx@xxxxxxxx.xx.xx >, Pat Heslop-Harrison <xxxx@xxxxxxxxx.xx.xx >, Helmut Greim [redacted], Wolfgang Dekant <xxxxxx@xxxx.xxx-wuerzburg.de>
Betreff: Re: US Oak Foundation funding on ED

OK guys this is how my weekend started!

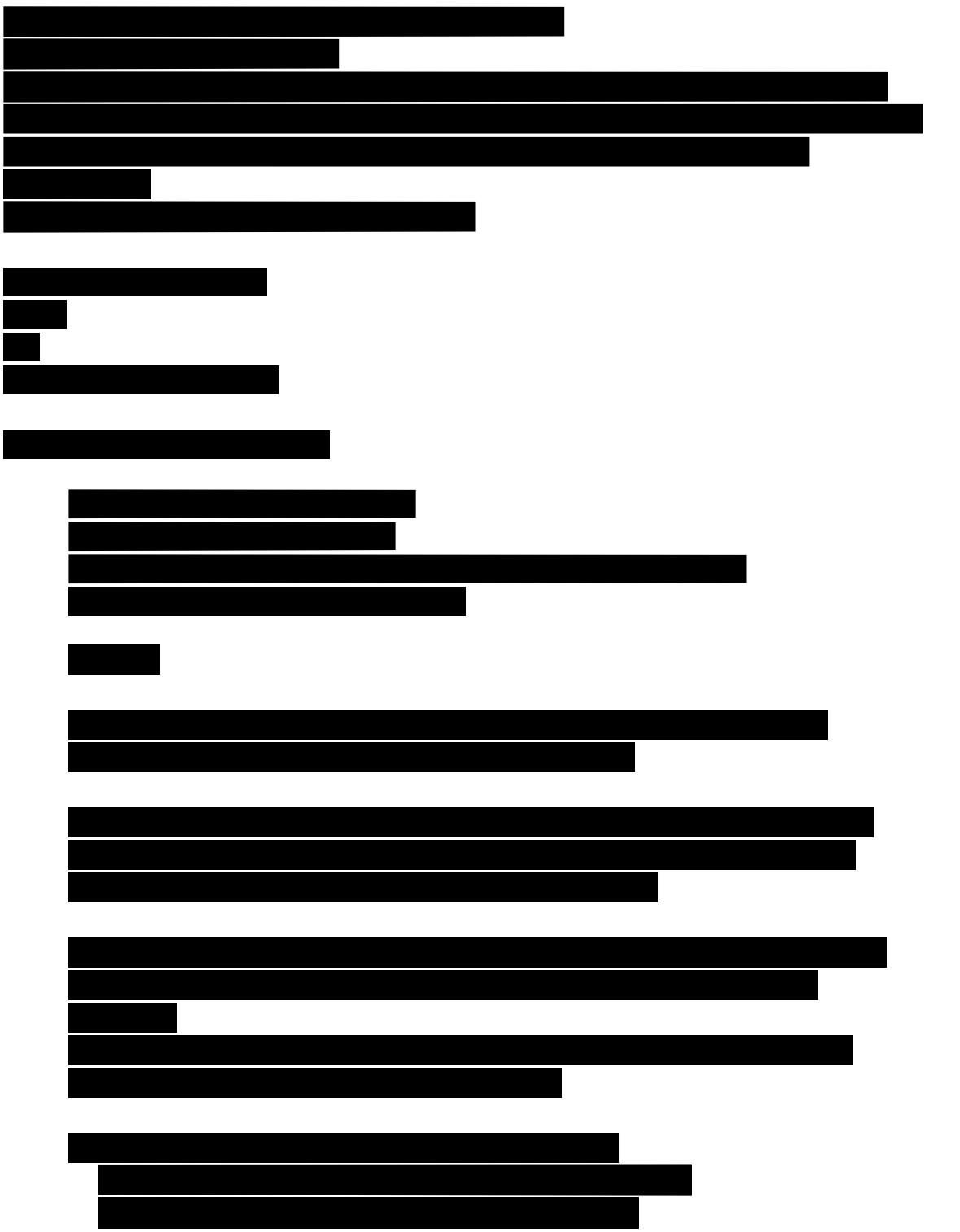
I've taken the latest version and dis-assembled it and tried to make it clearer why we are making this statement by explicitly showing what the dark side is proposing and why it is wrong. I'm sure it can be improved upon, so over to you for this. I turned off track changes when writing this because it was so difficult to read otherwise but if I know my laptop, the track changes will mysteriously reappear when I

attach the document.

One point: I've tried to really hammer home the clinical endocrinology aspect because (a) this is familiar to the commissioner, and (b) it ultimately has the biggest public impact because endocrine disorders are very common (maybe we should mention menopause, the commonest of the lot) and anything that 'doctors' do immediately elevates it to 'fact' status, whether or not that is accurate!

Enjoy your weekend – and I hope I didn't just make it worse.

Richard



From: SHARPE Richard
To: NOBLE Ann-Marie
Subject: FW: EDCs
Date: 17 July 2018 10:12:36

Date: Fri, 6 May 2016 13:27:39 +0100
Subject: Re: EDCs
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>,
Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>,
Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>,
"Greim, Helmut" [redacted]
"Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>,
[redacted]
CC: "xxxxxx@xxxx.xxxxxxxxxxxxx.xx" <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>,
[redacted]

I just re-read my e-mail and just wanted to say to Dan that I did not intend any criticism of him. Getting words down on paper is the most important first task as then we have a bone to chew upon, so I should have acknowledged his hard work in taking the first step for us all.

Richard

On 06/05/2016 13:10, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx> wrote:

>Richard
>
>It certainly resonates with me!
>
>I can sympathise with Dan's concerns following the way in which the
>outcome of the Berlin meeting is being portrayed. But I fully agree with
>you that if we resort to the same tactics we will not achieve anything.
>Our arguments must be evidence-based, level-headed and suitably
>circumspect.
>
>Best wishes,
>
>Alan
>
>-----Original Message-----
>From: SHARPE Richard [mailto:x.xxxxxx@xx.xx.xx
>Sent: 06 May 2016 13:04
>To: Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>; Colin Berry
><xxxxx@xxxxxxxxxxxxx.xx.xx>; Greim, Helmut
>[redacted]>; Heslop-Harrison, Pat (Prof.)
><xxxx@xxxxxxxxx.xx.xx[redacted]
>[redacted]
>Cc: Boobis, Alan R <x.xxxxxx@xxxxxxxx.xx.xx>;
[redacted]
>Subject: Re: EDCs
>
>I¹m not going to get near this today, but based on a quick read through,
>it will need considerable Œtoning down¹. I don¹t think we should be

>making sweeping interpretational statements (e.g. Absolutely no evidence
>that EDCs Š..), as then we are venturing into the same emotional
>territory as occupied by our counterparts. Instead, I think we need to
>give it a measured tone with emphasis solely on the differences between
>hazard and risk and on the critical importance of using evidence rather
>than presumption to guide risk evaluation and regulatory decision-making.
>It also needs to seek an advantage over the other side by pointing out
>that scaremongering and use of emotional arguments should have no place
>in any assessment nor should beliefs - only robust evidence. I also think
>it needs to mention that the goal of protecting the public from harmful
>exposures will never be achieved by basing it on simple
>characterisation/labelling, but only by obtaining sufficiently detailed
>evidence to show how and when a risk may be posed and ten managed
>(including banning a chemical if this is what the evidence supports).
>
>Sorry to just throw this into an e-mial for now, but I thought it might
>help to voice my knee jerk reaction, in case it resonates with anyone
>else.
>
>Best wishes
>
>Richard
>
>On 06/05/2016 11:30, "Daniel Dietrich" <Daniel.Dietrich@uni-konstanz.de>
>wrote:
>
>>Dear [redacted] and Dear colleagues.
[redacted]
>>Dan
>>Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>
>>Professor of Human and Environmental Toxicology, Faculty of Biology,
>>University of Konstanz P.O. Box 622 Universitätsstrasse 10
>>D-78457 Konstanz, Germany
>>
>>Telephone: [redacted]
>>Portable-Phone: [redacted]
>>Fax: [redacted]
>>email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>http://www.umwelttoxikologie.uni-konstanz.de
>>
>>
>>
>>
>>
>>
>>
>>Am 06.05.2016 08:33 schrieb "Colin Berry" unter
>>[redacted]
>>
>>>>Daniel,
>>>>I can make sure it goes to Sense about Science and The Science Media
>>>>Centre and [redacted] at SAS and [redacted] will mail it out
>>>>to their media contacts if I ask them, I am sure. I am on the Advisory
>>>>Boards of both.
>>>>Colin

>>>
>>>-----Original Message-----
>>>From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxx.xx
>>>Sent: Friday, May 6, 2016 7:05 AM
>>>To: Greim, Helmut; Heslop-Harrison, Pat (Prof.)
>>>Cc: Boobis, Alan R; xxxxxx@xxxx.xxxxxxxxxxxxx.xx; x.xxxxxx@xx.xx.xx;
>>>Colin Berry; [redacted]
>>>Subject: Re: EDCs
>>>
[redacted]
>>>Dan
>>>Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>
>>>Professor of Human and Environmental Toxicology, Faculty of Biology,
>>>University of Konstanz P.O. Box 622 Universitätsstrasse 10
>>>D-78457 Konstanz, Germany
>>>
>>>Telephone: [redacted]
>>>
>>>Portable-Phone: [redacted]
>>>Fax: [redacted]
>>>email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>http://www.umwelttoxikologie.uni-konstanz.de
>>>
>>>
>>>
>>>
>>>
>>>
>>>
>>>Am 05.05.2016 21:13 schrieb "Greim, Helmut" unter
>>><xxxxxx.xxxxx@xxx.xxxxxxxxxx.xx>:
>>>
[redacted]
>>>>helmut
>>>>
>>>>
>>>>Am 05.05.2016 19:39, schrieb Heslop-Harrison, Pat (Prof.):
[redacted]
>>>>>
>>>>> Pat
>>>>>
>>>>> Professor J.S. (Pat) Heslop-Harrison Department of Genetics
>>>>> University of Leicester Leicester LE1 7RH UK
>>>>>
>>>>> E-mail: xxxx@xx.xx.xx[redacted]
>>>>>
>>>>> Annals of Botany blog: www.AoBBlog.com [1]
>>>>> Websites: www.molcyt.com [2] [redacted] Chief Editor,
>>>>> Annals of Botany: www.annbot.com [3]
>>>>>
>>>>> Phone: [redacted]

>>>>> Mobile phone: [redacted]
>>>>> FAX: [redacted]
>>>>>
>>>>> ------------------------
>>>>>
>>>>> FROM: Boobis, Alan R [x.xxxxxx@xxxxxxxx.xx.xx]
>>>>> SENT: 05 May 2016 18:26
>>>>> TO: Helmut Greim; xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx;
>>>>> xxxxxx@xxxx.xxxxxxxxxxxx.xx; Heslop-Harrison, Pat (Prof.);
>>>>> x.xxxxxx@xx.xx.xx; xxxxx@xxxxxxxxxxxx.xx.xx
>>>>> CC: [redacted]
>>>>> SUBJECT: EDCs
>>>>>
>>>>> Dear all
>>>>>
>>>>> The comments at
>>>>>
>>>>>https://chemicalwatch.com/47135/official-edcs-statement-confirms-pot
>>>>>en
>>>>>cy-
>>>>>not-relevant-for-id
>>>>> [4] emphasize the need for an some commentary to explain the
>>>>>aspects of the statement emphasizing that identification is not the
>>>>>assessment of heath effects in exposed populations.
>>>>>
>>>>> Best wishes,
>>>>>
>>>>> Alan
>>>>>
>>>>>
>>>>> Links:
>>>>> ------
>>>>> [1] http://www.AoBBlog.com
>>>>> [2] http://www.molcyt.com
>>>>> [3] http://www.annbot.com
>>>>> [4]
>>>>>
>>>>>https://chemicalwatch.com/47135/official-edcs-statement-confirms-pot
>>>>>en
>>>>>cy-
>>>>>not-relevant-for-id
>>>
>>>
>>
>
>
>--
>The University of Edinburgh is a charitable body, registered in Scotland,
>with registration number SC005336.
>

From:	SHARPE Richard
To:	NOBLE Ann-Marie
Subject:	FW: Homeopathy
Date:	17 July 2018 10:11:10

Date: Tue, 3 May 2016 17:33:55 +0100
Subject: FW: Homeopathy
From: SHARPE Richard <x@xx
To: Colin Berry <x@xx,
"Boobis, Alan R" <x@xx,
"Greim, Helmut" [redacted],
"Heslop-Harrison, Pat (Prof.)" <x@xx

From: SHARPE Richard <x@xx
Date: Tuesday, 3 May 2016 at 17:33
To: Colin Berry <x@xx, "Boobis, Alan R" <a.boobis@imperial.ac.uk>, "Greim, Helmut" [redacted], "Heslop-Harrison, Pat (Prof.)" <x@xx
Subject: FW: Homeopathy

For your entertainment! http://youtu.be/HMGIbOGu8q0

From: Information Services <x@xx>
Date: Monday, 4 April 2016 20:23
To: [redacted]
Subject: Re: Homeopathy

That is brilliant – captures the absurdity by using humour. Great bit of script writing, especially the ending.
Cheers from [redacted]!

Richard

From: [redacted]
Reply-To: [redacted]
Date: Monday, 4 April 2016 13:50
To: Information Services <x@xx>, [redacted]
Subject: Homeopathy

[redacted]
http://youtu.be/HMGIbOGu8q0
[redacted]

[redacted]

Date: Thu, 28 Apr 2016 17:27:09 +0100
Subject: Re: meeting with Commissioner May 3
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
CC: "Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>,
Daniel Dietrich <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>,
Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>,
Wolfgang Dekant <xxxxxx@xxxx.xxxxxxxxxxxxx.xx>,
"Greim, Helmut" [redacted],
[redacted]

Thanks Aalan.
OK I'll aim to meet up with you all at midi.
My mobile number is [redacted] in case any changes.
Cheers

Richard

On 28/04/2016 15:49, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx> wrote:

>Richard
>
>We (Colin, Pat and I) are due in at 11:05.
>
>Best wishes,
>
>Alan
>
>Sent from my iPhone
>
>> On 28 Apr 2016, at 14:47, SHARPE Richard <x.xxxxxx@xx.xx.xx> wrote:
>>
>> Meeting up at Midi would be no problem for me, its just 1 more stop down
>> the line. So let me know your arrival time.
>> BW
>>
>> Richard
>>
>>> On 28/04/2016 14:31, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx> wrote:
>>>
>>> Richard
>>>
>>> The Eurostar gets into Midi station.
>>>
>>> Best wishes,
>>>
>>> Alan
>>>
>>> Sent from my iPhone
>>>
>>>> On 28 Apr 2016, at 14:29, SHARPE Richard <x.xxxxxx@xx.xx.xx> wrote:
>>>>
>>>> Thank you all for your speedy corrections/additions, which have dealt

>>>> with
>>>> everything that I had thought might need changing.
>>>> I think this is about as good and concise as we can aim for whilst
>>>>still
>>>> making the key points in a cogent and cohesive manner.
>>>> It will hopefully provide the basis for the commissioner's questions
>>>>to
>>>> us, which would be a great outcome.
>>>>
>>>> On an organisational point, I'm just wondering about when and how we
>>>> will
>>>> meet up at Berlaymont (I presume at the front entrance). Are those
>>>> arriving by train from UK terminating at Central station? If so, I
>>>>might
>>>> be able to meet up as I arrive early at the airport, and can time my
>>>> trip
>>>> into Central station accordingly.
>>>>
>>>> Best wishes
>>>>
>>>> Richard
>>>>
>>>>> On 28/04/2016 13:00, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
>>>>>wrote:
>>>>>
>>>>> Dear all
>>>>>
>>>>> I have added my suggestions to the version edited by others .
>>>>>
>>>>> Best wishes,
>>>>>
>>>>> Alan
>>>>>
>>>>> _____
>>>>> From: Heslop-Harrison, Pat (Prof.) <xxxx@xxxxxxxxx.xx.xx>
>>>>> Sent: 28 April 2016 12:03
>>>>> To: 'Daniel Dietrich'; Colin Berry; Wolfgang Dekant; SHARPE Richard;
>>>>> Greim, Helmut
>>>>> Cc: Boobis, Alan R; [redacted]
>>>>> Subject: RE: meeting with Commissioner May 3
>>>>>
>>>>> Dear All,
>>>>>

[redacted]

[redacted]

>>>>>
>>>>>
>>>>> Pat.
>>>>>
>>>>> Pat Heslop-Harrison
>>>>>
>>>>> Professor J.S. (Pat) Heslop-Harrison
>>>>> Department of Genetics,
>>>>> University of Leicester
>>>>> Leicester LE1 7RH UK
>>>>> xxxx@xx.xx.xx[redacted]
>>>>> Office: [redacted] Mobile: [redacted]
>>>>> FAX: [redacted]
>>>>> Web: www.molcyt.com [redacted]
>>>>> Blog: www.AoBBlog.com
>>>>> Chief Editor, Annals of Botany www.annbot.com
>>>>>
>>>>>
>>>>> -----Original Message-----
>>>>> From: Daniel Dietrich [mailto:xxxxxx.xxxxxxxx@xxxxxxxxxxx.xx
>>>>> Sent: 28 April 2016 11:28
>>>>> To: Colin Berry; Wolfgang Dekant; SHARPE Richard; Greim, Helmut
>>>>> Cc: Boobis, Alan R; Heslop-Harrison, Pat (Prof.)
>>>>> Subject: Re: meeting with Commissioner May 3
>>>>> Importance: High
>>>>>
>>>>> Dear Wolfgang
[redacted]

[redacted]
>>>>> Dan
>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT Professor of Human and
>>>>> Environmental Toxicology, Faculty of Biology, University of Konstanz
>>>>>
>>>>> Universitätsstrasse. 10
>>>>> D-78457 Konstanz, Germany
>>>>>
>>>>> Telephone: [redacted]
>>>>> [redacted]
>>>>> Portable-Phone: [redacted]
>>>>> Fax: [redacted]
>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>>
>>>>> Am 28.04.16 12:16 schrieb "Colin Berry" unter
>>>>> [redacted]:
>>>>>
>>>>>> Wolfgang,
>>>>>> I have made changes largely as a "precis" but you may disagree with
>>>>>> "identification" instead of "characterisation" in the first line.
>>>>>> However, I don't think the general rule is to characterise - that
>>>>>> might
>>>>>> be better.
>>>>>> Ignore anything you dislike
>>>>>> Regards
>>>>>> Colin
>>>>>>
>>>>>> -----Original Message-----
>>>>>> From: Wolfgang Dekant [mailto:xxxxxx@xxxx.xxxxxxxxxxxx].xx
>>>>>> Sent: Thursday, April 28, 2016 10:37 AM
>>>>>> To: Daniel Dietrich; Colin Berry; SHARPE Richard; Greim, Helmut
>>>>>> Cc: Boobis, Alan R; xxxx@xxxxxxxxx.xx.xx
>>>>>> Subject: Re: meeting with Commissioner May 3
>>>>>>
>>>>>> Dear all, [redacted]
>>>>>>
>>>>>> wd
>>>>>>
>>>>>>> Am 27.04.16 um 21:17 schrieb Daniel Dietrich:
>>>>>>> Dear Wolfgang And Richard:
[redacted]
>>>>>>> Dan
>>>>>>>
>>>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT
>>>>>>>
>>>>>>> Professor of Human and Environmental Toxicology, Faculty of

>>>>>>>Biology,
>>>>>>> University of Konstanz P.O. Box 622 Universitätsstrasse 10
>>>>>>> D-78457 Konstanz, Germany
>>>>>>>
>>>>>>> Telephone: [redacted]
>>>>>>>
>>>>>>> Secretary)
>>>>>>> Portable-Phone: [redacted]
>>>>>>> Fax: [redacted]
>>>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>>>
>>>>>>>
>>>>>>>
>>>>>>>
>>>>>>>
>>>>>>>
>>>>>>>
>>>>>>> Am 27.04.2016 17:03 schrieb "Colin Berry" unter
>>>>>>> [redacted]
>>>>>>>
>>>>>>>> I think that is super, Richard (and clinical, which will matter)
>>>>>>>> Colin Berry
>>>>>>>>
>>>>>>>> -----Original Message-----
>>>>>>>> From: SHARPE Richard [mailto:x.xxxxxx@xx.xx.xx
>>>>>>>> Sent: Wednesday, April 27, 2016 3:59 PM
>>>>>>>> To: Wolfgang Dekant; Greim, Helmut; Colin Berry
>>>>>>>> Cc: Boobis, Alan R; Daniel Dietrich; xxxx@xxxxxxxxx.xx.xx;
>>>>>>>> [redacted]
>>>>>>>> Subject: Re: meeting with Commissioner May 3
>>>>>>>>
>>>>>>>> Just to add a brief resume that might be included in the 1-page
>>>>>>>> briefing for the commissioner.
>>>>>>>>
>>>>>>>> So-called 'low dose/non-monotonic dose-response curves' for 1 or 2
>>>>>>>> endocrine-disrupting compounds (EDCs) in model systems has been a
>>>>>>>> key
>>>>>>>> argument for adopting a hazard-only based assessment process. It
>>>>>>>>is
>>>>>>>> now widely stated that non-monotonicity is a basic principle of
>>>>>>>> endocrine systems, whereas the opposite is actually the case. The
>>>>>>>> intrinsic homeostatic basis/regulation of all major endocrine
>>>>>>>> systems
>>>>>>>> would not operate if there was non-monotonicity. When this system
>>>>>>>> fails, you do not see the same disease at subnormal (low) and
>>>>>>>> supranormal (high) hormone levels but very different
>>>>>>>> diseases/symptoms with hormone deficiency versus hormone excess
>>>>>>>> (e.g.
>>>>>>>> Addisons v Cushings) that are treated successfully by
>>>>>>>> therapeutically returning hormone levels to normal. The whole of
>>>>>>>> clinical endocrinology is built around this and is based on
>>>>>>>>decades
>>>>>>>> of experience and evidence.
>>>>>>>>
>>>>>>>>
>>>>>>>> Homeostatic regulation may not apply to the hormonal regulation of
>>>>>>>> specific programming/organisational events (e.g. role of androgens
>>>>>>>> in fetal masculinisation) but the evidence we have from animal
>>>>>>>> studies is that only very high doses of EDCs (orders of magnitude
>>>>>>>> higher than human

>>>>>>>> exposure) can impair this process and for some of these there
>>>>>>>>appear
>>>>>>>> to be substantial human-rodent differences (no effect in humans)
>>>>>>>> based on the best available evidence.
>>>>>>>>
>>>>>>>> Therefore, to adopt a hazard-only approach to EDC regulation is
>>>>>>>> nonsensical as it ignores the available (strong) evidence that
>>>>>>>> endocrine systems work primarily on a straightforward dose
>>>>>>>>response
>>>>>>>> relationship.
>>>>>>>>
>>>>>>>> If nothing else, a bone for you all to chew on, as I'm sure the
>>>>>>>> wording can be improved.
>>>>>>>>
>>>>>>>> BW
>>>>>>>>
>>>>>>>> Richard
>>>>>>>>
>>>>>>>> On 27/04/2016 14:59, "Wolfgang Dekant"
>>>>>>>> <dekant@toxi.uni-wuerzburg.de>
>>>>>>>> wrote:
>>>>>>>>
>>>>>>>> Dear all,

>>>>>>>>>
>>>>>>>>> wd
>>>>>>>>>
>>>>>>>>> Am 27.04.16 um 09:55 schrieb Greim, Helmut:
>>>>>>>>> Dear all,

>>>>>>>>> Helmut
>>>>>>>>>
>>>>>>>>>
>>>>>>>>> Am 26.04.2016 23:06, schrieb Colin Berry:
>>>>>>>>> Dear Wolfgang,

>>>>>>>>>>> Daniel suggested I forward this, which I sent to him and
>>>>>>>>>>> Helmut earlier.
>>>>>>>>>>> Colin Berry
>>>>>>>>>>>
>>>>>>>>>>> Daniel,
>>>>>>>>>>> I agree about mixtures. The point you make is a
>>>>>>>>>>> difficult one but even if it is thought reasonable to use
>>>>>>>>>>>hazard
>>>>>>>>>>> Identification as a basis for intervention (pace the declared
>>>>>>>>>>> intention of IARC in their pre-amble) there must be data to
>>>>>>>>>>> support any assertion, or almost anything can be used to object
>>>>>>>>>>> to
>>>>>>>>>>> any process involving chemicals (the oxygen, glucose and sodium
>>>>>>>>>>> chloride are all deadly kind of nonsense.)
>>>>>>>>>>> Perhaps something like this should go in what we
>>>>>>>>>>> send.
>>>>>>>>>>>
>>>>>>>>>>> "In identifying any agent which has the potential to do harm,
>>>>>>>>>>> some mechanism of injury should be proposed, some target for
>>>>>>>>>>> disturbance should be identified, some likelihood of
>>>>>>>>>>>significant
>>>>>>>>>>> exposure characterised and some quantitative consideration as
>>>>>>>>>>>to
>>>>>>>>>>> the numbers of those exposed should be made. This will enable
>>>>>>>>>>> the potential benefit of the intervention to be assessed
>>>>>>>>>>>against
>>>>>>>>>>> its potential for harm and will enable the value of a
>>>>>>>>>>> regulatory intervention to be measured."
>>>>>>>>>>>
>>>>>>>>>>> This is very speculative and the result of an on-the-spot
>>>>>>>>>>> thought.
>>>>>>>>>>> Regards
>>>>>>>>>>> Colin
>>>>>>>>>>>
>>>>>>>>>>>
>>>>>>>>>>>
>>>>>>>>>>> -----Original Message-----
>>>>>>>>>>> From: Wolfgang Dekant [mailto:xxxxxx@xxxx.xxxxxxxxxxxx].xx
>>>>>>>>>>> Sent: Tuesday, April 26, 2016 6:55 AM
>>>>>>>>>>> To: Greim, Helmut; Boobis, Alan R
>>>>>>>>>>> Cc: xxxxxx@xxxx.xxxxxxxxxxxx.xx; SHARPE Richard; Daniel
>>>>>>>>>>> Dietrich; Colin Berry; xxxx@xxxxxxxxx.xx.xx
>>>>>>>>>>> Subject: Re: The Times article
>>>>>>>>>>>
>>>>>>>>>>> Dear all,

[redacted]

[redacted]
>>>>>>>>>>>> wd
>>>>>>>>>>>
>>>>>>>>>>>> Am 25.04.16 um 21:10 schrieb Greim, Helmut:
>>>>>>>>>>>> Dear all,
[redacted]
>>>>>>>>>>>> Helmut
>>>>>>>>>>>
>>>>>>>>>>>> Am 25.04.2016 17:30, schrieb Boobis, Alan R:
>>>>>>>>>>>>> Richard
>>>>>>>>>>>>>
>>>>>>>>>>>>> I agree with these points. We need to consider the
>>>>>>>>>>>>>alternative
>>>>>>>>>>>>> viewpoints and what is it we would like to realistically
>>>>>>>>>>>>> achieve.
>>>>>>>>>>>>>
>>>>>>>>>>>>> In my view we do need to emphasize the importance of risk
>>>>>>>>>>>>> assessment, as opposed to hazard identification for a range
>>>>>>>>>>>>>of
>>>>>>>>>>>>> socio-economic reasons (which we can elaborate); and the
>>>>>>>>>>>>>danger
>>>>>>>>>>>>> of considering risk in isolation, without considering
>>>>>>>>>>>>> alternative risks or benefits.
>>>>>>>>>>>>>
>>>>>>>>>>>>> Best wishes,
>>>>>>>>>>>>>
>>>>>>>>>>>>> Alan
>>>>>>>>>>>>> _____
>>>>>>>>>>>>> From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
>>>>>>>>>>>>> Sent: 25 April 2016 14:03
>>>>>>>>>>>>> To: Daniel Dietrich; Greim, Helmut; Wolfgang Dekant
>>>>>>>>>>>>> Cc: Colin Berry; Boobis, Alan R; xxxx@xxxxxxxxx.xx.xx
>>>>>>>>>>>>> Subject: Re: The Times article
>>>>>>>>>>>>>
>>>>>>>>>>>>> Dear All
>>>>>>>>>>>>>
>>>>>>>>>>>>> Whilst I agree in principle with what is written in the
>>>>>>>>>>>>> suggested text for the commissioner, I'm not sure that a
>>>>>>>>>>>>> sweeping dismissal of the 'views of the other side' on the

>>>>>>>>>>>>>> basis
>>>>>>>>>>>>>> of longstanding proven practice is necessarily the most
>>>>>>>>>>>>>> convincing approach. It can be seen as failing to move with
>>>>>>>>>>>>>>the
>>>>>>>>>>>>>> times, sticking ones head in the sand etc etc. We have to
>>>>>>>>>>>>>>think
>>>>>>>>>>>>>> of what the 'opposition thinkers' would present to the
>>>>>>>>>>>>>> commissioner, and whilst we can push some of that away on the
>>>>>>>>>>>>>> lack of convincing evidence, it is by no means as certain as
>>>>>>>>>>>>>>is
>>>>>>>>>>>>>> implied....if we are basing it on available evidence. The
>>>>>>>>>>>>>>human
>>>>>>>>>>>>>> epidemiological data is, in general, unconvincing but it is
>>>>>>>>>>>>>> constrained by all manner of difficulties and whilst many of
>>>>>>>>>>>>>> the
>>>>>>>>>>>>>> animal experimental studies are not relevant, not well enough
>>>>>>>>>>>>>> done or are confounded, based on the evidence I could not
>>>>>>>>>>>>>> simply
>>>>>>>>>>>>>> sweep it all aside. In particular, the mixtures issue is an
>>>>>>>>>>>>>> aspect that I find difficult to dismiss and in general the
>>>>>>>>>>>>>> studies on which it is based have been top quality.
>>>>>>>>>>>>>> I still don't see that it requires a different set of rules
>>>>>>>>>>>>>>for
>>>>>>>>>>>>>> its evaluation (i.e. I am not a believer in the 'low dose,
>>>>>>>>>>>>>> inverted U' thinking that is increasingly bandied around),
>>>>>>>>>>>>>>but
>>>>>>>>>>>>>> it unquestionably challenges the current risk assessment
>>>>>>>>>>>>>> process.
>>>>>>>>>>>>>> There is not a mention of this in the proposed commissioner
>>>>>>>>>>>>>> text, which I don't think is wise. To me, the wise approach
>>>>>>>>>>>>>>is
>>>>>>>>>>>>>> to acknowledge that these new developments need to be
>>>>>>>>>>>>>>factored
>>>>>>>>>>>>>> into the risk assessment and regulatory process (which will
>>>>>>>>>>>>>> take
>>>>>>>>>>>>>> some doing), but what would be sheer lunacy is to abandon
>>>>>>>>>>>>>>what
>>>>>>>>>>>>>> has been proven to work so well up until now. None of us can
>>>>>>>>>>>>>> see
>>>>>>>>>>>>>> that it will not continue to be the frontline, 'proven in
>>>>>>>>>>>>>> practice', optimal way to protect the public, but it has to
>>>>>>>>>>>>>> take
>>>>>>>>>>>>>> account of the new developments that are evidence-based. So
>>>>>>>>>>>>>> there has to be some middle path.
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> Whilst I'm on my soapbox, I also have never liked the idea of
>>>>>>>>>>>>>> using as a defence the argument about 'natural chemicals'
>>>>>>>>>>>>>>with
>>>>>>>>>>>>>> EDC activity being present in higher amounts than the
>>>>>>>>>>>>>> contaminants.
>>>>>>>>>>>>>> Its a weak defence that is easily attacked from several
>>>>>>>>>>>>>>angles.
>>>>>>>>>>>>>> Far better to rely on the proven principles of toxicology
>>>>>>>>>>>>>>etc.
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> I offer these gut reactions of mine as fuel for our thoughts
>>>>>>>>>>>>>> and discussions and will be happy to have them shot down in
>>>>>>>>>>>>>> flames!
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> All the best
>>>>>>>>>>>>>>

>>>>>>>>>>>>>> Richard
>>>>>>>>>>>>>>
>>>>>>>>>>>>>> On 25/04/2016 13:24, "Daniel Dietrich"
>>>>>>>>>>>>>> <Daniel.Dietrich@uni-konstanz.de>
>>>>>>>>>>>>>> wrote:
>>>>>>>>>>>>>>
[redacted]
>>>>>>>>>>>>>>>> Dan
>>>>>>>>>>>>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT Professor of
>>>>>>>>>>>>>>>>Human
>>>>>>>>>>>>>>>> and Environmental Toxicology, Faculty of Biology, University
>>>>>>>>>>>>>>>> of Konstanz
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>> Universitätsstrasse. 10
>>>>>>>>>>>>>>>> D-78457 Konstanz, Germany
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>> Telephone: [redacted]
>>>>>>>>>>>>>>>> [redacted]
>>>>>>>>>>>>>>>> Portable-Phone: [redacted]
>>>>>>>>>>>>>>>> Fax: [redacted]
>>>>>>>>>>>>>>>> email: Daniel.Dietrich@uni-konstanz.de
>>>>>>>>>>>>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>> Am 25.04.16 14:06 schrieb "Greim, Helmut" unter
>>>>>>>>>>>>>>>> <helmut.greim@lrz.tu-muenchen.de>:
>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>> Dear all,
[redacted]
>>>>>>>>>>>>>>>>> Regards
>>>>>>>>>>>>>>>>> Helmut
>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>> Am 25.04.2016 11:53, schrieb Wolfgang Dekant:
>>>>>>>>>>>>>>>>> Dear all, [redacted]
>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>> wd
>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>> Am 25.04.16 um 11:15 schrieb Daniel Dietrich:
>>>>>>>>>>>>>>>>> Dear Colleagues
[redacted]

[redacted]

>>>>>>>>>>>>>>>>>> Dan
>>>>>>>>>>>>>>>>>> Prof. Dr. Daniel Dietrich, Ph.D., FATS, ERT Professor of
>>>>>>>>>>>>>>>>>> Human and Environmental Toxicology, Faculty of Biology,
>>>>>>>>>>>>>>>>>> University of Konstanz
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>> Universitätsstrasse. 10
>>>>>>>>>>>>>>>>>> D-78457 Konstanz, Germany
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>> Telephone: [redacted]
>>>>>>>>>>>>>>>>>> [redacted]
[redacted]
>>>>>>>>>>>>>>>>>> Portable-Phone: [redacted]
>>>>>>>>>>>>>>>>>> Fax: [redacted]
>>>>>>>>>>>>>>>>>> email: xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx
>>>>>>>>>>>>>>>>>> http://www.umwelttoxikologie.uni-konstanz.de
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>> Am 25.04.16 10:42 schrieb "Greim, Helmut" unter
>>>>>>>>>>>>>>>>>> <xxxxxx.xxxxx@xxx.xxxxxxxxxx.xx>:
>>>>>>>>>>>>>>>>>>
[redacted]

>>>>>>>>>>>>>>>>>>>> Helmut
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> Am 24.04.2016 17:44, schrieb Colin Berry:
>>>>>>>>>>>>>>>>>>>> Do we send them papers in advance? This from Matt
>>>>>>>>>>>>>>>>>>>>Ridley
>>>>>>>>>>>>>>>>>>>> is good and my comments about hazard based systems and
>>>>>>>>>>>>>>>>>>>> reproducibility was focussed on IARC - do we send this
>>>>>>>>>>>>>>>>>>>> kind of thing?
>>>>>>>>>>>>>>>>>>>> Regards to all
>>>>>>>>>>>>>>>>>>>> Colin
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> -----Original Message-----
>>>>>>>>>>>>>>>>>>>> From: Boobis, Alan R [mailto:x.xxxxxx@xxxxxxxx.xx]
>>>>>>>>>>>>>>>>>>>> Sent: Sunday, April 24, 2016 3:05 PM
>>>>>>>>>>>>>>>>>>>> To: Greim, Helmut; xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx;
>>>>>>>>>>>>>>>>>>>> xxxxxx@xxxx.xxxxxxxxxxxx.xx; xxxx@xxxxxxxxx.xx.xx;
>>>>>>>>>>>>>>>>>>>> x.xxxxxx@xx.xx.xx; Colin Berry
>>>>>>>>>>>>>>>>>>>> Subject: Re: The Times article

>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> Helmut
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> I though this was a very helpful article in that it
>>>>>>>>>>>>>>>>>>>> identified many of the issues that concern us and would
>>>>>>>>>>>>>>>>>>>> be well worth discussing with the commissioner.
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> Best wishes,
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> A;an
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> _____
>>>>>>>>>>>>>>>>>>>> From: Greim, Helmut <xxxxxx.xxxxx@xxx.xx-muenchen.de>
>>>>>>>>>>>>>>>>>>>> Sent: 24 April 2016 14:58
>>>>>>>>>>>>>>>>>>>> To: Boobis, Alan R; xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx;
>>>>>>>>>>>>>>>>>>>> xxxxxx@xxxx.xxxxxxxxxxxx.xx; xxxx@xxxxxxxxx.xx.xx;
>>>>>>>>>>>>>>>>>>>> x.xxxxxx@xx.xx.xx[redacted]
>>>>>>>>>>>>>>>>>>>> Subject: The Times article
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> Dear all,

[redacted]

>>>>>>>>>>>>>>>>>>>> Best Helmut
>>>>>>>>>>>>>>>>>>>>
>>>>>>>>>>>>>>>>>>>> Stop misusing science to scare the world By Matt Ridley
>>>>>>>>>>>>>>>>>>>> De Niro's intervention in the MMR vaccine row
>>>>>>>>>>>>>>>>>>>>highlights
>>>>>>>>>>>>>>>>>>>> how the cherry-picking of data is warping our
>>>>>>>>>>>>>>>>>>>> understanding Science, humanity's greatest
>>>>>>>>>>>>>>>>>>>>intellectual
>>>>>>>>>>>>>>>>>>>> achievement, has always been vulnerable to infection
>>>>>>>>>>>>>>>>>>>>by
>>>>>>>>>>>>>>>>>>>> pseudoscience, which pretends to use the methods of
>>>>>>>>>>>>>>>>>>>> science, but actually subverts them in pursuit of an
>>>>>>>>>>>>>>>>>>>> obsession. Instead of evidence-based policymaking,
>>>>>>>>>>>>>>>>>>>> pseudoscience specialises in policy-based evidence
>>>>>>>>>>>>>>>>>>>> making.
>>>>>>>>>>>>>>>>>>>> Today, this infection is spreading.
>>>>>>>>>>>>>>>>>>>> Two egregious examples show just how easy it is to
>>>>>>>>>>>>>>>>>>>> subvert the scientific process. The campaign by Andrew
>>>>>>>>>>>>>>>>>>>> Wakefield against the MMR vaccine, recently boosted by
>>>>>>>>>>>>>>>>>>>> Robert De Niro's support, is pseudoscience.
>>>>>>>>>>>>>>>>>>>> So is the campaign against glyphosate ("Roundup")
>>>>>>>>>>>>>>>>>>>> weedkiller, which has now resulted in the European
>>>>>>>>>>>>>>>>>>>> parliament recommending a ban on its use by gardeners.
>>>>>>>>>>>>>>>>>>>> A large dossier claiming to find evidence that
>>>>>>>>>>>>>>>>>>>>glyphosate
>>>>>>>>>>>>>>>>>>>> is "probably carcinogenic" was published last year by
>>>>>>>>>>>>>>>>>>>>the
>>>>>>>>>>>>>>>>>>>> International Agency for Research on Cancer (IARC),
>>>>>>>>>>>>>>>>>>>>part
>>>>>>>>>>>>>>>>>>>> of the World Health Organisation.
>>>>>>>>>>>>>>>>>>>> What
>>>>>>>>>>>>>>>>>>>> could be more scientifically respectable?
>>>>>>>>>>>>>>>>>>>> Yet the document depends heavily on the work of an
>>>>>>>>>>>>>>>>>>>> activist employed by a pressure group called the
>>>>>>>>>>>>>>>>>>>> Environmental Defense
>>>>>>>>>>>>>>>>>>>> Fund:
>>>>>>>>>>>>>>>>>>>> Christopher
>>>>>>>>>>>>>>>>>>>> Portier, whose conflict of interest the IARC twice

>>>>>>>>>>>>>>>>>>>> omitted to disclose.
>>>>>>>>>>>>>>>>>>>> Portier chaired the committee that proposed a study on
>>>>>>>>>>>>>>>>>>>> glyphosate and then served as technical adviser to the
>>>>>>>>>>>>>>>>>>>> IARC's glyphosate report team, even though he is not a
>>>>>>>>>>>>>>>>>>>> toxicologist.
>>>>>>>>>>>>>>>>>>>> He has since been campaigning against glyphosate.
>>>>>>>>>>>>>>>>>>>> The IARC study is surely pseudoscience. It relies on a
>>>>>>>>>>>>>>>>>>>> tiny number of cherry-picked studies, and even these
>>>>>>>>>>>>>>>>>>>> don't
>>>>>>>>>>>>>>>>>>>> support its conclusion.
>>>>>>>>>>>>>>>>>>>> The evidence that it causes cancer in humans is
>>>>>>>>>>>>>>>>>>>> especially tenuous, based on three epidemiological
>>>>>>>>>>>>>>>>>>>> studies with confounding factors and small sample
>>>>>>>>>>>>>>>>>>>>sizes
>>>>>>>>>>>>>>>>>>>> "linking" it to Non-Hodgkin lymphoma (NHL). The study
>>>>>>>>>>>>>>>>>>>> ignored the US Agricultural Health Study, which has
>>>>>>>>>>>>>>>>>>>>been
>>>>>>>>>>>>>>>>>>>> tracking some
>>>>>>>>>>>>>>>>>>>> 89,000 farmers and their spouses for 23 years.
>>>>>>>>>>>>>>>>>>>> The study found "no association between glyphosate
>>>>>>>>>>>>>>>>>>>> exposure and all cancer incidence or most of the
>>>>>>>>>>>>>>>>>>>>specific
>>>>>>>>>>>>>>>>>>>> cancer subtypes we evaluated, including NHL . . ."
>>>>>>>>>>>>>>>>>>>> Many other studies found very little cancer risk from
>>>>>>>>>>>>>>>>>>>> glyphosate use, but the IARC argued that they included
>>>>>>>>>>>>>>>>>>>> some data generated by industry.
>>>>>>>>>>>>>>>>>>>> Well, of course they did, because we rightly demand
>>>>>>>>>>>>>>>>>>>>that
>>>>>>>>>>>>>>>>>>>> industry, not the taxpayer, pays for and does the
>>>>>>>>>>>>>>>>>>>>safety
>>>>>>>>>>>>>>>>>>>> testing of its products and makes the results public.
>>>>>>>>>>>>>>>>>>>>The
>>>>>>>>>>>>>>>>>>>> IARC appeared to ignore work by the German Federal
>>>>>>>>>>>>>>>>>>>> Institute for Risk Assessment, managing the glyphosate
>>>>>>>>>>>>>>>>>>>> dossier for the European Commission, which judged
>>>>>>>>>>>>>>>>>>>> glyphosate safe.
>>>>>>>>>>>>>>>>>>>> As
>>>>>>>>>>>>>>>>>>>> did the European Food Safety Authority, whose head
>>>>>>>>>>>>>>>>>>>> accused the IARC and Portier of bringing in the
>>>>>>>>>>>>>>>>>>>> "Facebook
>>>>>>>>>>>>>>>>>>>> age of science".
>>>>>>>>>>>>>>>>>>>> When Portier's role and the IARC's findings were
>>>>>>>>>>>>>>>>>>>>revealed
>>>>>>>>>>>>>>>>>>>> by David Zaruk, who blogs under the name the
>>>>>>>>>>>>>>>>>>>>Risk-Monger,
>>>>>>>>>>>>>>>>>>>> pressure started coming from many groups to censor his
>>>>>>>>>>>>>>>>>>>> science-policy blog.
>>>>>>>>>>>>>>>>>>>> The publisher EurActiv was forced to shut down Zaruk's
>>>>>>>>>>>>>>>>>>>> entire blog in the week of the European parliament
>>>>>>>>>>>>>>>>>>>>vote.
>>>>>>>>>>>>>>>>>>>> This is how Big Green behaves in Brussels, routinely.
>>>>>>>>>>>>>>>>>>>> Dose for dose, glyphosate is half as toxic as vinegar,
>>>>>>>>>>>>>>>>>>>> and one tenth as carcinogenic as caffeine. Not that
>>>>>>>>>>>>>>>>>>>> coffee's dangerous
>>>>>>>>>>>>>>>>>>>> - but the chemicals in it, like those in virtually any
>>>>>>>>>>>>>>>>>>>> vegetable, are dangerous in lab tests at absurdly high
>>>>>>>>>>>>>>>>>>>> concentrations. So is dihydrogen monoxide, for that
>>>>>>>>>>>>>>>>>>>> matter, if you inhale it, drink it to excess or let its
>>>>>>>>>>>>>>>>>>>> gaseous form burn your skin (that's H2O, by the way).
>>>>>>>>>>>>>>>>>>>> Besides, risk is hazard plus exposure, a point ignored
>>>>>>>>>>>>>>>>>>>>by

>>>>>>>>>>>>>>>>>>>> the IARC.
>>>>>>>>>>>>>>>>>>>> If
>>>>>>>>>>>>>>>>>>>> you routinely put coffee down your throat, you are
>>>>>>>>>>>>>>>>>>>> exposing yourself to the infinitesimal hazard caffeine
>>>>>>>>>>>>>>>>>>>> represents. If you spray a little Roundup on your
>>>>>>>>>>>>>>>>>>>>garden
>>>>>>>>>>>>>>>>>>>> path, you are not even exposing yourself to the more
>>>>>>>>>>>>>>>>>>>> infinitesimal hazard of glyphosate.
>>>>>>>>>>>>>>>>>>>> Roundup is probably the safest herbicide ever, with no
>>>>>>>>>>>>>>>>>>>> persistence in the environment. But the Green Blob
>>>>>>>>>>>>>>>>>>>>hates
>>>>>>>>>>>>>>>>>>>> it for three reasons.
>>>>>>>>>>>>>>>>>>>> It's
>>>>>>>>>>>>>>>>>>>> off-patent and therefore cheap. It was invented by
>>>>>>>>>>>>>>>>>>>> Monsanto, a company that had the temerity to make a
>>>>>>>>>>>>>>>>>>>> contribution to reducing famine and lowering food
>>>>>>>>>>>>>>>>>>>>prices
>>>>>>>>>>>>>>>>>>>> through innovation in agriculture. And some genetically
>>>>>>>>>>>>>>>>>>>> modified crops have been made resistant to it, so that
>>>>>>>>>>>>>>>>>>>> they can be weeded after planting by spraying, rather
>>>>>>>>>>>>>>>>>>>> than
>>>>>>>>>>>>>>>>>>>> tilling the
>>>>>>>>>>>>>>>>>>>> ground: this no-till farming is demonstrably better for
>>>>>>>>>>>>>>>>>>>> the environment, by the way.
>>>>>>>>>>>>>>>>>>>> Under the influence, at least in part of the IARC
>>>>>>>>>>>>>>>>>>>>report,
>>>>>>>>>>>>>>>>>>>> the European parliament voted last week to advise the
>>>>>>>>>>>>>>>>>>>> commission to ban glyphosate immediately for
>>>>>>>>>>>>>>>>>>>> "non-professionals" - ie gardeners - but allow it for
>>>>>>>>>>>>>>>>>>>> seven years for farmers. However, a lie is halfway
>>>>>>>>>>>>>>>>>>>>round
>>>>>>>>>>>>>>>>>>>> the world before the truth has got its boots on:
>>>>>>>>>>>>>>>>>>>>already
>>>>>>>>>>>>>>>>>>>> retailers worldwide are dropping glyphosate, Waitrose
>>>>>>>>>>>>>>>>>>>> included.
>>>>>>>>>>>>>>>>>>>> Much the same happened with the ban on neonicotinoid
>>>>>>>>>>>>>>>>>>>> pesticides, which was pushed through Brussels by a
>>>>>>>>>>>>>>>>>>>> tsunami
>>>>>>>>>>>>>>>>>>>> of angry emails from greens, in the teeth of clear
>>>>>>>>>>>>>>>>>>>> scientific advice that honey bee numbers were
>>>>>>>>>>>>>>>>>>>>increasing
>>>>>>>>>>>>>>>>>>>> and that alternative insecticides were worse.
>>>>>>>>>>>>>>>>>>>> James Gurney, a microbiologist who blogs on a site
>>>>>>>>>>>>>>>>>>>>called
>>>>>>>>>>>>>>>>>>>> the League of Nerds, describes the level of scholarship
>>>>>>>>>>>>>>>>>>>> in
>>>>>>>>>>>>>>>>>>>> the IARC report as "on a par with Andrew Wakefield of
>>>>>>>>>>>>>>>>>>>> MMR/autism fame".
>>>>>>>>>>>>>>>>>>>> In the case of Mr Wakefield's claim that the measles,
>>>>>>>>>>>>>>>>>>>> mumps and rubella
>>>>>>>>>>>>>>>>>>>> (MMR) vaccine causes autism, the push-back against
>>>>>>>>>>>>>>>>>>>> pseudoscience largely succeeded in this country, though
>>>>>>>>>>>>>>>>>>>> not before real harm had been done.
>>>>>>>>>>>>>>>>>>>> Journalists found that Mr Wakefield had failed to
>>>>>>>>>>>>>>>>>>>>declare
>>>>>>>>>>>>>>>>>>>> financing from lawyers preparing to sue vaccine makers
>>>>>>>>>>>>>>>>>>>> and
>>>>>>>>>>>>>>>>>>>> had taken blood samples at his own children's party;
>>>>>>>>>>>>>>>>>>>> further research failed to replicate his results. His
>>>>>>>>>>>>>>>>>>>> paper was retracted and he was struck off the medical
>>>>>>>>>>>>>>>>>>>> register, the General Medical Council calling him

>>>>>>>>>>>>>>>>>>>> dishonest and irresponsible. His message is now
>>>>>>>>>>>>>>>>>>>>falling
>>>>>>>>>>>>>>>>>>>> on
>>>>>>>>>>>>>>>>>>>> fertile ground in the United States, however, where
>>>>>>>>>>>>>>>>>>>> measles epidemics have resumed as a result.
>>>>>>>>>>>>>>>>>>>> In both these cases, superficial plausibility is lent
>>>>>>>>>>>>>>>>>>>>to
>>>>>>>>>>>>>>>>>>>> the scares by history. Earlier pesticides were more
>>>>>>>>>>>>>>>>>>>> dangerous:
>>>>>>>>>>>>>>>>>>>> copper sulphate (still used as a fungicide by "organic"
>>>>>>>>>>>>>>>>>>>> farmers) is toxic; DDT insecticide did wipe out
>>>>>>>>>>>>>>>>>>>>predatory
>>>>>>>>>>>>>>>>>>>> birds; paraquat herbicide was used in suicides. But
>>>>>>>>>>>>>>>>>>>> Roundup is far, far less dangerous than these.
>>>>>>>>>>>>>>>>>>>> Likewise, early vaccines did carry risks. In the 1950s
>>>>>>>>>>>>>>>>>>>> polio vaccines, grown in monkey tissue, were
>>>>>>>>>>>>>>>>>>>>contaminated
>>>>>>>>>>>>>>>>>>>> with SV40, a virus associated with cancer in monkeys.
>>>>>>>>>>>>>>>>>>>> Many
>>>>>>>>>>>>>>>>>>>> children were infected with the virus as a result.
>>>>>>>>>>>>>>>>>>>> Fortunately, SV40 proved neither infectious nor
>>>>>>>>>>>>>>>>>>>> carcinogenic in human beings, but it was a bullet
>>>>>>>>>>>>>>>>>>>>dodged.
>>>>>>>>>>>>>>>>>>>> Today such contamination is impossible.
>>>>>>>>>>>>>>>>>>>> Pseudoscience is bad enough when it infects
>>>>>>>>>>>>>>>>>>>>astrologers,
>>>>>>>>>>>>>>>>>>>> 9/11 truthers and crop-circle makers. But when its
>>>>>>>>>>>>>>>>>>>> symptoms show up in mainstream bodies, such as the
>>>>>>>>>>>>>>>>>>>>World
>>>>>>>>>>>>>>>>>>>> Health Organisation, it's time to be worried.
>>>>>>>>>>>> --
>>>>>>>>>>>> Prof. Dr. Wolfgang Dekant
>>>>>>>>>>>> Department of Toxicology
>>>>>>>>>>>> University of Wuerzburg
>>>>>>>>>>>> Versbacher Str. 9
>>>>>>>>>>>> 97078 Wuerzburg
>>>>>>>>>>>> Tel.: [redacted]
>>>>>>>>>>>> Fax: [redacted]
>>>>>>>>>> --
>>>>>>>>>> Prof. Dr. Wolfgang Dekant
>>>>>>>>>> Department of Toxicology
>>>>>>>>>> University of Wuerzburg
>>>>>>>>>> Versbacher Str. 9
>>>>>>>>>> 97078 Wuerzburg
>>>>>>>>>> Tel.: [redacted]
>>>>>>>>>> Fax: [redacted]
>>>>>>
>>>>>> --
>>>>>> Prof. Dr. Wolfgang Dekant
>>>>>> Department of Toxicology, University of Wuerzburg Versbacher Str. 9,
>>>>>> 97078 Wuerzburg, Germany Tel. [redacted]
>>>>>> Fax: [redacted]
>>>>>> Mobil: [redacted]
>>>>
>>>> The University of Edinburgh is a charitable body, registered in
>>>> Scotland, with registration number SC005336.
>>
>> The University of Edinburgh is a charitable body, registered in
>> Scotland, with registration number SC005336.

[redacted]

Date: Wed, 27 Apr 2016 12:59:17 +0100
Subject: Re: Conference Call regarding the Meeeting with Commissioner,
Wednesday 27th April, 15:00 - 16:00 CEST
From: SHARPE Richard <R.Sharpe@ed.ac.uk>
To: Helmut Greim [redacted]

From: SHARPE Richard <r.sharpe@ed.ac.uk>
Date: Wednesday, 27 April 2016 at 12:59
To: Helmut Greim [redacted]
Subject: Re: Conference Call regarding the Meeeting with Commissioner, Wednesday 27th April, 15:00 - 16:00 CEST

Hi [redacted]

I was just checking out he dial-in information ahead of our conference call in an hours time, and I'm a bit confused.
In dailling from the UK, do I use the German number that you cite in your e-mail [redacted]) or do I use one of the +44 numbers for the UK (which doesn't seem right).
Thanks for your help.

Richard

From: Helmut Greim <helmut.greim@lrz.tu-muenchen.de>
Date: Thursday, 21 April 2016 11:57
To: "a.boobis@imperial.ac.uk" <a.boobis@imperial.ac.uk>, "Daniel.Dietrich@uni-konstanz.de" <Daniel.Dietrich@uni-konstanz.de>, "dekant@toxi.uni-wuerzburg.de" <dekant@toxi.uni-wuerzburg.de>, "phh4@leicester.ac.uk" <phh4@leicester.ac.uk>, "R.Sharpe@ed.ac.uk" <R.Sharpe@ed.ac.uk>, [redacted]
Cc: "'Greim, Helmut'" [redacted]
Subject: Conference Call regarding the Meeeting with Commissioner, Wednesday 27th April, 15:00 - 16:00 CEST

Dear Sirs,

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]
[redacted]
for

****

Prof. Dr. med. Helmut Greim
Institute of Toxicology and Environmental Hygiene
Technical University of Munich
Hohenbachernstr. 15-17
D-85354 Freising-Weihenstephan
Germany
Phone: [redacted]
Fax: [redacted]
E-Mail: helmut.greim@lrz.tum.de

****

[redacted]

Date: Tue, 26 Apr 2016 14:36:01 +0100
Subject: Re: The Times article
From: SHARPE Richard <R.Sharpe@ed.ac.uk>
To: "Greim, Helmut" [redacted]
CC: Wolfgang Dekant <dekant@toxi.uni-wuerzburg.de>,
"Boobis, Alan R" <a.boobis@imperial.ac.uk>,
Daniel Dietrich <Daniel.Dietrich@uni-konstanz.de>,
Colin Berry <colin@sircolinberry.co.uk>,
"phh4@leicester.ac.uk" <phh4@leicester.ac.uk>

Hi Helmut

Well I'm an endocrinologist not a toxicologist and I'm certainly not in favour of a hazard-based approach. Whether I am representative or not is another question, although my strong feeling is that, at least in the UK, most endocrinologists would consider a hazard approach to be foolhardy.

The approach I've always tried to make to give non experts understandable perspective is that in clinical endocrinology it is the dose that makes the disease, with entirely different disorders associated with too little or too much of any of the major hormones, something that forms the foundations of practising clinical endocrinology as we know it - and it works in successful management of the patients. This at least drives a coach and horses through the non-monotonic dose-resposne fiasco, but it also emphasises that it is all about dose (exposure).

Talk tomorrow

Best wishes

Richard

On 26/04/2016 12:37, "Greim, Helmut" <helmut.greim@lrz.tu-muenchen.de> wrote:

>Dear Richard,
[redacted]
>Helmut
>
>
>Am 26.04.2016 10:04, schrieb SHARPE Richard:
>> Just online in EHP and highly relevant
>>
>> On 26/04/2016 06:54, "Wolfgang Dekant" <dekant@toxi.uni-wuerzburg.de>
>> wrote:
>>
>>> Dear all, [redacted]

[redacted]

>>>
>>> wd
>>>
>>> Am 25.04.16 um 21:10 schrieb Greim, Helmut:
>>>> Dear all,

[redacted]

>>>> Helmut
>>>>
>>>> Am 25.04.2016 17:30, schrieb Boobis, Alan R:
>>>>> Richard
>>>>>
>>>>> I agree with these points. We need to consider the alternative
>>>>> viewpoints and what is it we would like to realistically achieve.
>>>>>
>>>>> In my view we do need to emphasize the importance of risk
>>>>> assessment,
>>>>> as opposed to hazard identification for a range of socio-economic
>>>>> reasons (which we can elaborate); and the danger of considering risk
>>>>> in isolation, without considering alternative risks or benefits.
>>>>>
>>>>> Best wishes,
>>>>>
>>>>> Alan
>>>>> _____
>>>>> [redacted]

ehp ENVIRONMENTAL HEALTH PERSPECTIVES
http://www.ehponline.org

Scientific Issues Relevant to Setting Regulatory Criteria to Identify Endocrine Disrupting Substances in the European Union

Rémy Slama, Jean-Pierre Bourguignon, Barbara Demeneix, Richard Ivell, Giancarlo Panzica, Andreas Kortenkamp, and Thomas Zoeller

http://dx.doi.org/10.1289/EHP217

Received: 14 September 2015
Revised: 17 February 2016
Accepted: 5 April 2016
Published: 25 April 2016

Note to readers with disabilities: *EHP* will provide a 508-conformant version of this article upon final publication. If you require a 508-conformant version before then, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

NIH National Institute of Environmental Health Sciences

Environ Health Perspect DOI: 10.1289/EHP217
Advance Publication: Not Copyedited

Scientific Issues Relevant to Setting Regulatory Criteria to Identify Endocrine Disrupting Substances in the European Union

Rémy Slama[1], Jean-Pierre Bourguignon[2], Barbara Demeneix[3], Richard Ivell[4], Giancarlo Panzica[5], Andreas Kortenkamp[6], and Thomas Zoeller[7]

[1]Inserm and Univ. Grenoble Alpes, IAB joint research center, Team of Environmental Epidemiology, Grenoble, France; [2]Pediatric Endocrinology, CHU Liège and Neuroendocrinology Unit, GIGA Neurosciences, Univ. Liège, Belgium; [3]UMR CNRS/MNHN 7221, Dept. RDDM, Muséum National d'Histoire Naturelle, 75005 Paris, France; [4]School of Biosciences & School of Veterinary Medicine and Science, University of Nottingham, UK; [5]Dept. Neuroscience, University of Torino, and Neuroscience Institute Cavalieri Ottolenghi (NICO), Orbassano, Italy; [6]Brunel University London, Institute of Environment, Health and Societies, Uxbridge, UK; [7]University of Massachusetts, Biology Department, Amherst, Massachusetts, USA

Address correspondence to Rémy Slama, E-mail: remy.slama@ujf-grenoble.fr

Running title: Criteria to identify endocrine disruptors

Acknowledgments: The authors acknowledge the support of the Endocrine Society for meetings related to endocrine disruptors.

Competing financial interests: None. Additional information: RS, JPB, BD, RI, GP and TZ have had travel fees covered by the Endocrine Society (non-profit organization) for travel and accommodation expenses to meetings related to endocrine disruptors.

ABSTRACT

Background: Endocrine Disruptors (EDs) are defined by WHO as exogenous compounds or mixtures that alter function(s) of the endocrine system and consequently cause adverse effects in an intact organism, or its progeny, or (sub)populations. European regulations on pesticides, biocides, cosmetics, and industrial chemicals require the European Commission to establish scientific criteria to define EDs.

Objectives: We address the scientific relevance of four options for the identification of EDs proposed by the European Commission.

Discussion: Option 1, which does not define EDs and implies to use interim criteria unrelated to the WHO definition of EDs, is not relevant. Options 2 and 3 rely on the WHO definition for EDs, which is widely accepted by the scientific community, with option 3 introducing additional categories based on the strength of evidence (suspected EDs and endocrine active substances). Option 4 adds potency to the WHO definition, as a decision criterion. We argue that potency is dependent on the adverse effect considered, is scientifically ambiguous and note that potency is not used as a criterion to define other particularly hazardous substances such as carcinogens and reproductive toxicants. The use of potency requires a context that goes beyond hazard identification and corresponds to risk characterization, in which potency (or, more relevantly, the dose-response function) is combined with exposure levels.

Conclusions: There is scientific agreement regarding the adequacy of the WHO definition of EDs. The potency concept is not relevant to the identification of particularly serious hazards such as EDs. As is common practice for carcinogens, mutagens and reproductive toxicants, a multi-level classification of ED based on the WHO definition, and not considering potency, would be relevant (corresponding to option 3 proposed by the European Commission).

Introduction

The regulation of chemicals identifies specific classes of health hazards such as carcinogens, mutagens and reprotoxicants. Endocrine disruptors (EDs) are a new type of hazard identified by research. WHO defined an ED as "…an exogenous substance or mixture that alters the function(s) of the endocrine system and consequently causes adverse effects in an intact organism, or its progeny, or (sub)populations" (WHO/IPCS 2002). Following the first scientific reference to EDs (Colborn et al. 1993), a large body of research has considerably improved our understanding of their effects in wildlife and humans (e.g., Braun et al. 2011; Delfosse et al. 2014; Frye et al. 2012; Heindel et al. 2015; Kortenkamp et al. 2011; Shelton et al. 2014; UNEP/WHO 2013; Warner et al. 2014; Woodruff et al. 2011).

In 1999, the European Union (EU) became the first major economy to develop a strategy for the regulation of EDs (European Commission 1999). Subsequently, EDs have been addressed in at least four acts of EU law: the water framework directive (European Parliament 2000), REACH (the European Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals)(European Parliament 2006), the Cosmetics Regulation (European Parliament 2009a), the Plant Protection Products Regulation (PPPR)(European Parliament 2009b), as well as the Biocidal Products Regulation (European Parliament 2012). The two latter regulations required the European Commission to establish scientific criteria to identify substances with endocrine disrupting properties before December 2013.

The PPPR and the BPR specify that substances with ED properties used as pesticides or biocides will not receive approval for their use, with certain exceptions (e.g., if exposure is negligible). Thus, these laws are not based on risk assessment for EDs present in biocides and pesticides, but only require hazard identification if exposure is not negligible. This corresponds to so-called "hazard-based cut-off criteria" (see Figure 1 for the distinction

between hazard – a source of potential health effects – and risk – the actual impact of a substance in a population, in terms of disease probability or number of attributable disease cases). This hazard-based approach to pesticide and biocide regulation has been opposed by companies that market pesticides and biocides (CEFIC 2013; European commission 2015; European Crop Protection Association 2014).

In addition, editors of pharmacology and toxicology journals condemned in an editorial the proposed European Commission recommendations on ED regulations, which they claimed were based on scientifically unfounded precaution, defied common sense and well-established risk assessment principles; they called for the consideration of adverse effects and potency (Dietrich et al. 2013). Their editorial was criticized for being based on a factually incorrect interpretation of the proposed regulatory framework and for ignoring the programming role of the endocrine system during development (Bergman et al. 2013, Gore et al. 2013). Its authors were also called upon to provide information about potential conflicts of interest (Grandjean and Ozonoff 2013).

At a meeting convened by the EU Commission including signatories of the Dietrich et al. editorial and scientists with a strong base in ED research, a consensus was reached on the definition of EDs, on the existence of non-monotonic dose-responses and on the difficulties of determining thresholds for EDs (European commission 2013).

Despite the obligations to establish scientific criteria to identify EDs by December 2013, as specified by EU laws (European Parliament 2009b, 2012), no such criteria were published to date by the European Commission. Instead, the European Commission published a roadmap listing four options for defining criteria for identifying EDs and initiated an assessment of their impact (European Commission 2014)(Table 1). One of the options included in the

roadmap (option 4) would use potency as a decision criterion during the process of hazard identification.

The disregard for the obligations laid down in EU law led Sweden and several other EU countries to sue the European Commission. In December 2015, the European Court of Justice ruled that the European Commission acted unlawfully in failing to develop ED criteria and that an impact assessment was unnecessary (European Court of Justice 2015). This judgment heightened the urgency of developing scientifically-based regulatory criteria for identifying EDs.

Objectives

We elaborate some principles of ED regulation and specifically discuss the scientific relevance of each option considered by the European Commission to identify an ED, reviewing the availability of accepted definitions of EDs, endocrine active substances, and the relevance of the concept of potency for hazard identification. A parallel with carcinogens is drawn. The relevance of impact assessment studies to define scientific criteria is finally discussed.

Discussion

I. Proposed options regarding criteria for EDs in Europe

The general intention of defining ED criteria is "to ensure a high level of protection to human health and the environment and to strengthen the functioning of the internal market" (European Commission 2014). The four options proposed (European Commission 2014) are detailed in Table 1 and summarized below:

- *Option 1* consists of no policy change and no specification of criteria;
- *Option 2* relies on the World Health Organization (WHO) definition to identify EDs (WHO/IPCS 2002). This option a) identifies EDs as substances known or presumed to

cause endocrine-mediated adverse effects in humans or animal species living in the environment; b) stipulates that endocrine-mediated adverse effects should not be a non-specific secondary consequence of other toxic effects; c) defines *adverse effects* (as discussed below); d) excludes substances for which there is information demonstrating that the effects are not relevant for humans and for animal species living in the environment; and finally e) lists the step-by-step procedure to be followed for the identification;

- *Option 3* relies on the identification of ED as in Option 2 and further defines *suspected endocrine disruptors* and *endocrine active substances* (see below);
- *Option 4* relies on the WHO/IPCS definition of ED, and includes *potency* as element of hazard characterization. Potency is not defined, nor is the manner in which it would be combined with the ED definition.

The European Commission (2014) indicated that Option 1 (*no specification of criteria*) would run counter to the requirements of regulations calling for an operational definition of EDs. Moreover, the PPPR and BPR laws mention *interim* criteria, and these would likely apply. According to these interim criteria, all substances classified as carcinogenic category 2 or toxic for reproduction category 2 shall be considered as EDs (European Parliament 2009b). These interim criteria based on the definitions of carcinogens and reproductive toxicants have no scientific relevance to the WHO/IPCS definition of endocrine disruptors (WHO/IPCS 2002), so that Option 1 would not be scientifically justified. Consequently, we do not discuss this option further.

II. Availability of a definition of EDs

Option 2 of the roadmap defines EDs and *adverse effect*. At a workshop convened in 1996 in Weybridge (UK) by the European Commission, WHO and other institutions, an ED was defined as "an exogenous substance that causes adverse health effects in an intact organism,

or its progeny, secondary to changes in endocrine function" (quoted by EFSA Scientific Committee 2013). Several definitions were subsequently suggested by Canadian, Japanese and other institutions (reviewed by Kortenkamp et al. 2011), after which the International Program on Chemical Safety (IPCS), in collaboration with experts from Canada, Japan, the USA, and the EU, defined an ED as "…an exogenous substance or mixture that alters the function(s) of the endocrine system and consequently causes adverse effects in an intact organism, or its progeny, or (sub)populations" (WHO/IPCS 2002). The main differences with the Weybridge definition are the consideration of mixtures and of effects in populations or subpopulations.

The definition issued from the workshop convened by the US-Environmental Protection Agency (EPA) in 1995 in Raleigh (Kavlock et al. 1996), which is still referred to by EPA (EPA 2015), differs from the WHO/IPCS definition by lack of reference to adverse effects. As discussed below, substances acting on the endocrine system without evidence of an adverse health effect would be defined as endocrine active substances under Option 3.

It can be noted that for other categories of health hazards, specific adverse health effects are often referred to, as is the case for carcinogens or reprotoxins, while for mutagens there is only a reference to a mode of action. The WHO/IPCS definition of EDs refers to both a mode of action and an adverse effect at the scale of organs, organisms or populations. Consequently, conclusions about the nature of an ED require the integration of biochemical, toxicological, ecotoxicological/human data.

EFSA recommended that the WHO/IPCS definition be "adopted as a basis for the criteria for the identification of EDs" (EFSA Scientific Committee 2013). The European Commission roadmap acknowledges that "there is general consensus on the WHO/IPCS (2002) definition of an ED" (European Commission 2014).

The ED definition mentions *adverse effects*. Adverse effects were defined as a "change in the morphology, physiology, growth, development, reproduction or lifespan of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences" (WHO/IPCS 2009). The EC roadmap explicitly refers to this definition. This definition covers health effects at the individual level such as occurrence of diabetes or obesity, IQ loss, as well as congenital malformations, or changes not visible at the individual but only at the population level, such as alteration of the sex-ratio. It excludes, among others, transient changes in hormone levels that would not induce health effects in the short or long term. To our knowledge this definition has not been questioned. The expression of "(sub)population" in WHO/IPCS definition refers to effects that may concern the population as a whole or a specific subgroup (e.g. based on gender, age, genetic susceptibility, etc.).

III Suspected EDs and Endocrine Active Substances (Option 3)

In addition to defining an ED as in Option 2, Option 3 proposes two additional categories, suspected endocrine disruptors and endocrine active substances (EAS), that express the strength of evidence for a given compound.

Suspected endocrine disruptors are defined in the roadmap as "Substances where there is some evidence for endocrine-mediated adverse effects from humans, animal species living in the environment or from experimental studies, but where the evidence is not sufficiently strong to place the substance in Category I…" (European Commission 2014). This definition is close to the WHO/IPCS definition of a *possible endocrine disruptor* ("an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub)populations.") (WHO/IPCS 2002). *Endocrine active substances* are defined in the European Commission roadmap as:

"Substances for which there is some (…) potential for endocrine disruption mediated adverse effects in intact organisms and where the evidence is not sufficiently convincing to place the substance in category I [ED] or II [suspected ED]" (European Commission 2014). We believe that the terminology of *endocrine active substance* does not convey this lower level of evidence (a hierarchy such as ED [category I], presumed ED and suspected ED, similar to that of carcinogens shown in Table 1, would better fit this purpose). In contrast, an *Endocrine active substance* is defined by EFSA as "any chemical that can interact directly or indirectly with the endocrine system, and subsequently result in an effect on the endocrine system, target organs and tissues" (EFSA Scientific Committee 2013). The term is used to cover "all substances that in some way interfere with the endocrine system, but not necessarily induce adverse effects". This definition transmits the notion that there is evidence regarding the mode of action of the substance (interference with the endocrine system), but not regarding the induction of adverse effects, which is in line with the terminology of endocrine active substances. Therefore, we suggest to use the EFSA definition for EAS instead of the EC roadmap definition.

IV. Introduction of potency as a criterion for hazard identification (Option 4)

Option 4 of the roadmap is based on the WHO/IPCS definition of an ED, with potency as an added criterion. This option echoes approaches developed by the UK and German authorities with the explicit intention of limiting the number of substances that would fall under the hazard-based cut-off criteria of the PPPR and BPR (discussed in Kortenkamp et al. 2011). A publication from the German Federal institute for risk assessment also suggested to consider potency to identify EDs (Marx-Stoelting et al. 2015).

Potency is not well-defined; it is not in the glossary of terms of the environmental health criteria published by the International Program on Chemical Safety (IPCS 2009). The term is

presented in a publication sponsored by ECETOC, the European Centre for Ecotoxicology and Toxicology of Chemicals, a non-profit association of companies with interests in the manufacture and use of chemicals, as being "primarily based on the dose causing a specific toxic effect" without being clearly defined (Hennes et al. 2014). A publication from the German Federal institute for risk assessment indicates that “Potency relates to the dose levels at which certain effects occur.” (Marx-Stoelting et al. 2015). The International Union of Pharmacology defines potency as “an expression of the activity of a drug, in terms of the concentration or amount needed to produce a defined effect; an imprecise term that should always be further defined (see EC_{50}, IC_{50}, etc.)” (where EC_{50} is further defined as “The molar concentration of an agonist that produces 50% of the maximal possible effect of that agonist. Other percentage values (EC_{20}, EC_{40}, etc.) can be specified.”) (Neubig et al. 2003).

Hence, in pharmacology, potency is related to the dose-response function: a substance that at a certain dose causes 50% of its possible maximal effect magnitude (e.g., rate of animals with a specific disease) is considered more potent than another substance for which the same effect magnitude is attained at a larger dose. As already mentioned (Neubig et al. 2003), sometimes doses other than those leading to 50% of a given effect are used, such as 10% of a given effect, without apparent scientific justification of how these cut-off values are chosen. Thus, potency is simply a point of the dose-response function, corresponding to the dose at which this dose-response function intersects an arbitrary response level (Figure 2A).

Note that the step by step procedure of the EC roadmap (Options 2 and 3) mentions that it is necessary to « evaluate whether endocrine disruption is due to a specific endocrine-mediated mode of action and not to a non-specific secondary consequences of other toxic effects » (European Commission 2014). Consequently, effects that would occur at very high doses at which general toxicity is observed would generally not be enough to qualify the

compound as an ED, without the need to explicitly introduce concepts related to the dose at which effects occur.

The introduction of potency as a criterion in hazard identification would lead to several difficulties. First, this concept is not suited for compounds for which non-monotonic dose-response functions are possible, as is the case for EDs (Vandenberg et al. 2012). Second, the introduction of potency as a decision criterion may force the establishment of dichotomous regulatory cut-off values that are entirely arbitrary and not science-based, such that an ED with a potency of 10 mg/kg/day might be classified as an ED, while an ED with a potency 11 mg/kg/day (hence causing the same effect at an exposure of 11 instead of 10 mg/kg/day) would not be classified as an ED. Third, potency comparisons are influenced by the effect magnitude that is chosen to define the doses to be compared (i.e., whether one considers a 10% or a 50% increase, see Figure 2A), and by the health endpoint considered to define potency. Overall, potency is not a relevant concept for hazard identification.

Even in the context of risk management, potency alone is of little use. Indeed, dose-response functions, from which potency is defined, are not meaningful alone, and need to be interpreted in relation to exposure, which allows estimation of the level of risk for a given population (Figure 1). Low potency compounds with shallow dose-response functions and very frequent exposures (Figure 2B) may present greater risks at the population level than more potent chemicals with steep dose-response functions but less frequent exposure (Figure 2C). Well-established examples illustrating that the dose-response (or potency) cannot be considered alone to predict risk include airborne fine particulate matter ($PM_{2.5}$)(WHO 2014) and low exposures during critical windows of vulnerability like fetal development, such as those demonstrated for effects of PCBs on intellectual quotient (Jacobson and Jacobson 1996; Schantz et al. 2003). Accordingly, the EFSA scientific committee stated "… that, to assess

whether or not a (predefined) level of concern is reached for an ED, potency should not be used alone but should take account of actual or predicted exposure." (EFSA Scientific Committee 2013). Indeed, potency replaces dose-response curves by a single point of the curve, which results in a strong loss of information. If a risk-based and not hazard-based management is chosen, the relevant approach is to take into account the variations of the dose-response function over the whole range of exposures and combine it with actual exposures, for all relevant health outcomes, i.e. to explicitly perform a risk assessment study – but this goes beyond the steps required for hazard identification.

In the context of the PPPR and BPR, where some substances are to be regulated mostly on the basis of their hazard (at least if exposure is not negligible) and not their risk, considering dose-response functions (or potency) at the step of hazard identification would lead to reintroducing a logic of risk assessment. The discussion of whether or not the hazard-based logic of the PPPR and BPR for EDs should be modified into a risk-based regulation is a matter of policy. If deemed relevant by regulators, risk assessment should not be reintroduced partially (by considering only a component of risk assessment), nor "by the back door", i.e., indirectly, by requiring consideration of a criterion related to risk assessment such as potency. Rather, if necessary, this should be done explicitly, by modifying the legislation.

V. Parallel with hazard identification in the field of carcinogens

Another key argument against adopting criteria for EDs considering potency is consistency with the identification of other hazards of similar concern, such as carcinogens or reproductive toxicants. Several other types of chemical hazards are explicitly referred to in the EU regulation, including carcinogens, mutagens, reprotoxins. Carcinogens are defined as "a substance or a mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumors in well-performed experimental

studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans" (European Parliament 2008). For carcinogens, the EU defines three categories for carcinogenic substances (1A, 1B and 2, the latter corresponding to suspected carcinogens, Table 2). The classification of a substance in any category is based on a scientific assessment of the hazard (hazard identification) and does not take into consideration other components of the risk assessment scheme (Figure 1) such as "potency". Opting for options 2 or 4 would separate EDs from other hazards of equivalent concerns because the number of hazard categories would differ (in the case of Option 2, for which a substance is either identified as an ED or not, not alerting industry, consumers or policy-makers to *suspected* EDs) or because potency would be considered (Option 4). This would run counter to the policy choice of the legislation to consider EDs as being of equivalent concern to carcinogens, mutagens and reprotoxicants. Overall, the example of carcinogens shows that criteria defining a serious hazard need not be complex, nor need to resort to potency and risk-related concepts.

VI. Impact assessment studies are not designed to help defining hazards

The European Commission is carrying out an impact assessment as a preliminary step before deciding among the four options. Impact assessment studies provide an assessment of the potential economic**,** social and environmental impacts of alternative policy options. They would make sense if policy options were currently examined (e.g., between hazard-based regulation of pesticides or risk-based regulation), or after the implementation of a policy to judge its results. Here the relevant regulations (PPPR, BPR, REACH laws) have already been enacted but not applied.

Scientific criteria should rely on a scientific foundation. It is not the evaluation of the impact of a family of compounds that should guide their scientific definition; rather, the adoption of a

scientific definition conditions any impact evaluation. Continuing the previous parallel with other health hazards, carcinogens were defined prior to obtaining a clear picture of the number of existing carcinogens, and independently of their impact. Similarly, it would not be necessary to perform an impact assessment study before defining X-rays or explosives.

Studies of the impact of some EDs on disease burden and cost in Europe have already been published (Trasande et al. 2015). The economic cost associated with exposure to non-banned EDs in the EU was estimated to be 157 billion Euros per year (Trasande et al. 2015).

If option A leads to the identification of 10 substances that are EDs while option B identifies 50 further substances, will option B be preferred to limit the health impact of EDs or will option A be chosen to limit constraints on the industrial sector? Economic and health impacts are subject to quick changes as a function of exposure levels, development of substitutes or alternative industrial processes, existence of companies with relevant substitutes... Will the impact assessment be updated to take these changes into account, and the criteria modified accordingly?

In its ruling against the European Commission, the European court of justice stated that "the definition of scientific criteria to identify properties disrupting the endocrine system can only be done in an objective manner based on scientific data relative to the endocrine system, independently from any other consideration, and in particular from any economic consideration." (European Court of Justice 2015). Making a scientific definition dependent on the results of an assessment of its impact would be a dangerous precedent for public health and science in general.

Conclusion

The laws passed by the European parliament during the last decade constitute an innovative approach to limit health risks posed by EDs.

We have presented and discussed each option proposed by the European Commission to identify EDs (European Commission 2014), and provided specific recommendations (Table 3). Only options 2 and 3 comply with science. There is scientific consensus on the relevance of the WHO/IPCS definition of an ED (WHO/IPCS 2002). Option 4 modifies this definition by introducing the notion of potency, which is absent from the WHO/IPCS definition and from the criteria identifying carcinogens, which are hazards of equivalent concern to EDs. We believe that, because of the parallel with definitions of carcinogenic hazards (which have different categories based on evidence levels) and because it calls for the identification of suspected EDs, Option 3 is more relevant. This will provide a simple classification conveying the weight of the scientific evidence regarding the likelihood for the compound to be an ED: endocrine disruptors (expressing certainty), suspected endocrine disruptors, and endocrine active substances (see Table 2).

We recognize that scientific uncertainty remains with regard to the finer detail of mechanisms, the exact extent of health and environmental effects of EDs and their impact at the population level. There are also great uncertainties as to the number of substances likely to be identified as EDs. However, as demonstrated by the 40 years of work by the International Agency for Research on Cancer to identify carcinogens (Pearce et al. 2015), the availability of a clear definition of the hazard considered is a necessary first step. Once defining criteria are available, one can develop appropriate testing methods, identify substances and manage risk. Some of the test methods that will be required for regulatory purposes need to be developed and agreed upon.

There is no scientific or public health justification for the delay in the adoption of scientific criteria for EDs.

As scientists, we believe that impact assessment studies should not be used to define scientific criteria, nor be used as an argument for postponing the publication of a scientific definition. We are concerned that an impact assessment study could be used to bend science towards an outcome defined by aspects external to science. We are convinced that the (vague) notion of potency has no place in a hazard identification context. We are concerned that scientific definitions are being distorted in order to modify the spirit of a law which requires hazard-based management of EDs present in pesticides and biocides if exposure is not negligible, and not a risk-based management, thereby muddling science and policy. We believe that scientific criteria identifying EDs should follow the logic of the EU criteria for other serious hazards such as carcinogens and reproductive toxicants. We regret that several years have been spent on trying to issue scientific criteria defining a hazard that actually has been defined years earlier by a state-of-the-science report from WHO. We fear that the most plausible explanation for this delay is not a lack of scientific consensus but rather that postponing the publication of the scientific criteria is a way to postpone the full application of the 2009 pesticide regulation and 2012 biocide European regulation. This postponement is all the more worrying since these scientific criteria are but one of the first steps towards identifying EDs and providing more efficient protection of public health in the European Union.

References

Braun JM, Kalkbrenner AE, Calafat AM, Yolton K, Ye X, Dietrich KN, et al. 2011. Impact of early-life bisphenol a exposure on behavior and executive function in children. Pediatrics 128:873-882.

CEFIC. 2013. CEFIC's response - addressing the four discussion topics included in the Community strategy for endocrine disruptors. Available: http://www.asktheeu.org/fr/request/650/response/3056/attach/18/19.sanco.ddg2.e.3%202013%202884470%20annex.pdf [accessed 3 April 2016].

Colborn T, vom Saal FS, Soto AM. 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ Health Perspect 101:378-384.

Delfosse V, Maire AL, Balaguer P, Bourguet W. 2014. A structural perspective on nuclear receptors as targets of environmental compounds. Acta Pharmacol Sin.

Dietrich DR, Aulock S, Marquardt H, Blaauboer B, Dekant W, Kehrer J, et al. 2013. Scientifically unfounded precaution drives european commission's recommendations on edc regulation, while defying common sense, well-established science and risk assessment principles. Chem Biol Interact 205:A1-5.

EFSA Scientific Committee. 2013. Scientific opinion on the hazard assessment of endocrine disruptors:Scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment. EFSA Journal 11:3132. Available: http://www.efsa.europa.eu/fr/efsajournal/pub/3132 [accessed 3 April 2016].

EPA. 2015. What is endocrine disruption? Available: https://www.epa.gov/endocrine-disruption/what-endocrine-disruption [accessed 3 April 2016].

European Commission. 1999. Community strategy for endocrine disruptors - a range of substances suspected of interfering with the hormone systems of humans and wildlife.

Fed Reg COM (1999) 706. Available: http://ec.europa.eu/environment/archives/docum/99706sm.htm [accessed 3 April 2016]

European commission. 2013. Minutes of the expert meeting on endocrine disruptors held in the office of the chief scientific adviser on oct. 24 2013. Available: http://ec.europa.eu/archives/commission_2010-2014/president/chief-scientific-adviser/documents/minutes_endocrine_disruptors_meeting_241013_final.pdf [accessed 23 March 2016].

European Commission. 2014. Roadmap-defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection product regulation and biocidal products regulation. Available: http://ec.europa.eu/smart-regulation/impact/planned_ia/docs/2014_env_009_endocrine_disruptors_en.pdf [accessed 3 April 2016]

European commission. 2015. Report on public consultation on defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection product regulation and biocidal products regulation. Brussels: European Commission, Health and Food Safety. Available: http://ec.europa.eu/health/endocrine_disruptors/docs/2015_public_consultation_report_en.pdf [Accessed 23 March 2016].

European Court of Justice. 2015. Règlement (UE) n°528/2012 - Produits biocides - Recours en carence - Spécification des critères scientifiques pour la détermination des propriétés perturbant le système endocrinien - Défaut de la part de la Commission d'adopter des actes délégués - Obligation d'agir. Available: http://curia.europa.eu/juris/document/document_print.jsf?doclang=FR&text=&pageIndex=0&part=1&mode=lst&docid=173067&occ=first&dir=&cid=750233 [Accessed 23 March 2016]

European Crop Protection Association. 2014. ECPA's position on the criteria for the determination of endocrine disrupting properties under regulation 1107/2009. Available: http://www.ecpa.eu/files/attachments/23734_ECPA position paper on endocrine disruptors - 10 March 2014.pdf [Accessed 23 March 2016].

European Parliament. 2000. Directive 2000/60/EC of the European Parliament and of the Council establishing a framework for the community action in the field of water policy. Available: http://eur-lex.europa.eu/resource.html?uri=cellar:5c835afb-2ec6-4577-bdf8-756d3d694eeb.0004.02/DOC_1&format=PDF [Accessed 23 March 2016]

European Parliament. 2006. Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Available: [Accessed 23 March 2016]

European Parliament. 2008. Regulation (EC) No 1272/2008 of the European Parliament and of the council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing directives 67/548/EEC and 1999/45/EC, and amending regulation (EC) No 1907/2006. Fed Reg No 1272/2008. Available: http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A02008R1272-20150601 [Accessed 23 March 2016]

European Parliament. 2009a. Regulation (EC) No 1223/2009 of 30 November 2009 on cosmetic products. Available: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:02009R1223-20150416&from=EN [Accessed 23 March 2016]

European Parliament. 2009b. Regulation (EC) No 1107/2009 of 21 October 2009 concerning the placing of plant protection products on the market and repealing council directives 79/117/EEC and 91/414/EEC. Available: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32009R1107 [Accessed 23 March 2016]

European Parliament. 2012. Regulation (EU) No 528/2012 of 22 May 2012 concerning the making available on the market and use of biocidal products (BPR). Available: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02012R0528-20140425&from=EN [Accessed 23 March 2016]

Frye CA, Bo E, Calamandrei G, Calza L, Dessi-Fulgheri F, Fernandez M, et al. 2012. Endocrine disrupters: A review of some sources, effects, and mechanisms of actions on behaviour and neuroendocrine systems. J Neuroendocrinol 24:144-159.

Grandjean P, Ozonoff D. 2013. Transparency and translation of science in a modern world. Environ Health 12:70.

Heindel JJ, vom Saal FS, Blumberg B, Bovolin P, Calamandrei G, Ceresini G, et al. 2015. Parma consensus statement on metabolic disruptors. Environ Health 14:54.

Hennes C, Batke M, Bomann W, Duhayon S, Kosemund K, Politano V, et al. 2014. Incorporating potency into eu classification for carcinogenicity and reproductive toxicity. Regul Toxicol Pharmacol 70:457-467.

IPCS. 2009. Principles and methods for the risk assessment of chemicals in food. (Environmental Health Criteria). 240. International Programme on Chemical Safety. Available: http://www.inchem.org/documents/ehc/ehc/ehc240_index.htm [Accessed 23 March 2016]

Jacobson JL, Jacobson SW. 1996. Dose-response in perinatal exposure to polychlorinated biphenyls (PCBs): The Michigan and North Carolina cohort studies. Toxicol Ind Health 12:435-445.

Kavlock RJ, Daston GP, DeRosa C, Fenner-Crisp P, Gray LE, Kaattari S, et al. 1996. Research needs for the risk assessment of health and environmental effects of endocrine disruptors: A report of the U.S. EPA-sponsored workshop. Environ Health Perspect 104 Suppl 4:715-740.

Kortenkamp A, Martin O, Faust M, Evans R, McKinlay R, Orton F, et al. 2011. State of the art of assessment of endocrine disrupters. Available: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf [Accessed 23 March 2016]

Marx-Stoelting P, Braeuning A, Buhrke T, Lampen A, Niemann L, Oelgeschlaeger M, et al. 2015. Application of omics data in regulatory toxicology: Report of an international BfR expert workshop. Arch Toxicol 89:2177-2184.

Neubig RR, Spedding M, Kenakin T, Christopoulos A, International Union of Pharmacology Committee on Receptor N, Drug C. 2003. International union of pharmacology committee on receptor nomenclature and drug classification. XXXVIII. Update on terms and symbols in quantitative pharmacology. Pharmacol Rev 55:597-606.

Pearce N, Blair A, Vineis P, Ahrens W, Andersen A, Anto JM, et al. 2015. IARC monographs: 40 years of evaluating carcinogenic hazards to humans. Environ Health Perspect 123:507-514.

Schantz SL, Widholm JJ, Rice DC. 2003. Effects of PCB exposure on neuropsychological function in children. Environmental Health Perspectives 111:357-376.

Shelton JF, Geraghty EM, Tancredi DJ, Delwiche LD, Schmidt RJ, Ritz B, et al. 2014. Neurodevelopmental disorders and prenatal residential proximity to agricultural pesticides: The CHARGE study. Environ Health Perspect 122:1103-1109.

Trasande L, Zoeller RT, Hass U, Kortenkamp A, Grandjean P, Myers JP, et al. 2015. Estimating burden and disease costs of exposure to endocrine-disrupting chemicals in the european union. J Clin Endocrinol Metab 100:1245-1255.

UNEP/WHO. 2013. World Health Organization, United Nation Environmental Program. In: Bergman, A., Heindel, J.J., Jobling, S., Kidd, K.A., Zoeller, R.T. (Eds.), State of the science of endocrine disrupting chemicals. Available:

http://www.who.int/ceh/publications/endocrine/en/index.html [Accessed 23 March 2016]

Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR, Jr., Lee DH, et al. 2012. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev 33:378-455.

Warner M, Wesselink A, Harley KG, Bradman A, Kogut K, Eskenazi B. 2014. Prenatal exposure to dichlorodiphenyltrichloroethane and obesity at 9 years of age in the Chamacos study cohort. Am J Epidemiol 179:1312-1322.

WHO. 2014. WHO expert meeting: Methods and tools for assessing the health risks of air pollution local, national and international level (meeting report). Available: http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2014/who-expert-meeting-methods-and-tools-for-assessing-the-health-risks-of-air-pollution-at-local,-national-and-international-level [Accessed 23 March 2016]

WHO/IPCS. 2002. Global assessment of the state-of-the-science of endocrine disruptors. WHO/PCS/EDC/02.2. Available: http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/ [Accessed 23 March 2016]

WHO/IPCS. 2009. Principles and methods for the risk assessment of chemicals in food. (Environmental Health Criteria).World Health Organisation. International Program on Chemical Safety. Available: http://www.who.int/foodsafety/publications/chemical-food/en/ [Accessed 23 March 2016]

Woodruff TJ, Zota AR, Schwartz JM. 2011. Environmental chemicals in pregnant women in the United States: NHANES 2003-2004. Environmental Health Perspectives 119:878-885.

Table 1: Four options to identify endocrine-disrupting substances in the EC 2014 roadmap (European Commission 2014).

Option	Details	Comments
1	No criteria are specified. The interim criteria set in the BPR and PPPR continue to apply.	Would run counter the PPPR and BPR, which require scientific criteria to be defined. Would lead to the interim criteria (which are not coherent with the WHO/IPCS (2002) definition of EDs) to be used.
2	WHO/IPCS definition (WHO/IPCS 2002) to identify ED (hazard identification). ED are identified as: a) Substances which are i) known or presumed to have caused endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects in animal species living in the environment or ii) where there is evidence from experimental studies (in vivo), possibly supported with other information (e.g. (Q)SAR, analogue and category approaches) to provide a strong presumption that the substance has the capacity to cause endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects on animal species living in the environment; b) the experimental studies used to determine if a substance is an endocrine disruptor shall provide clear evidence of endocrine-mediated adverse effects in the absence of other toxic effects, or if occurring together with other toxic effects, the endocrine-mediated adverse effects should not be a non-specific secondary consequence of other toxic effects; c) An adverse effects is a change in the morphology, physiology, growth, development, reproduction, or, life span of an organism, system, or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences, as stated in (WHO/IPCS 2009); d) where there is (e.g. mechanistic) information demonstrating that the effects are clearly not relevant for humans and not relevant at population level to animal species living in the environment, then the substance should not be considered an endocrine disruptor; e) The identification shall follow a step by step procedure as follows: i) gather all available data; ii) assess the	

	data quality, reliability, reproducibility and consistency; iii) consider adversity and mode of action together in a weight of evidence approach based on expert judgment; iv) evaluate whether endocrine disruption is due to a specific endocrine-mediated mode of action and not to a non-specific secondary consequences of other toxic effects; v) evaluate human and wildlife relevance; vi) final (eco)toxicological evaluation indicating, where possible, whether the adverse effect is in relation to human health or environment (vertebrates and/or invertebrate populations), and where possible which are the axes or mechanisms concerned (e.g. estrogenic, androgenic, thyroid and/or steroidogenic axes)	
3	WHO/IPCS definition (WHO/IPCS 2002) to identify ED (hazard identification) as in option 2. Introduction of additional categories based on the different strength of evidence for fulfilling the WHO/IPCS definition: **Category I:** *endocrine disruptors* (as defined in 2a-2d). **Category II:** *suspected endocrine disruptors*, defined as substances where there is some evidence for endocrine-mediated adverse effects from humans, animal species living in the environment or from experimental studies, but where the evidence is not sufficiently strong to place the substance in Category I. If, for example, limitations in the studies make the quality of evidence less convincing, Category II could be more appropriate. Points 2b, 2c (definition of adverse effect) and 2d above remain valid for Category II. **Category III:** *endocrine active substances*, defined as substances for which there is some in vitro or in vivo evidence indicating a potential for endocrine disruption mediated adverse effects in intact organisms and where the evidence is not sufficiently convincing to place the substance in category I or II. The allocation to categories shall follow a step-by-step procedure (identical to that listed in 2e above).	The definition of *endocrine active substances* (category III) does not follow the definition provided by EFSA, which refers to substances that can interfere or react with the endocrine system (without evidence of adverse effect).
4	WHO/IPCS definition (WHO/IPCS 2002) to identify ED (hazard identification) and inclusion of potency as element of hazard characterization	Potency is not defined. Option 4 introduces elements of risk assessment. No step-by-step procedure provided as in 2 and 3.

BPR: Biocide Products Regulation (EU); PPPR: Plant Protection Products Regulation (EU).

Table 2: Categories of carcinogenic substances, as defined by the EU CLP regulation (EC, No. 1272/2008 on classification, labeling and packaging of substances and mixtures). In the right-hand column, we have added the 3 levels for EDs proposed in Option 3 of the European Commission roadmap (2014).

Carcinogens [a]		**Endocrine Disrupting Chemicals (option 3 of the EC Roadmap)**	
Hazard Class		**Hazard Class**	
Category 1A	Substances known to have carcinogenic potential for humans [b]	**I**	Substances known to be an endocrine disruptor
Category 1B	Substances presumed to have carcinogenic potential for humans [b]	**II**	Suspected endocrine disruptors
Category 2	Suspected human carcinogens [c]	**III**	Endocrine active substances

a. A carcinogen is defined as a substance or a mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumors in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans (European Parliament 2008) .
b. A substance is classified in Category 1 for carcinogenicity on the basis of epidemiological and/or animal data. A substance may be further distinguished as: Category 1A, known to have carcinogenic potential for humans, classification is largely based on human evidence, or category 1B, presumed to have carcinogenic potential for humans, classification is largely based on animal evidence.
c. According to the EU regulation, the placing of a substance in Category 2 (Suspected human carcinogens) is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or 1B, based on strength of evidence together with additional considerations. Such evidence may be derived either from limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Table 3: Recommendations.

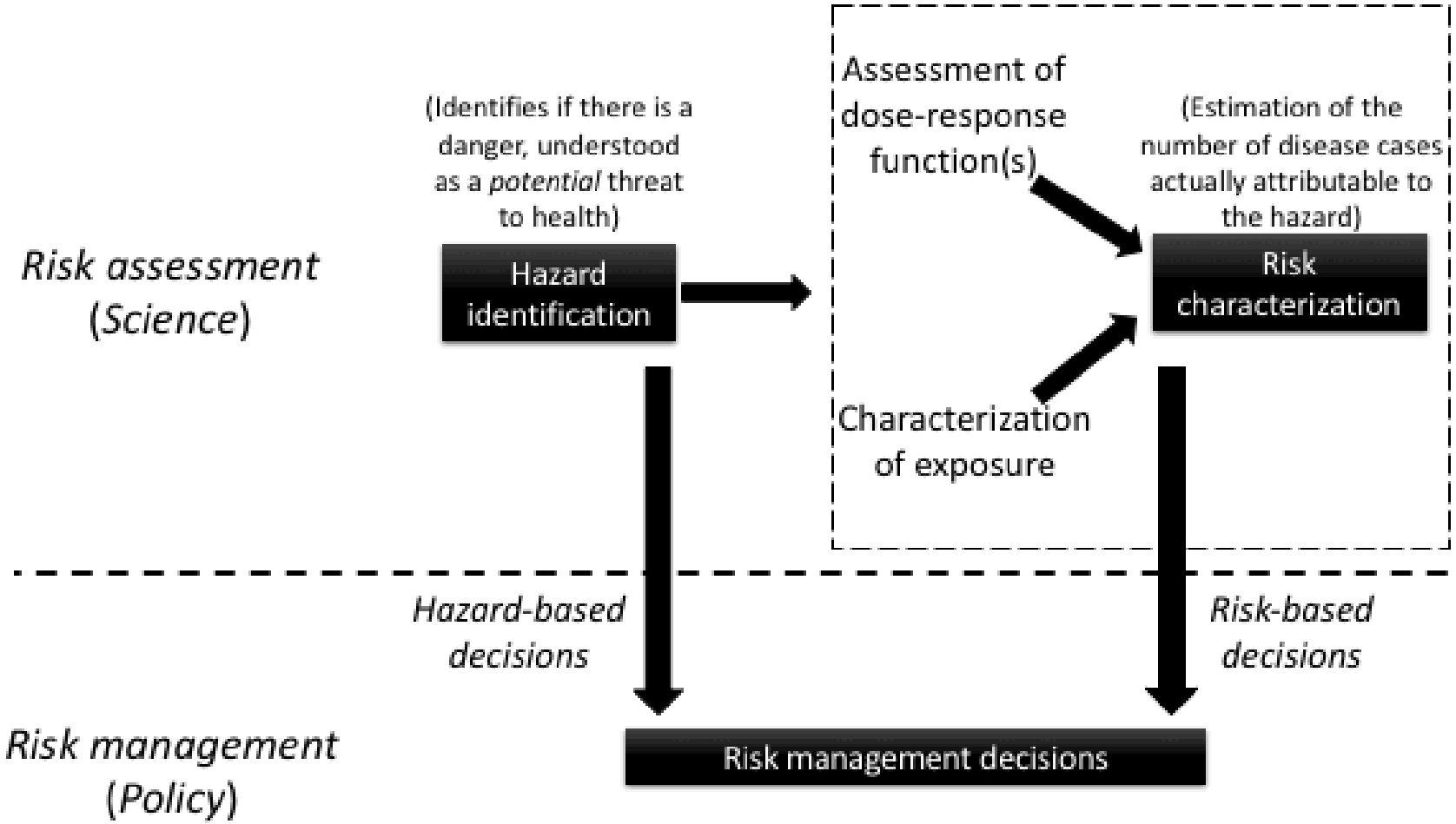
RECOMMENDATION	RATIONALE
1. Refer to the WHO/IPCS (2002) definition of EDs, potential (suspected) ED, and adverse effects; and to the EFSA definition of endocrine active substances.	Follow scientific consensus.
2. Identify hazards without referring to potency.	Potency is poorly defined, endpoint dependent, is not used to define other hazards of equivalent concern such as carcinogens and belongs to risk assessment, not hazard identification.
3. Consider hazard identification and risk characterization as separate issues. Do not use scientific criteria to move from a hazard-based to a risk-based regulation for specific substances	Any change in the spirit of the law should be done explicitly in the law, not via a delegate act.
4. Establish scientific ED criteria irrespective of an impact assessment study	Impact assessment studies are not meant to provide scientific definitions.
5. Incorporate the level of evidence in characterization of EDs (option 3)	Proven to be relevant for carcinogens and other hazardous substances of equivalent concern to EDs.

Figure Legends

Figure 1: Hazard-based versus risk-based management of hazards. Note that the step of risk characterization is sometimes (ambiguously) termed hazard characterization.

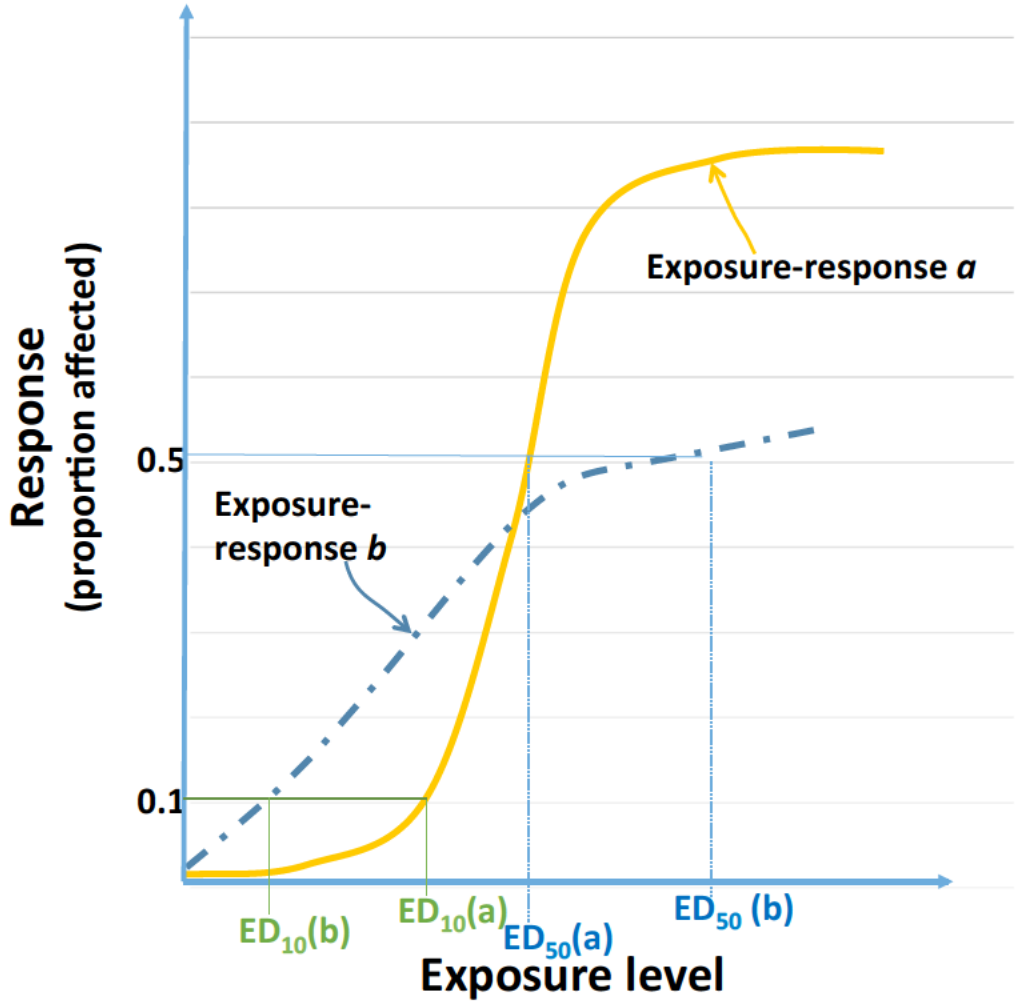
Figure 2: Illustration of issues with the potency concept with hypothetical dose-response functions and distributions of exposure. **A)** Situation of dose-response functions that cross: If potency is defined as the dose ED_{50} leading to 50% of a given response, then chemical with the dose-response function *a* is considered more potent than chemical with exposure-response function *b*; if potency is defined as the dose leading to 10% of the response (ED_{10}), then chemical with dose-response *a* is less potent than chemical with exposure-response *b*. **B)** Shallow dose-response function (and low potency) with a large proportion of highly exposed subjects, hence entailing a possibly high risk. **C)** Steep dose-response function (and high potency) with a low proportion of highly exposed subjects, hence entailing a possibly similar or lower risk. Blue bars in B) and C) represent the distribution of exposure in the population.

Figure 1.

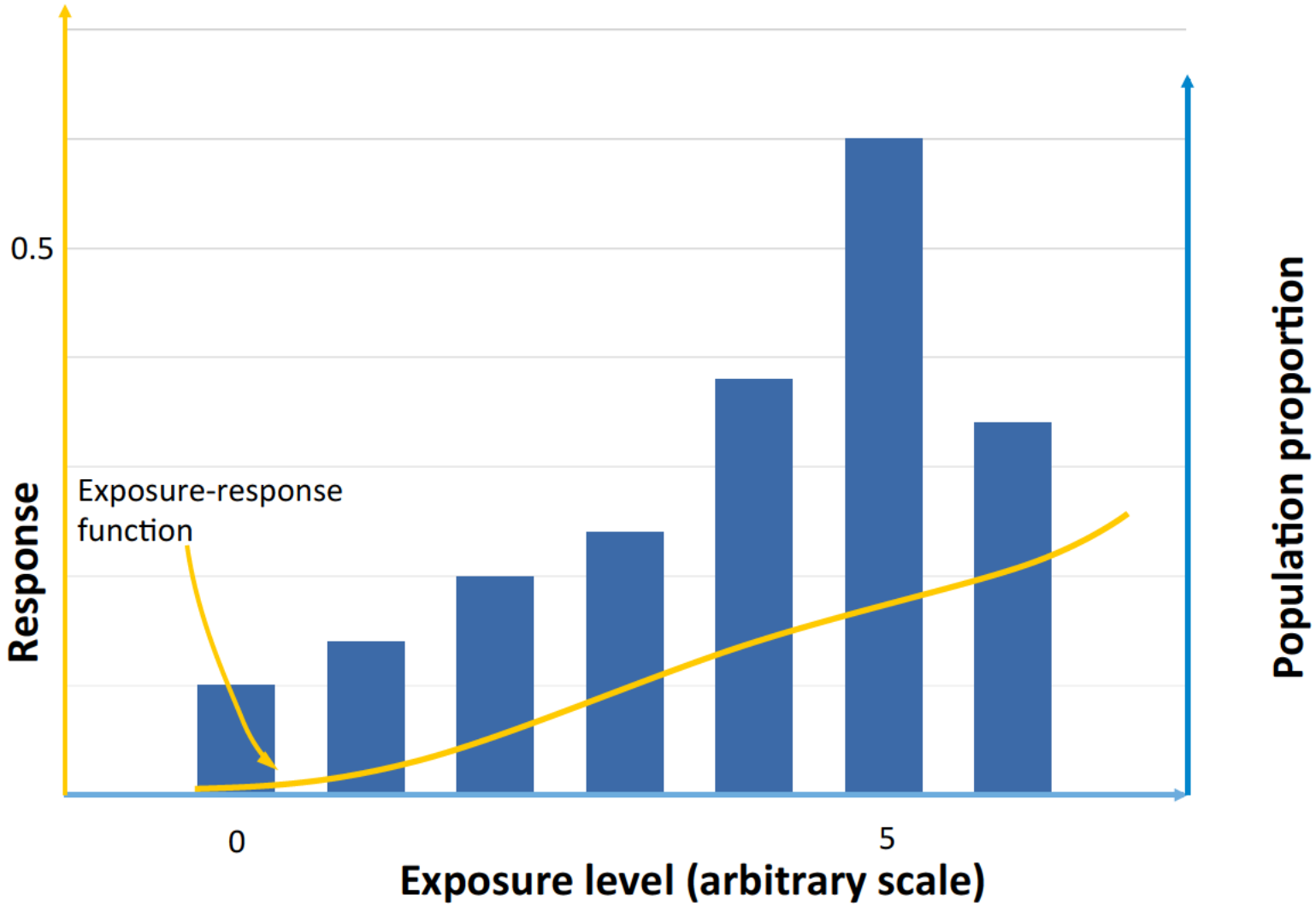

Risk assessment
(Science)
(Identifies if there is a danger, understood as a *potential* threat to health)
Hazard identification
Assessment of dose-response function(s)
(Estimation of the number of disease cases actually attributable to the hazard)
Risk characterization
Characterization of exposure
Hazard-based decisions
Risk-based decisions
Risk management
(Policy)
Risk management decisions

Environ Health Perspect DOI: 10.1289/EHP217
Advance Publication: Not Copyedited

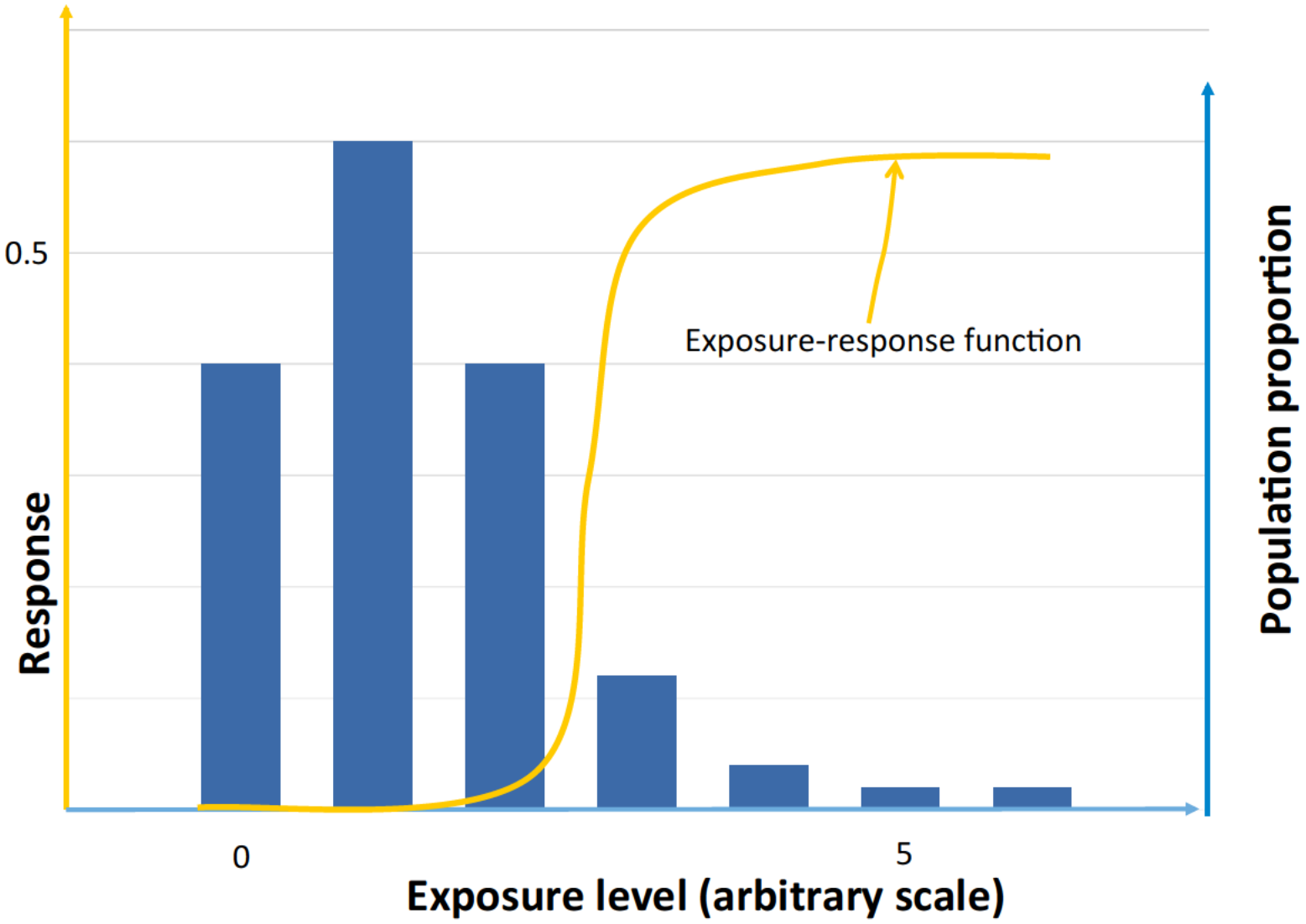
Figure 2.



Environ Health Perspect DOI: 10.1289/EHP217
Advance Publication: Not Copyedited



Environ Health Perspect DOI: 10.1289/EHP217
Advance Publication: Not Copyedited



[redacted]

Date: Thu, 21 Apr 2016 10:07:31 +0100
Subject: Re: meeting with Commissioner May 3
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
CC: "Greim, Helmut" [redacted]
"Heslop-Harrison, Pat (Prof.)" <xxxx@xxxxxxxxx.xx.xx>,
"xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx" <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>,
"xxxxxx@xxxx.xxxxxxxxxxxx.xx" <xxxxxx@xxxx.xxxxxxxxxxxx.xx>,
[redacted]

Thanks Alan, Helmut
I'm also now booked into [redacted]

Richard

On 21/04/2016 09:34, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx> wrote:

>Richard
>
>A number of us are staying at [redacted]
>
>Best wishes,
>
>Alan
>
>Sent from my iPhone
>
>> On 21 Apr 2016, at 10:32, SHARPE Richard <x.xxxxxx@xx.xx.xx> wrote:
>>
>> Which hotel(s) are you guys staying at?
>> Richard
>>
>>> On 20/04/2016 08:31, "Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx> wrote:
>>>
>>> Helmut
>>>
>>> Many thanks indeed.
>>>
>>> Best wishes,
>>>
>>> Alan
>>>
>>> _____
>>> From: Greim, Helmut [redacted]
>>> Sent: 20 April 2016 08:02
>>> To: Heslop-Harrison, Pat (Prof.)
>>> Cc: Boobis, Alan R; xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx;
>>> xxxxxx@xxxx.xxxxxxxxxxxx.xx; x.xxxxxx@xx.xx.xx;
>>> [redacted]
>>> Subject: RE: meeting with Commissioner May 3
>>>
>>> Dear all,
[redacted]

[redacted]

>>> Helmut
>>>
>>> Am 19.04.2016 17:39, schrieb Heslop-Harrison, Pat (Prof.):
>>>> Dear All,
>>>>
[redacted]
>>>>
>>>> Pat.
>>>>
>>>> Professor J.S. (Pat) Heslop-Harrison
>>>> Department of Genetics,
>>>> University of Leicester
>>>> Leicester LE1 7RH UK
>>>> Phh4@le.ac.uk Twitter [redacted]
>>>> Office: [redacted] Mobile: [redacted]
>>>> FAX: [redacted]
>>>> Web: www.molcyt.com ([redacted])
>>>> Blog: www.AoBBlog.com
>>>> Chief Editor, Annals of Botany www.annbot.com
>>>>
>>>>
>>>> -----Original Message-----
>>>> From: Boobis, Alan R [mailto:a.boobis@imperial.ac.uk]
>>>> Sent: 19 April 2016 15:13
>>>> To: Greim, Helmut; Daniel.Dietrich@uni-konstanz.de;
>>>> dekant@toxi.uni-wuerzburg.de; Heslop-Harrison, Pat (Prof.);
>>>> r.sharpe@ed.ac.uk
>>>> Subject: RE: meeting with Commissioner May 3
>>>>
>>>> Helmut
>>>>
>>>> That would be OK for me, up until 17:00 CET.
>>>>
>>>> Best wishes,
>>>>
>>>> Alan
>>>>
>>>> -----Original Message-----
>>>> From: Greim, Helmut [redacted]
>>>> Sent: 19 April 2016 15:09
>>>> To: Boobis, Alan R <a.boobis@imperial.ac.uk>;
>>>> Daniel.Dietrich@uni-konstanz.de; dekant@toxi.uni-wuerzburg.de;
>>>> phh4@leicester.ac.uk; r.sharpe@ed.ac.uk
>>>> Subject: meeting with Commissioner May 3
>>>>
>>>> Dear all,
[redacted]
>>>> Helmut

>>
>>
>> --
>> The University of Edinburgh is a charitable body, registered in
>> Scotland, with registration number SC005336.
>>

[redacted]

Date: Tue, 19 Apr 2016 13:41:28 +0100
Subject: Re: meeting with Commissioner May 3
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: "Greim, Helmut" [redacted],
"Boobis, Alan R" <x.xxxxxx@xxxxxxxx.xx.xx>
CC: "xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx" <xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx>,
"xxxxxx@xxxx.xxxxxxxxxxxx.xx" <xxxxxx@xxxx.xxxxxxxxxxxx.xx>,
"xxxx@xxxxxxxxx.xx.xx" <xxxx@xxxxxxxxx.xx.xx>,
"xxxxx@xxxxxxxxxxxxx.xx.xx" xxxxx@xxxxxxxxxxxxx.xx.xx

There is a chance I may be able to make next Tuesday 17:00 CET, but I am at an important meeting from 13.30 in another location and with no clear idea of what time it will finish.

Best wishes

Richard

On 19/04/2016 13:02, "Greim, Helmut" <[redacted]> wrote:

>Dear all,
[redacted]
>Helmut
>
>Am 19.04.2016 13:54, schrieb Boobis, Alan R:
>> Helmut
>>
>> My apologies, but I will be at WHO meeting in Geneva on Friday
>> (possibly available for a call at 17:00 CET at the airport). Monday
>> and Tuesday next week I am tied up chairing the SAB for an EU project.
>> Again, possibly available at 17:00 on Tuesday from the airport.
>>
>> Best wishes,
>>
>> Alan
>>
>> -----Original Message-----
>> From: Greim, Helmut [redacted]
>> Sent: 19 April 2016 12:33
>> To: Boobis, Alan R <x.xxxxxx@xxxxxxxx.xx.xx>;
>> xxxxxx.xxxxxxxx@xxxxxxxxxxxx.xx; xxxxxx@xxxx.xxxxxxxxxxxxx.xx;
>> xxxx@xxxxxxxxx.xx.xx; x.xxxxxx@xx.xx[redacted]
>> Subject: meeting with Commissioner May 3
>>
>> Dear all,
[redacted]
>> Helmut
>

[redacted]

Date: Thu, 7 Apr 2016 10:02:11 +0100
Subject: Re: Meeting with Commissioner May 3
From: SHARPE Richard <x.xxxxxx@xx.xx.xx>
To: "Greim, Helmut" [redacted],
Colin Berry <xxxxx@xxxxxxxxxxxxx.xx.xx>
CC: "x.xxxxxx@xxxxxxxx.xx.xx" <x.xxxxxx@xxxxxxxx.xx.xx>,
"xxxx@xxxxxxxxx.xx.xx" <xxxx@xxxxxxxxx.xx.xx>

Hi Helmut

I have just replied to [redacted] and said I can attend (depending on funding) on May 3-4 and happy to participate also in the meeting with Dr. Andriukaitis of DG Sante.

Best wishes

Richard

On 07/04/2016 09:58, "Greim, Helmut" <[redacted]> wrote:

>Dear Colin,
[redacted]
>Helmut
>
>Am 07.04.2016 10:24, schrieb Colin Berry:
>> Dear All,
>> I am sorry that I am committed In London until late on the 3rd. Is
>> it worth my coming for this meeting only on the 4th? I would need
>> support for my fare.
>> Colin Berry
>>
>> -----Original Message-----
>> From: Greim, Helmut [redacted]
>> Sent: Wednesday, April 6, 2016 3:22 PM
>> To: Colin Berry; x.xxxxxx@xx.xx.xx; x.xxxxxx@xxxxxxxx.xx.xx;
>> xxxx@xxxxxxxxx.xx.xx
>> Subject: Meeting with Commissioner May 3
>>
>> Dear all,
>>
[redacted]

[redacted]
>>
>> Sincerely,
>> Helmut