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GRACE - the EU risk research project sold out to industry

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Content

Summary

The overall objective of the EU project GRACE (GMO Risk Assessment and Communication of Evidence) is to look at the risks of genetically engineered plants. Once completed it is supposed to have a significant impact on future methods and criteria to be used in the risk assessment of genetically engineered plants before market authorisations. Therefore, it is essential that it employs the highest standards regarding conflicts of interest, credibility and scientific scrutiny.

Testbiotech has voiced criticism of the way the GRACE-Consortium has been put together. Some of the leading experts involved in GRACE have close affiliations to institutions such as ILSI , ILSI (International Life Sciences Institute) and ISBR (International Society for Biosafety Research), which are funded completely or to a large extent by industry. There are even experts involved with GRACE who are contracted to work for companies such as Monsanto.

Testbiotech has also criticised the publication and the presentation of the results of the GRACE feeding trial with genetically engineered maize MON810 in the journal *Archives of Toxicology.* Testbiotech has further:

- exposed flaws in the presentation of the results from feeding trials, especially in regard to total serum protein concentration and pancreas weight and the increase in blood glucose levels. Contrary to the claims made in the publication, the data from feeding trials do indeed give some indication of health impacts in rats fed with genetically engineered maize.
- shown there are major flaws in the declaration of interests. In particular, these concern affiliations with Monsanto, ILSI and ISBR.
- revealed close contacts between GRACE experts and the editorial board of the *Archives of Toxicology*. These findings give the impression that the journal was not chosen for publication because of scientific reasoning, but because of personal networks established within a dubious context. Testbiotech therefore questioned whether in this case the conditions for a rigorous and independent peer review had been met.
- found evidence that the journal *Archives of Toxicology* itself is far too closely connected to industry, for example, several editors have close ties to the tobacco industry.

The coordinator of the GRACE Consortiums, the chief-editor of the *Archives of Toxicology* and the EU Commission have all responded to the Testbiotech reports. In their responses, they neither contest the close affiliations between the editors of *Archives of Toxicology* and the corresponding author of the publication, nor make any comment on the close relationship of the journal with industry. They do, however, dispute other points relating to conflicts of interest, flaws in scientific standards and presentation of the results: They do, however, dispute other points relating to conflicts of interest, flaws in scientific standards and

presentation of the results:

- The GRACE Consortium asserts that the results of the feeding study are reported correctly in the publication, and the scientific standards of the publication comply with required international standards.
- The Consortium sees no reason to withdraw the publication, but Testbiotech is welcome to send a comment to the *Archives of Toxicology* for publication.
- The Consortium believes that the ISBR should simply be seen as a scientific organisation and therefore no conflicts of interest can emerge from membership.
- The Consortium asserts that leading GRACE experts are not active within ILSI.
- The Consortium believes that it is not necessary to explicitly mention that US company Monsanto is amongst the clients of some GRACE experts.
- The editor-in-chief of *Archives of Toxicology* is rejects any concerns that is influenced or funded by any interests of industry.
- The EU Commission states that the participation of industry within GRACE was intended from the beginning.

Testbiotech took a closer look at these statements and came to the following conclusions:

- the existing data from feeding trials do provide relevant indications for health impacts that were not, or at least not correctly, presented in the disputed publication.
- Testbiotech appreciates that the raw data has been made accessible. However, it is a matter of concern that there is a lack of independence amongst experts responsible for data collection and analysis.
- the public availability of the raw data cannot in any case be a ground for accepting insufficient peer review standards of the data before publication. Independent and comprehensive peer review standards have to be applied in order to compare the conclusions from the publication with the original data.
- the statements made by GRACE on conflicts of interest are not correct and/ or strongly misleading.
- there are strong reasons to question the statement made by the editor-in-chief of the *Archives of Toxicology* saying that he was never influenced by interests of industry.
- Testbiotech will not accept the invitation to send a comment to the *Archives of Toxicology* for further discussion because the journal is in a difficult position to defend its own reputation and cannot be considered as a neutral platform.
- Testbiotech is of the opinion that the answer given by the Commission is without substance and partially misleading.

Testbiotech has urged the EU Commission several times to take action. Some of its recommendations are:

- given the importance of this study, Testbiotech recommends the retraction of the paper. Re-publication should only be considered under a rigorous peer review process and in a journal with a scientific reputation not tarnished by questionable cooperation with industry, and which is not impacted by any affiliations to the authors and has the highest standards regarding conflicts of interest.
- the EU-Commission should ensure that the experts who participated in the peer review process before the publication are named.
- the whole GRACE-project and the interconnected EU Project G-TwYST should be subjected to thorough examination to avoid further conflicts of interest.
- plans to publish further results from GRACE or G-TwYST in the *Archives of Toxicology* have to be rejected.
- this case should be a starting point to assess and reorganise the current EU programs and infrastructures in the context of risk research organised by the EU Commission.

Introduction

In October 2014, the results of 90-day feeding study with genetically engineered maize MON810 were published in the journal *Archives of Toxicology* (Zeljenková et al., 2014). The study is part of the EU research project GRACE (GMO Risk Assessment and Communication of Evidence).[1] According to the EU Commission, the results of GRACE will have an impact on future methods and criteria of risk assessment for the market authorisation of genetically engineered plants.[2] Testbiotch is of the opinion that in the light of the importance of this project highest standards regarding conflict of interest, credibility and scientific scrutiny have to be applied.

Testbiotech has criticised the composition of the GRACE-Consortium (Bauer-Panskus & Then, 2013), as well as the process of publication and the presentation of the results in the journal *Archives of Toxicology* (Bauer-Panskus & Then, 2014). Testbiotech received a number of responses.

1. The Testbiotech analysis

1.1 Conflicts of interest at GRACE

In 2013 a report published by Testbiotech (Bauer-Panskus & Then, 2013) showed that several members of the GRACE consortium[3] have strong ties with institutions that are financed by industry, either completely or to large extent. Amongst those institutions are International Life Sciences Institute (ILSI) and International Society for Biosafety Research (ISBR).

The International Life Sciences Institute (ILSI) is financed by food, pharmaceutical and agrochemical companies. For example, its European branch (ILSI Europe) lists following members and supporting companies:[4] BASF, Bayer CropScience, Cargill, Coca-Cola, Danone, Dow Europe, DuPont de Nemours, General Mills, Kellogg, Mars, McDonald's, Merck Consumer Healthcare. Monsanto, Nestlé, PepsiCo International, Pfizer Consumer Healthcare. Currently, a staff member of Monsanto is president of ILSI's most influential body, the Board of Trustees.[5] As the Testbiotech report revealed, several GRACE experts have current or past connections to ILSI. Amongst those is also the coordinator of the GRACE project, Joachim Schiemann. Further GRACE experts with links to ILSI are Patrick Rüdelsheim, Jörg Romeis, Esther Kok, Gjis Kleter, Jean-Michel Wal und Pablo Steinberg.

The International Society for Biosafety Research (ISBR) has close ties to the biotech and agrochemical

1 http://www.grace-fp7.eu/
2 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:157:0001:0048:EN:PDF
3 GRACE experts are listed at www.grace-fp7.eu/content/julius-k%C3%BChn-institut-bundesforschungsinstitut-f%C3%BCr-kulturpflanzen-jki-germany
4 http://www.ilsi.org/Documents/ILSI_2013_Member_List.pdf
5 http://www.ilsi.org/Pages/Leadership.aspx

industry and other industry groups such as ILSI. The general funding of ISBR has not been disclosed, but its conferences are sponsored by biotech corporations such as Monsanto, Bayer, Dow AgroSciences, DuPont and Syngenta as well as by the biotech industry's global umbrella association, CropLife International. In addition, the ISBR's Board of Directors consists almost exclusively of scientists with industry or ILSI affiliations (table 1). As the Testbiotech report revealed, eight GRACE experts have ties with ISBR. Amongst those is also the coordinator of the GRACE project, Joachim Schiemann, who was president of ISBR from 2004-2008. Further GRACE experts concerned are Patrick Rüdelsheim, Kristina Sinemus, Klaus Minol, Jeremy Sweet, Ralf Wilhelm, Jörg Romeis and Wendy Craig.

Table 1: Examples of industry affiliations of members of ISBR's Board of Directors[6]

Name	ISBR position	Affiliation
Morven A. McLean	President	„ILSI's lead for sustainable agriculture and nutrition security across the organization internationally“
Alan Gray	President-elect	Co-author of several ILSI publications[7]
Monica Garcia-Alonso	Secretary	„worked for Syngenta for 19 years“
Donald MacKenzie	Treasurer	DuPont / Pioneer
Karen Hokanson	Director	Consultant for the Donald Danforth Plant Science Center, a research center funded by Monsanto[8]
Alan Raybould	Director	Syngenta

A third relevant lobby organisation in this context is the Public Research and Regulation Initiative (PRRI). This organisation lobbies for GMOs in international bodies such as the Convention of Biological Diversity (CBD). Scientists involved in PRRI have advocated lower regulatory standards for genetically engineered plants. PRRI is sponsored by Syngenta Foundation, CropLife International, US Grain Council, Monsanto and Arborgen.[9] Members of PRRI who also participate in GRACE are:[10] Joachim Schiemann, Jörg Romeis, Atanas Atanassov und Justus Wesseler.

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6 http://isbr.info/Board_of_Directors

7 Roberts, A., Devos, Y., Raybould, A., Bigelow, P., & Gray, A. (2013) Environmental risk assessment of GE plants under low-exposure conditions. Transgenic research, 23(6): 971-983. http://link.springer.com/article/10.1007/s11248-013-9762-z
Wolt, J.D., Keese, P., Raybould, A., Fitzpatrick, J.W., Burachik, M., Gray, A., ... & Wu, F. (2010) Problem formulation in the environmental risk assessment for genetically modified plants. Transgenic research, 19(3): 425-436. http://link.springer.com/article/10.1007/s11248-009-9321-9

8 http://www.zoominfo.com/CachedPage/?archive_id=0&page_id=6913215340&page_url=//maize.danforthcenter.org/scientists-research/research-institutes/institute-for-international-crop-improvement/team&page_last_updated=2014-08-14T07:29:06&firstName=Karen&lastName=Hokanson

9 https://web.archive.org/web/20090709062104/http://pubresreg.org/index.php?option=com_content&task=view&id=12&Itemid=29

10 http://www.prri.net/prri-members/

1.2 Flaws in the process of publication

The results of the GRACE (Zeljenkova et al., 2014) 90-day feeding trial with genetically engineered maize MON810 were published in October 2014 in the *Archives of Toxicology*. Corresponding author of the study is Pablo Steinberg from University of Hannover, Germany. The authors come to the conclusion that no negative health impacts were observed in the group of rats fed with MON810.

Testbiotech (Bauer-Panskus & Then, 2014) exposed flaws in the presentation of the results from feeding trials, especially in regard to total serum protein concentration and pancreas weight and the increase in blood glucose levels. Contrary to the description in the publication, the data from feeding trials did indeed give some indication of health impacts in rats fed with genetically engineered maize.

At the same time, none of the relevant conflicts of interests were mentioned. Amongst others, it is not mentioned that Pablo Steinberg is active in an ILSI working group and Joachim Schiemann has been actively involved with ISBR for many years. Also not mentioned is the fact that the producer of the genetically engineered maize, the US company Monsanto, is amongst the clients of Kerstin Schmidt and Jörg Schmidtke, who are themselves also part of the GRACE publishing team.

Testbiotech has revealed that there are close contacts between Pablo Steinberg and Jan G. Hengstler (the editor-in- chief of the *Archives of Toxicology*) and Hermann M. Bolt (the deputy editor-in-chief) and at least four more members of the editorial board of the *Archives of Toxicology.* Steinberg himself is also one of the editors of the journal. The contacts amongst those experts are manifested in joint publications, membership in organisations (see below) and joint activities. The research shows some further striking personal constellations:

- Steinberg as well as Hengstler and other editors of the *Archives of Toxicology* such as Franz Oesch, Hansruedi Glatt und Albrecht Seidel worked at the Institute of Toxicology at the University of Mainz, Germany.
- Steinberg is a member of the advisory board of the Leibniz Research Centre for Working Environment and Human Factors, while Hengstler is director of this institute and Bolt was his predecessor.
- Steinberg, Hengstler and Olavi Pelkonen (another editor) are co-signers on a controversially disputed call to the EU Commission to prevent stricter regulation of so-called endocrine disrupters.[11] Other signatories to this letter also have close affiliations with industry. [12]

[11] Dietrich, D.R., Aulock, S.V., Marquardt, H., Blaauboer, B., Dekant, W., Kehrer, J., Hengstler, J., Collier, A., Gori, G.B., Pelkonen. O., Lang, F., Barile, F.A., Nijkamp, F.P., Stemmer, K., Li, A., Savolainen, K., Hayes, A.W., Gooderham, N., Harvey, A. (2013) Scientifically unfounded precaution drives European Commission's recommendations on EDC regulation, while defying common sense, well-established science and risk assessment principles. Chemico-Biological Interactions,.

[12] http://www.environmentalhealthnews.org/ehs/news/2013/eu-conflict-list
Bergman, Å., Andersson, A.M., Becher, G., van den Berg, M., Blumberg, B., Bjerregaard, P., ... & Zoeller, R.T.

- In addition, there are several joint articles by Steinberg and other editors of the *Archives of Toxicology* such as Jan G. Hengstler, Franz Oesch, Abrecht Seidel und Hansruedi Glatt.

It is also striking that the institutions mentioned (Institute of Toxicology at the University of Mainz, Leibniz Research Centre for Working Environment and Human Factors (IfADo) and the *Archives of Toxicology* are known for close their cooperation with the tobacco industry (see below). These findings create the impression that the journal was not chosen for publication because of scientific reasoning but because of personal networks established within a dubious context.

Testbiotech is therefore questioning whether the conditions for a rigorous and independent peer review were met. There is the impression that this is a case of “self publication” .

1.3 Archives of Toxicology - too close to industry

The Testbiotech report reveals that the journal *Archives of Toxicology* has close affiliations to industry. It is striking that several of the editors of the journal have close ties to tobacco industry. Research with the database Legacy Tobacco Documents Library (LTDL)[13] shows that amongst the members of the editorial board of the journal, there are several experts who formerly worked, or still work, at institutes that have cooperated with the tobacco industry for many years. An overview of these affiliations is given in Table 2.

(2013) Science and policy on endocrine disrupters must not be mixed: a reply to a ‚common sense‘ intervention by toxicology journal editors. Environmental Health, 12(1): 69. http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=23981468
Grandjean, P., & Ozonoff, D. (2013) Transparency and translation of science in a modern world. Environmental Health, 12(1): 70. http://www.ehjournal.net/content/12/1/70#B11
Gore, A.C., Balthazart, J., Bikle, D., Carpenter, D.O., Crews, D., Czernichow, P., ... & Watson, C.S. (2013): Policy decisions on endocrine disruptors should be based on science across disciplines: a response to Dietrich et al..European Journal of Endocrinology, 169(6): E1-E4. http://www.eje-online.org/content/169/6/E1.full

[13] http://legacy.library.ucsf.edu/

Table 2. Members of the editorial board of the *Archives of Toxicology* with affiliations to the tobacco industry

Name	function at *Archives of Toxicology*	Professional background
Jan G. Hengstler	Editor-in-Chief	Director at Leibniz Research Centre for Working Environment and Human Factors (IfADo), before Institute of Toxicology, University of Mainz
Hermann M. Bolt	Deputy Editor-in-Chief	Former Director at IfADo
Hansruedi Glatt,	Member of the editorial board	Former Institute of Toxicology, University of Mainz, now German Institute of Human Nutrition.
Franz Oesch	Member of the editorial board	Former head of department at the Institute of Toxicology, University of Mainz. Now head of consulting „Oesch-Tox Toxicological Consulting and Expert Opinions GmbH&Co.KG“
Olavi Pelkonen	Member of the editorial board	University Oulu (Finland)
Albrecht Seidel	Member of the editorial board	Institute of Toxicology, University of Mainz, Germany, now Gernot Grimmer-Foundation[14]

Documents found in the LTDL database show that the former editor-in-chief of the *Archives of Toxicology*, Prof. Hermann Bolt (now listed as deputy editor-in-chief), invited scientists from the German Philip Morris owned laboratory, INBIFO (Institut für biologische Forschung) in Cologne, or the Philip Morris Contract Research Center in Belgium, to review studies, including studies on the effects on health from smoking. Until 2008, Hermann Bolt was Director of the Institute of Work Physiology, University of Dortmund (now Leibniz Research Centre for Working Environment and Human Factors) which conducted research for Philip Morris from 2001 to 2004 and received US-$ 230.000 for one of the studies.

1.4 What Testbiotech is demanding

Testbiotech has urged the EU Commission several times to take action. The recommendations are:

- Given the importance of this study, Testbiotech recommends the retraction of the paper. Re-publication should only be considered under a rigorous peer review process and in a journal with a scientific reputation not tarnished by questionable cooperation with industry, and which is not impacted by any affiliations to the authors and has the highest standards regarding conflicts of interest.
- The EU Commission should ensure that the experts who participated in the peer review process before the publication are named.
- Data derived from a further one year feeding study with MON810 performed by the GRACE team should be published as soon as possible. Further, urine samples should be taken from the rats used in

[14] Prof. Gernot Grimmer, conducted several studies on behalf of tobacco industry. Amongst others, funding was organised via *Verum Foundation*, which was originally created by tobacco industry.

this feeding trial to conclude on some uncertainties from existing data.

- The whole GRACE-project and the interconnected EU Project G-TwYST should be subjected to thorough examination to avoid further conflicts of interest.

2. Responses to the Testbiotech report

The GRACE Consortium as well as the editors of the *Archives of Toxicology* and the EU Commission responded to the reports of Testbiotech. An overview is provided in Table 3.

Table 3. Overview of responses to the Testbiotech report on the GRACE publication

Date	Content	Link to internet
2.10.14	Publication of Zeljenkova et al.	www.grace-fp7.eu/sites/default/files/GRACE-FeedingTrials_AB_ArchToxicol_2014.pdf
7.11.14	Testbiotech report	www.testbiotech.org/en/node/1107
10.11.14	1. Open Letter from the GRACE Consortium	www.grace-fp7.eu/content/grace-rejects-testbiotech%E2%80%99s-criticisms-gmo-feeding-study
18.11.14	Reply from Testbiotech to GRACE and 2. letter to the EU Commission	www.testbiotech.org/en/node/1115
25.11.14	2. Open letter from GRACE Consortium	www.grace-fp7.eu/content/open-letter-totestbiotech-ev-response-its-letter-grace
2.12.14	Letter from editor of *Archives of Toxicology*	http://www.testbiotech.org/node/1128
8.12.14	Reply from Testbiotech to GRACE / *Archives of Toxicology* and 3. Letter to the EU Commission	http://www.testbiotech.org/en/node/1123
10.12.14	GRACE gives specific information to journalist, Testbiotech is asked for comment	Not published, but available at Testbiotech
17.12.14	Letter from the EU Commission to Testbiotech	www.testbiotech.org/node/1127

None of these responses deny that there are close contacts between the editors of the *Archives of Toxicology* and Pablo Steinberg. No comment is made on the close relationship of the journal with industry. Other points such as conflicts of interest, flaws in scientific standards and presentation of the results are disputed.

2.1 First open letter from the GRACE Consortium

In its first open letter, the GRACE Consortium asserts that the results of the feeding study are reported correctly in the publication. They argue that Testbiotech did not make the necessary distinction between statistically significant and biologically relevant findings. They further assert that the scientific standards of the publication comply with required international standards and make the following statement:

„The research within GRACE is carried out according to established scientific standards and under

conditions of well-documented quality control and good practices. Additionally, the GRACE consortium attaches great value to dialogue and transparency, among others by involving stakeholders during various stages of the research design, execution, and result interpretation.“

2.2 Second open letter from the GRACE Consortium

In its second open letter, the GRACE Consortium focuses on the demands of Testbiotech. They see no reason to retract the paper, but invite Testbiotech to send a comment to the *Archives of Toxicology*. Further, the experts involved in the peer review process at the *Archives of Toxicology* could not be named because they are not known to the authors of the article. The reason given for the experimental protocol was that no data could be made available from the ongoing one-year feeding trial. Furthermore, they state that any allegation of data manipulation had to be rejected because the raw data had been made available:

„All raw data generated in the course of our studies published by Zeljenková et al (2014) are freely accessible. In addition, we are offering interested parties the possibility to compare the original data (…) with the raw data published. Consequently, the allegation that we have tried to manipulate the results of our feeding trials can be completely rejected.“

2.3 Letter from the editor of the Archives of Toxicology

In the letter from the editor-in-chief of the *Archives of Toxicology*, Jan G. Hengstler, Testbiotech is again invited to send a comment on Zeljenkova et al. (2014) to be published in the journal. Hengstler also strongly rejects the allegation that he was influenced by industry:

„Moreover, it is not correct that I am funded or influenced by industry. I have never received money or favors from industry. I have also never served as a paid industry consultant, and have no undisclosed financial ties to industry. Furthermore, and to avoid any misunderstanding, it is not my opinion that cooperation projects funded by either the chemical or pharmaceutical industry are unethical by default.“

He further states that it is usual practice for journals to publish articles by their own editors if some specific rules are obeyed. Hengstler disputes that his participation in a study on the risks of Bisphenol A co-authored by many experts from industry, indicates ties to industry. The authors of this article were selected by a committee of the German Society of Toxicology. Finally, he claims that Testbiotech itself has some conflicts of interest because it receives funding from a retailing company.

2.4 GRACE communication to journalists

In December 2014, Testbiotech was asked to comment on a communication from GRACE to German journalists. The letter is available at Testbiotech, but was not published by GRACE. In this letter, Joachim Schiemann confirms that he was a co-founder of ISBR, and active within the Board of Directors from 2002-2012 and even president of ISBR from 2004-2008. He underlines the fact that the official mission of ISBR is to promote the practice and application of science in the field of agricultural biotechnology and does not imply any personal benefits to himself, or conflicts of interest. In general, membership in a scientific organisation does necessarily imply conflicts of interests. He also states he has not had any active role at ILSI for several years.

Further, Schiemann states that Kerstin Schmidt, one of the authors of the article, made public that she provides consulting services to biotech and pharmaceutical companies. Therefore, it was not necessary to explicitly mention that US company, Monsanto is one of her clients.

Finally, the communication says that Pablo Steinberg is definitely not a member of ILSI. He only authored a chapter in an ILSI book, which is not something that would give rise to any conflicts of interest. While he was member of the board of editors at the *Archives of Toxicology,* he was excluded from the peer review of the article.

2.5 Response from the EU Commission

The EU Commission welcomed the public discussion and affirmed that the selection process for the project involved independent and highly qualified experts, and was based on international peer reviewing standards. Also that the participation of industry within GRACE was intended from the beginning:

> „The need for linking up with existing activities (e.g. International Society for Biosafety Research) was explicitly mentioned in the call text and interaction with a wide range of stakeholders, including local, regional and national authorities, science organisations, but also industry, were specific requirements of the topic.“

The Testbiotech demands were not discussed in any detail.

3. Checking the facts

In the following paragraphs, some of the statements mentioned have been subjected to some double checks. As a result, the findings and conclusions from the original report of Testbiotech (Bauer-Panskus & Then, 2014) were mostly confirmed. These findings suggest that the credibility of the experts Schiemann, Hengstler and Steinberg is questionable.

3.1 The presentation of the results from the feeding study

Testbiotech has not complained about the manipulation of the raw data but has criticised flaws in data interpretation (Bauer_Panskus & Then, 2014).

Further, Testbiotech once again reviewed and discussed the results presented in the publication and double-checked with an experienced toxicologist. The existing data do not allow any conclusions on evidence of damage to health in rats fed with genetically engineered maize MON810, but they do provide relevant indications for health impacts that were not, or not correctly, presented in the disputed publication. For the parameters for which statistically significant and biologically relevant effects were identified, the Testbiotech report provides substantiated reasons, i.e. dose-dependent changes, a consideration of individual data and references. Therefore, the GRACE consortium allegations have to be rejected (see Testbiotech, 2014).

3.2 Conflicts of interest amongst GRACE experts

Statements made by Joachim Schiemann (on behalf of the GRACE-Project) about conflicts of interests are not correct and/ or strongly misleading:

- ISBR cannot simply be seen as a neutral, industry-independent organisation. There is no doubt about the dominant influence of industry. Membership in ISBR needs to be identified as potential conflict of interest in the context of the publication under dispute. For example, invitations to conferences for members of ISBR may lead to private benefits for the individuals. According to the definition of OECD (2007), this has to be considered as a conflict of interest.[15]

- Pablo Steinberg is not a member of ILSI (which only foresees membership for companies or institutions), but he is an active member of an ILSI working group. A publication co-authored by Steinberg was published in December 2014 in the journal Food and Chemical Toxicology (Edwards et al., 2014). Membership in the ILSI working group should have been declared in the context of the publication.

- Maize MON810 used in the feeding trial is produced by Monsanto. Monsanto is a client of Kerstin Schmidt and Jörg Schmidtke and therefore this specific information should have been disclosed in the context of the publication. Even more to the point, these experts should never have been allowed to participate in the EU project in the first place.

[15] „Conflict of interest occurs when an individual or a corporation (either private or governmental) is in a position to exploit his or their own professional or official capacity in some way for personal or corporate benefit.“ http://stats.oecd.org/glossary/detail.asp?ID=7206

3.3 Editors of the Archives of Toxicology too closely tied to industry

The statement made by Jan G. Hengstler, that he is not funded or influenced by industry is highly questionable. As further Testbiotech research shows, the institute IfADo conducted studies which were sponsored by the tobacco company Philip-Morris at least up to the year 2012 (for details see annex). Hengstler himself is named as co-author of a study that was sponsored by the tobacco industry (Borza et al., 2008). Other *Archives of Toxicology* editors such as Franz Oesch, Albrecht Seidel, Hansruedi Glatt and Olavi Pelkonen have also been involved in studies for tobacco industry.

Hengstler is further a member of the European Steering Committee of EBTC (Evidence-based Toxicology Collaboration),[16] which is sponsored by the oil and chemical industry.[17]

His contribution to the publication on the risks of Bisphenol A[18] at least raises some questions: For example it should not be overlooked that several members of the specific committee the German Society of Toxicology also has very close ties with industry.[19]

4. Further discussion

Responses to Testbiotech cover a range of further comments and opinions. Here a brief discussion:

- Testbiotech should send a comment to the *Archives of Toxicology* for further discussion in a public forum

This invitation has not been accepted by Testbiotech because the journal is in a difficult position to defend its own reputation and cannot be considered a neutral platform.

- Data from feeding trials are publicly available and therefore they cannot be manipulated.

Testbiotech appreciates that the raw data are accessible. However, the lack of independence from industry among the experts responsible for conducting the trials, collecting and analysing the data data still is a matter of concern. This can only lead to a lack of confidence in the overall process of data generation. Several steps in context of the trials are relevant: For example the conditions of blinding (those who collect the data should not know which animals are in the group with MON810 maize diet), the preparation of the feed, as well as the selection and the cultivation of the plants can have significant impact on relevant data and final results. In any case, public availability of the raw data is not an argument for accepting insufficient peer review

[16] http://www.ebto x.com/steering-committee/
[17] http://www.ebtox.com/sponsors/
[18] Hengstler, J.G., Foth, H., Gebel, T., Kramer, P.J., Lilienblum, W., Schweinfurth, H., ... & Gundert-Remy, U. (2011) Critical evaluation of key evidence on the human health hazards of exposure to bisphenol A. Critical reviews in toxicology, 41(4): 263-291. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3135059/
[19] See for example co-autor Heidi Foth of University Halle, which was sponsered by tobacco industry for a period of 20 years.

standards of the data before publication. Independent and comprehensive peer review standards have to be applied in every case.

- Data from the ongoing one-year feeding trial can not made public before it is finalised

It is indeed debatable whether data from a GRACE feeding trial that is not yet finished should be made public at all. The blinding code must not be broken. However, it could be discussed if the data can be accessed without breaking the code.

- Many stakeholders, including NGOs have been invited to participate in the GRACE project and can thereby influence the project

Testbiotech has participated in several GRACE project meetings and has also filed written comments. For example, Testbiotech raised concerns about conflicts of interest as early as 2013. Furthermore, Testbiotech presented written comments on the results of the feeding study before its publication. These contributions were neither answered in substance nor did they have any discernible impact.

- Industry has to be integrated into the GRACE-project

Many industry representatives are indeed taking part in the stakeholder meetings at GRACE, many more than from NGOs. However, this is not part of the Testbiotech criticism. The real problem is that leading GRACE experts are not sufficiently independent of industry and relevant conflicts of interest are not made transparent.

- Testbiotech has its own conflicts of interests

Testbiotech lists its most relevant funding sources on its webpage. An analysis of the funding background shows that Testbiotech funding comes from an environment, which is sceptical about the use of genetically engineered plants in agriculture. A comparison with conflicts of interest as discussed under GRACE is highly misleading. Publicly funded research projects that deal with the risks of genetically engineered plants must be completely independent of companies, which make a profit from selling such products, and is of highest relevance. This degree of independence is not ensured within the GRACE consortium.

5. Conclusions

Testbiotech is reaffirming its demands and recommendations.

Testbiotech is of the opinion that is primarily the task of the EU-Commission to make sure that credibility and scientific standards are safeguarded within the GRACE project. The answer provided by the Commission so far has to be considered as being without substance and partially misleading.

The EU Commission will have to deal with similar issues again in the very near future. Testbiotech has been informed[20] of a plan to publish all further results from feeding trials conducted under GRACE and also under the EU project TwYST (which is coordinated by Steinberg and conducted in parallel) in the *Archives of Toxicology*. Consequently, the described constellation between Steinberg, Hengstler, Bolt and other experts will become part of the EU research project, and the *Archives of Toxicology* and its editors will become a cooperation partner. This is likely to cause further substantial damage to the credibility of these projects. Testbiotech urges the EU-Commission to make sure that no further results from GRACE or G-TwYST are published in the *Archives of Toxicology*.

Further, Testbiotech is convinced that the problems at GRACE are a symptom for more general problems of current EU processes used to organise risk research independently of industry. This case can be seen as a starting point to assess and reorganise the current programs and infrastructures in this context.

Our recommendations to the EU Commission are:

- establish much higher standards to avoid conflicts of interest of experts involved in publicly funded research projects and for experts working with the EU authorities;
- give full transparency on the experts involved in the selection of the specific EU projects;
- enable the participation of civil society groups active in areas such as consumer protection, environment, and animal welfare in the selection of goals, subjects and experts of the EU funded risk research. Those who are bearing the risks (or are representing them) should be involved in the decision-making processes;
- encourage EU Member States to also start similar initiatives;
- further mechanisms should be developed for additional funding of public risk research by establishing mandatory financial contributions from industry.

[20] This information was provided at a meeting of the EU project G-TwYST at 16/17.12. 2014 in Vienna www.g-twyst.eu/

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Annex: The Leibniz Research Centre for Working Environment and Human Factors (IfADo) and the tobacco industry

From 2000 until 2012, there was a fairly intensive research cooperation between experts from IfADo and Philip Morris. Herrmann M. Bolt led the IfADo until 2008, and Jan G. Hengstler has been acting as director since 2009. Both experts are also editor-in-chief and deputy editor-in-chief at the Archives of Toxicology. The cooperation between IfADo and Philip Morris resulted in many publications, poster presentations and workshops. Table 1 provides an overview listing of some of the relevant activities.

Table 1: Overview of some IfADo publications and activities that are related to its cooperation with the tobacco company Philip Morris

Year	Documents	Funding
2000/1	Application of Hermann M. Bolt (IfADo) at Philip Morris for the Project „Development and Application of an in vitro System for Detection and Quantification of Urothelial Genotoxicity of Tobacco Smoke-Specific Constituents Utilizing Classical Genotoic Endpoints and cDNA Expression Profiling“ Application at http://legacy.library.ucsf.edu/tid/oyt30i00 Contract: http://legacy.library.ucsf.edu/tid/vuf20i00	Philip Morris Research Grant
2004	Final report for project „Development and Application of an in vitro System for Detection and Quantitation of Urothelial Genotoxicity of Tobacco Smoke-Specific Constitutents Utilizing Classical Genotoic Endpoints and cDNA Expression Profiling“ Overview on conferences and posters till 2004: http://legacy.library.ucsf.edu/tid/dxe82i00	Philip Morris Research Grant
2005	Publication Wolf, A., Kutz, A., Plöttner, S., Behm, C., Bolt, H.M., Föllmann, W., Kuhlmann, J. (2005) The effect of benzo (a) pyrene on porcine urinary bladder epithelial cells analyzed for the expression of selected genes and cellular toxicological endpoints. Toxicology, 207(2): 255-269. http://www.sciencedirect.com/science/article/pii/S0300483X04005712	Philip Morris Incorporated
2007	Conference-abstract Ploettner, S., Behm, C., Bolt, H.M., Foellmann, W. (2007) CYP1A1 induction by cigarette smoke condensate in urothelial cells-A result of complex combination interactions. In: Naunyn-Schmiedebergs Archives of Pharmacology, 375: 80-81. New York, USA, Springer.	No information
2008	Publication Plöttner, S., Borza, A., Wolf, A., Bolt, H.M., Kuhlmann, J., Föllmann, W. (2008) Evaluation of Time Dependence and Interindividual Differences in Benzo [a] pyrene-Mediated CYP1A1 Induction and Genotoxicity in Porcine Urinary Bladder Cell Cultures∗. Journal of Toxicology and Environmental Health, Part A, 71(13-14): 969-975. http://www.tandfonline.com/doi/abs/10.1080/15287390801989184	Philip Morris External Research Program
2008	Publication Borza, A., Plöttner, S., Wolf, A., Behm, C., Selinski, S., Hengstler, J.G., Roos, P.H., Bolt, H.M., Kuhlmann, J., Föllmann, W. (2008) Synergism of aromatic amines and benzo [a] pyrene in induction of Ah receptor-dependent genes. Archives of toxicology, 82(12): 973-980. http://link.springer.com/article/10.1007/s00204-008-0381-z	Philip Morris External Research Program

Year	Documents	Funding
2009	Publication Plöttner, S., Selinski, S., Bolt, H.M., Degen, G. H., Hengstler, J.G., Roos, P.H., Föllmann, W. (2009) Distinct subtypes of urinary bladder epithelial cells with inducible and non-inducible cytochrome P450 1A1. Archives of toxicology, 83(2): 131-138. http://link.springer.com/article/10.1007/s00204-008-0329-3	No information
2012	Publication (conference article) Plöttner, S., Behm, C., Bolt, H. M., & Föllmann, W. (2012). Effects of cigarette smoke condensate on primary urothelial cells in vitro. Journal of Toxicology and Environmental Health, Part A, 75(19-20), 1194-1205. http://www.tandfonline.com/doi/full/10.1080/15287394.2012.709166	Philip Morris External Research Program
2014	Publication (Review) Bolt, H. M. (2014). Causation of human urothelial cancer: there are challenging new data!. Archives of toxicology, 88(10), 1769-1770. http://link.springer.com/article/10.1007/s00204-014-1339-y	No information