Environ Sci Pollut Res (2018) 25:15265–15267
DOI 10.1007/s11356-017-0321-7

ERRATUM

Erratum to: The OECD validation program of the H295R steroidogenesis assay: Phase 3. Final inter-laboratory validation study

Markus Hecker[1,2] · Henner Hollert[3] · Ralph Cooper[4] · Anne-Marie Vinggaard[5] · Yumi Akahori[6] · Margaret Murphy[7] · Christine Nellemann[5] · Eric Higley[2] · John Newsted[8] · John Laskey[9] · Angela Buckalew[4] · Stefanie Grund[10] · Sibylle Maletz[3] · John Giesy[2,7] · Gary Timm[11]

Published online: 23 October 2017
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Erratum to: Environ Sci Pollut Res (2011) 18: 503
https://doi.org/10.1007/s11356-010-0396-x

In the original article wrong unites were quoted in Table 3 (page 508) and Table 4 (page 510) as well as in the paragraph 3.2 Core chemical exposure experiments on page 509. Also in paragraph 2.3 Selection and testing of chemicals the link to the Supplemental Materials (ESM) was missing. The correct versions of the tables and the paragraph as well as the ESM link are provided below.

3.2 Core chemical exposure experiments

There were chemical-specific differences in the response of T production after exposure of H295R cells to the 12 core chemicals (Table 3). With a few exceptions, the observed chemical-specific responses of T production were comparable among laboratories and could be grouped into three different types of effects: inducers, inhibitors, and negative reference chemicals. Among the inducers, exposure to trilostane resulted in the greatest fold changes (>10-fold induction) in T concentra-

The online version of the original article can be found at https://doi.org/10.1007/s11356-010-0396-x

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11356-017-0321-7) contains supplementary material, which is available to authorized users.

✉ Markus Hecker
markus.hecker@usask.ca

[1] ENTRIX, Inc., Sasaktoon, SK S7N 5B3, Canada

[2] Department of Veterinary Biomedical Sciences and Toxicology Centre, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

[3] Department of Ecosystem Analysis, Institute for Environmental Research, RWTH Aachen University, 52074 Aachen, Germany

[4] Endocrinology Branch, RTD, NHEERL, ORD, US Environmental Protection Agency, Research Triangle Park, NC, USA

[5] Department of Toxicology & Risk Assessment, National Food Institute, Technical University of Denmark, Soborg, Denmark

[6] Chemicals Evaluation and Research Institute, Chemicals Assessment Center, Saitama, Japan

[7] Department of Biology & Chemistry, City University of Hong Kong, Kowloon, Hong Kong, SAR, China

[8] ENTRIX, Inc., Okemos, MI 48864, USA

[9] Senior Environmental Employment Program, National Caucus on Black Aged, Research Triangle Park, NC, USA

[10] Department of Zoology, University of Heidelberg, 69120 Heidelberg, Germany

[11] Office of Science Coordination & Policy, US Environmental Protection Agency, Washington, DC, USA

tion when compared to SCs. The least fold changes were observed for the atrazine exposures where induction of T production was less than 1.5-fold with the exception of Lab 2, at which maximum induction was 2.4-fold. No effect on T production was observed after exposure to atrazine at Lab 6. Exposure to prochloraz resulted in a greater than 15-fold reduction of T production at the greatest concentration tested (100 μM) at all laboratories with the exception of Lab 4 where an up to 4.5-fold reduction was observed. The greater LOEC reported for Lab 2 is likely a function of the relatively great variation among replicate experiments at 0.01 μM (CV=35%). It is unclear why T production by cells was more sensitive to the exposure with prochloraz at Labs 1 and 3. However, a concentration-dependent response was observed starting at 0.01 μM, which is similar to the response patterns at the other labs. Therefore, it cannot be excluded that the significant reduction at 0.0001 and 0.001 μM represents an artifact. Exposure to the other inhibitors resulted in less than 4-fold changes in T production. When chemicals exhibited a less than 1.5-fold change in T production, they were categorized as negatives. This threshold was defined based on the average variation observed across all laboratories among replicate experiments. Some of these negative chemicals could have been categorized as inhibitors in individual cases (molinate: Lab 4; benomyl: Lab 1). However, even in situations where inhibition was observed at an individual laboratory, changes were always less than 2-fold and typically were not concentration-dependent. For instance, exposure to nonoxynol-9 resulted in a decrease in T concentrations at non-cytotoxic concentrations at two of five laboratories for which data was available. Relative to the SCs, inhibition of T production at Lab 1 was 29% (1 μM), while at Lab 2, it was 47% (10 μM). However, it should be noted that, at Lab 2, exposure to 10 μM nonoxynol-9 resulted in an average increase in cell viability (138% viable cells relative to the SCs), and thus the observed reduction in T production may be an artifact due to the correction for cell viability, especially as no such increase was observed by any of the other groups. The greatest letrozole concentration resulted in a significant decrease in T at all laboratories.

Table 3 Lowest observed effect concentrations (LOECs; measured by Dunnett's or Mann Whitney U test [mu]) and strength and direction of change (⇩= >0.5-fold; ⇩⇩ = 0.5- to >0.25-fold; ⇩⇩⇩ = 0.25- to >0.1-fold; ⇩⇩⇩⇩ = ≤0.1-fold; ⇧ = <2-fold; ⇧⇧ = 2- to <fold; ⇧⇧⇧ = 4- to <20-fold; ⇧⇧⇧⇧ = ≥20-fold) for testosterone (T) and estradiol (E2) after exposure to the twelve core chemicals. Ranges refer to maximum values measured in repeated experiments. nd – not detectable; — chemical not analyzed. Gray shaded cells – uncertainty due to interference of the antibody based hormone detection system with the test chemical

	Fold-Change (Testosterone)									
	Lab 1[a]		Lab 2		Lab 3		Lab 4		Lab 6	
	LOEC [μM]	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*
Prochloraz	0.0001	⇩⇩⇩⇩	0.1	⇩⇩⇩⇩	0.0001	⇩⇩⇩⇩	0.01	⇩⇩⇩⇩	0.01	⇩⇩⇩
Aminoglutethimide	100[d]	⇩⇩⇩	100[d]	⇩⇩	10	⇩⇩⇩	100[d]	⇩⇩	100[d]	⇩⇩⇩
Letrozole	100[d]	⇩⇩	100[d]	⇩⇩	100[a,d]	⇩⇩	100[d]	⇩⇩	100[d]	⇩⇩
Nonoxynol-9	10[c,d]	⇩	10[c,d]	⇩	nd[e]		10[c,d]	⇩	10[c,d]	⇩⇩
Molinate	nd		nd		100	⇩	nd		nd	
Benomyl	nd		nd		nd		nd [mu]		nd	
EDS	nd		nd		nd		nd		nd	
HCG	nd		nd		nd		nd		nd	
Paraben	10	⇧	nd		1	⇧	nd		nd	
Atrazine	100[d]	⇧	1	⇧	100[d]	⇧	nd		nd	
Forskolin	10	⇧⇧	1	⇧⇧	1	⇧	1	⇧⇧	1	⇧⇧
Trilostane	0.1 [mu]	⇧⇧⇧	0.01 [mu]	⇧⇧⇧	1 [mu]	⇧⇧⇧⇧	1 [mu]	⇧⇧⇧⇧	0.01 [mu]	⇧⇧⇧⇧
	Fold-Change (Estradiol)									
	Lab 1[a]		**Lab 2**		**Lab 3**		**Lab 4**		**Lab 6**	
	LOEC [μM]	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*	*LOEC [μM]*	*Max Change*
Letrozole	0.001	⇩⇩	0.001	⇩⇩	0.0001 [mu]	⇩⇩⇩	0.01	⇩⇩⇩	0.01	⇩⇩
Prochloraz	0.1	⇩⇩	1	⇩	0.1	⇩⇩	1	⇩⇩	0.1	⇩⇩
Aminoglutethimide	100[d]	⇩⇩	10 [mu]	⇩⇩	10	⇩⇩	100[b,d]	⇩⇩	100[d]	⇩⇩
Benomyl	nd		nd		nd[a]		nd[a]		nd	
EDS	nd		nd		nd		nd		nd	
Nonoxynol-9	nd		nd		nd		nd		nd	
HCG	nd		nd	⇧	nd[a]		nd[a]		nd	
Paraben	nd [mu]	⇧⇧⇧	10	⇧	10 [mu]	⇧⇧	nd	⇧⇧	nd	
Molinate	100[d]	⇧⇧ [mu]	100[d]	⇧	100[d] [mu]	⇧⇧	100[d] [mu]	⇧⇧	100[d]	⇧⇧
Atrazine	10	⇧⇧⇧	1 [mu]	⇧⇧⇧	1 [mu]	⇧⇧⇧⇧	10 [mu]	⇧⇧⇧	0.1	⇧
Forskolin	0.01 [mu]	⇧⇧⇧⇧	0.1 [mu]	⇧⇧⇧⇧	0.1 [mu]	⇧⇧⇧⇧	0.1 [mu]	⇧⇧⇧⇧	0.01 [mu]	⇧⇧
Trilostane	1 [mu]	⇧⇧⇧⇧	100	⇧	0.1 [mu]	⇧⇧⇧⇧	1 [mu]	⇧⇧⇧⇧	1 [mu]	⇧⇧⇧

[a] Only one experiment was conducted or considered for data evaluation

[b] Not statistically significant; $p = 0.051$

[c] Greatest concentration cytotoxic

[d] Effects occurred at greatest non-cytotoxic concentration; no dose-response

[e] Cytotoxicity observed at concentration at which effects occurred at other laboratories = 10

Table 4 Lowest observed effect concentrations (LOECs; measured by Dunnett's test) and strength and direction of change (⇓ = >0.5-fold; ⇓⇓ = 0.5- to >0.25-fold; ⇓⇓⇓ = 0.25- to >0.1-fold; ⇓⇓⇓⇓ = ≤0.1-fold; ⇑ = <2-fold; ⇑⇑ = 2- to <fold; ⇑⇑⇑ = 4- to <20-fold; ⇑⇑⇑⇑ = ≥20-fold) observed for the 16 test chemicals. nd – not detectable. Chemicals tested at the second laboratories (2nd Lab) were as follows; Lab2: Piperonyl butoxide, ketoconazole, prometon, DEHP, flutamide and danazol; Lab3: Bisphenol A, fenarimol, genistein, finasteride and dinitrophenol; Lab4: Spironolactone, mifepristone, tricrecyl phosphate, dimethoate and glyphosate

	Testosterone			
	LOEC [μM]		Max Change	
	1st Lab[b]	2nd Lab[c]	1st Lab	2nd Lab
Ketoconazole	1	1	⇓⇓⇓	⇓⇓⇓
Genistein	10	10	⇓⇓	⇓⇓⇓
Finasteride	10	100[d]	⇓⇓	⇓⇓
Bisphenol A	10	10	⇓⇓	⇓
Dinitrophenol	0.0001	100[d]	⇓	⇓⇓
Piperonyl butoxide	10	10	⇓	⇓
Spironolactone	1	1	⇓⇓⇓	⇓⇓
Fenarimol	nd	10	nd	⇓⇓
Danazol	nd	nd	nd	nd
DEHP	nd	nd	nd	nd
Dimethoate	nd	nd	nd	nd
Flutamide	nd	nd	nd	nd
Glyphosate	nd	nd	nd	nd
Prometon	nd	nd	nd	nd
Tricrecyl phosphate	10	nd	⇑	nd
Mifepristone	0.1	nd	⇑	nd

	Estradiol			
	LOEC [μM]		Max Change	
	1st Lab	2nd Lab	1st Lab	2nd Lab
Danazol	1	10	⇓⇓⇓	⇓⇓
Ketoconazole	10	10	⇓⇓	⇓⇓
Fenarimol	nd	1	nd	⇓⇓
Finasteride	nd	100[d]	nd	⇓
Glyphosate	nd	nd	nd	nd
Dinitrophenol	nd	nd	nd	nd
Spironolactone	nd	nd	nd	nd
Piperonyl butoxide	nd	nd	nd	nd
Dimethoate	10	nd	⇑⇑	nd
Flutamide	10	nd	⇑⇑	nd
Tricrecyl phosphate	10	nd	⇑⇑⇑	nd
Bisphenol A	10	1	⇑⇑	⇑⇑
DEHP	1[a]	1	⇑⇑	⇑⇑
Mifepristone	0.1	1	⇑⇑	⇑⇑
Prometon	100[d]	100[d]	⇑⇑⇑⇑	⇑⇑
Genistein	10	10	⇑⇑⇑⇑	⇑⇑⇑⇑

[a] considered because there was a clear concentration-response at all but the greatest concentration

[b] lead laboratory (Lab 1)

[c] participating laboratory (Labs 2,3 and 4)

[d] Effects occurred at greatest non-cytotoxic concentration; no dose-response