



10th Berlin-Workshop on Developmental Toxicology

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10th Berlin-Workshop on Developmental Toxicology



Welcome

to the **10th Berlin-Workshop on Developmental Toxicity** at the **German Federal Institute for Risk Assessment (BfR)**

➤ *25 years after the “1st Berlin Workshop”*

The **BfR** is the scientific body of the Federal Republic of Germany that prepares expert reports and opinions on risks related to food ingestion and exposure to consumers including risk assessments of industrial chemicals, biocides and pesticides.

10th Berlin-Workshop on Developmental Toxicology



Main goals of the

“**Berlin DevTox Workshops**” held in Berlin during the last 25 years

- **Harmonization of terminology** used in Developmental Toxicology,
- **Improvement of risk assessment** in regulatory developmental toxicology.
- **Application of alternative methods** for assessing developmental effects.

Agreed among experts from **academia, industry and regulatory authorities** that international harmonization of terminology is urgently needed for a better risk assessment of chemicals.

The activities of the “Berlin DevTox Workshops” were part of the “IPCS harmonization programme”.



1st Berlin-Workshop on Developmental Toxicology



The idea of the “**Berlin DevTox Workshops**” started 1995 with the 1st version of an internationally developed glossary of terms for structural developmental abnormalities in common laboratory animals, published by the **IFTS** Committee on International Harmonization of Nomenclature in Developmental Toxicology, and represents considerable progress toward harmonization of terminology in this area.

The purpose of this effort was to provide a common vocabulary that will reduce confusion and ambiguity in the description of developmental effects, **particularly in submissions to regulatory agencies worldwide.**

[Teratology](#). 1997 Apr;55(4):249-92.

Terminology of developmental abnormalities in common laboratory mammals (version 1).

[Wise LD](#)¹, [Beck SL](#), [Beltrame D](#), [Beyer BK](#), [Chahoud I](#), [Clark RL](#), [Clark R](#), [Druga AM](#), [Feuston MH](#), [Guittin P](#), [Henwood SM](#), [Kimmel CA](#), [Lindstrom P](#), [Palmer AK](#), [Petre JA](#), [Solomon HM](#), [Yasuda M](#), [York RG](#).

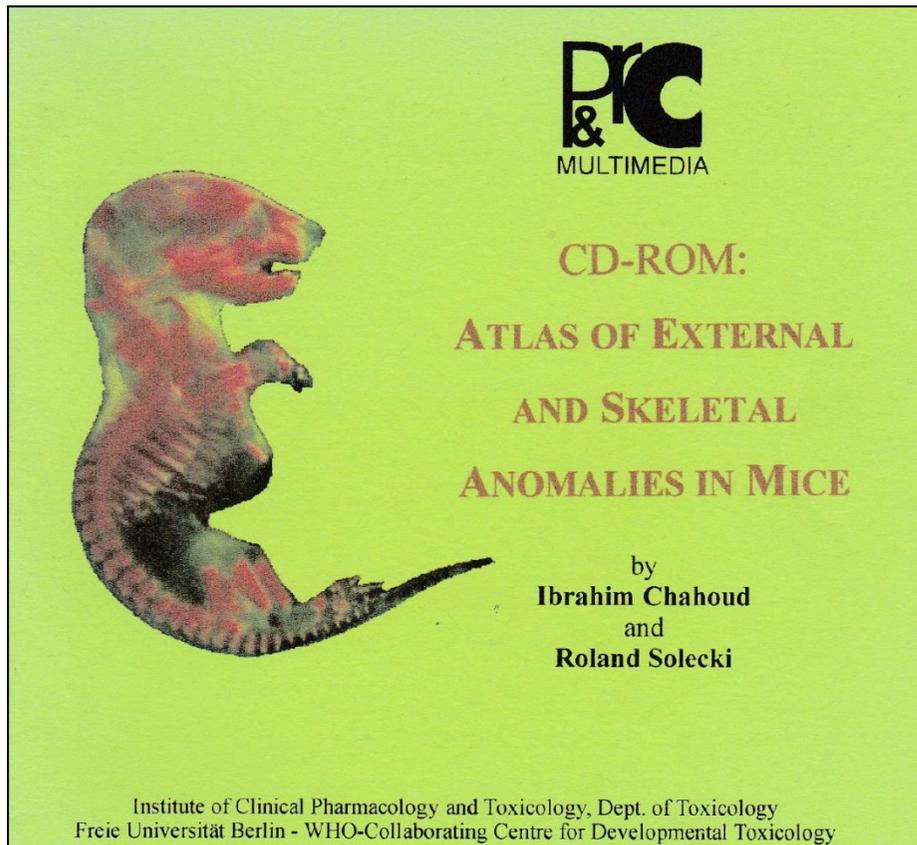
1st Berlin-Workshop on Developmental Toxicology



The second idea of the 1st “**Berlin DevTox Workshop**” was to discuss the project for an “Atlas of External and Skeletal Anomalies”.

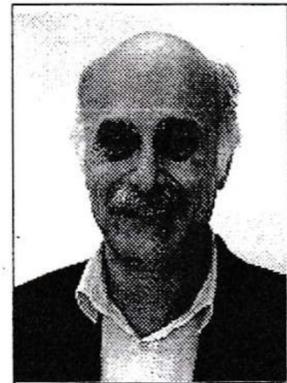
Three different atlases were published afterwards on CD-ROM:

Anomalies in Rats, Anomalies in Rabbits, Anomalies in Mice



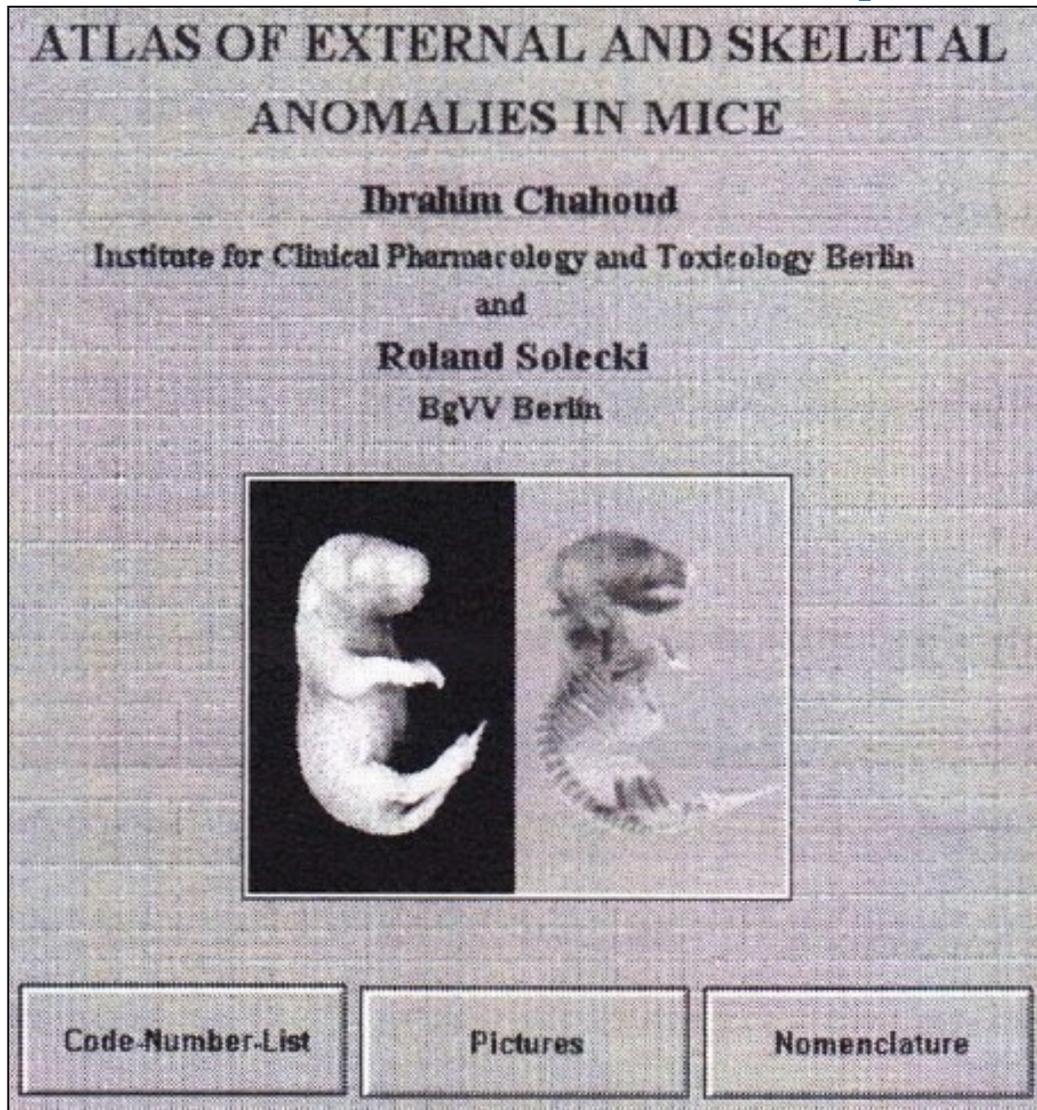
The objectives of the “Atlas of External and Skeletal Anomalies in Mice” are:

1. To provide suitable pictures for external (visceral) and skeletal anomalies as a background tool for a worldwide harmonization of the terminology used in reproductive toxicology.
2. To facilitate the diagnosis and harmonize the nomenclature of anomalies on the basis of practical images.
3. To furnish practical illustrations for seminars and university lectures.
4. To provide a background tool for the harmonization of picture based terminology in reproductive toxicology.



PROF. I. CHAHOUD

1st Berlin-Workshop on Developmental Toxicology



- The glossary was organized into broad sections for **external, visceral, and skeletal observations**, then subdivided into regions, structures, or organs.
- Numbering is sequential, and not in any regional or hierarchical order.
- Updates of the glossary were planned based on comments received.

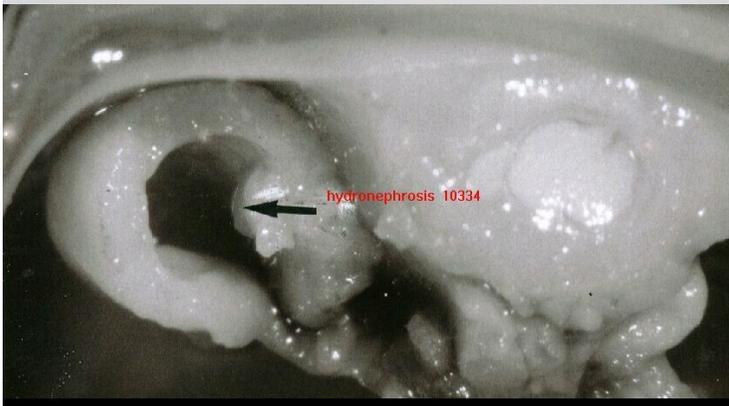
The Atlas consists of three sections:

- **first section**, anatomical names of various regions of the skeletons listed
- **second section** with the nomenclature of single anomalies,
- **third section** contains alternative terms and remarks if necessary.

2nd Berlin-Workshop on Developmental Toxicology



The 2nd “**Berlin DevTox Workshop**” in 1998 started a process of discussion that lead to a harmonization of terminology used for classification of structural anomalies including the **definition of “malformation”** and **“variation”**.



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● *Special Article*

**CLASSIFICATION TERMS IN DEVELOPMENTAL TOXICOLOGY:
NEED FOR HARMONISATION**

REPORT OF THE SECOND WORKSHOP ON THE TERMINOLOGY IN DEVELOPMENTAL
TOXICOLOGY BERLIN, 27–28 AUGUST 1998

IBRAHIM CHAHOUD,* JOCHEN BUSCHMANN,† RUTH CLARK,‡ ALICE DRUGA,§ HEIN FALKE,¶
ALI FAQI,* ERNST HANSEN,# BARBARA HEINRICH-HIRSCH,** JUERGEN HELLWIG,††
WOLFGANG LINGK,** MEG PARKINSON,‡‡ FRANCISCO J. R. PAUMGARTTEN,§§
RUDOLF PFEIL,** THOMAS PLATZEK,** ANTHONY R. SCIALLI,¶¶ JENNIFER SEED,##
RALF STAHLMANN,* BEATE ULBRICH,*** XIANDONG WU,††† MINEO YASUDA,‡‡‡
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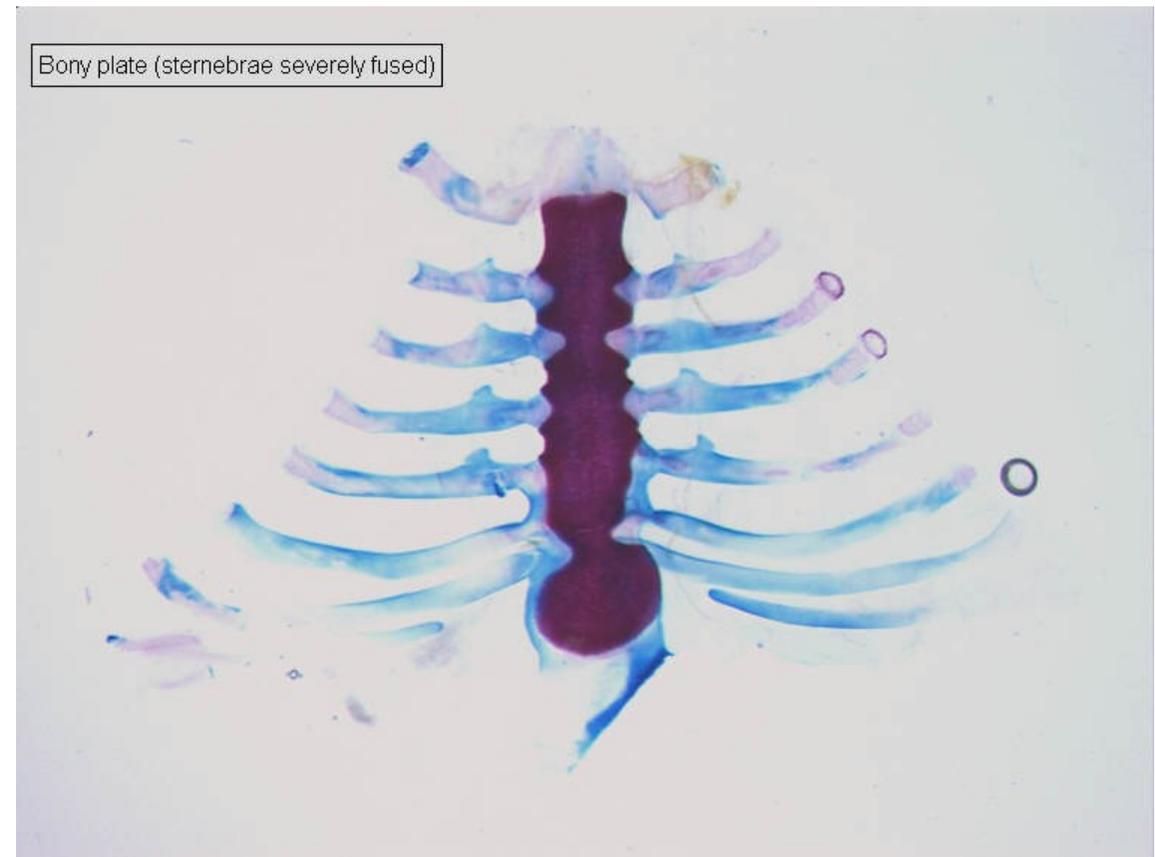
2nd Berlin-Workshop on Developmental Toxicology



Definition:

Malformation (Chahoud et al., 1999)

“permanent structural change that is likely to adversely affect the survival or health of the species under investigation”



2nd Berlin-Workshop on Developmental Toxicology



Definition:

Variation (Chahoud et al., 1999)

“a change that occurs within the normal population under investigation and is unlikely to adversely affect survival or health”

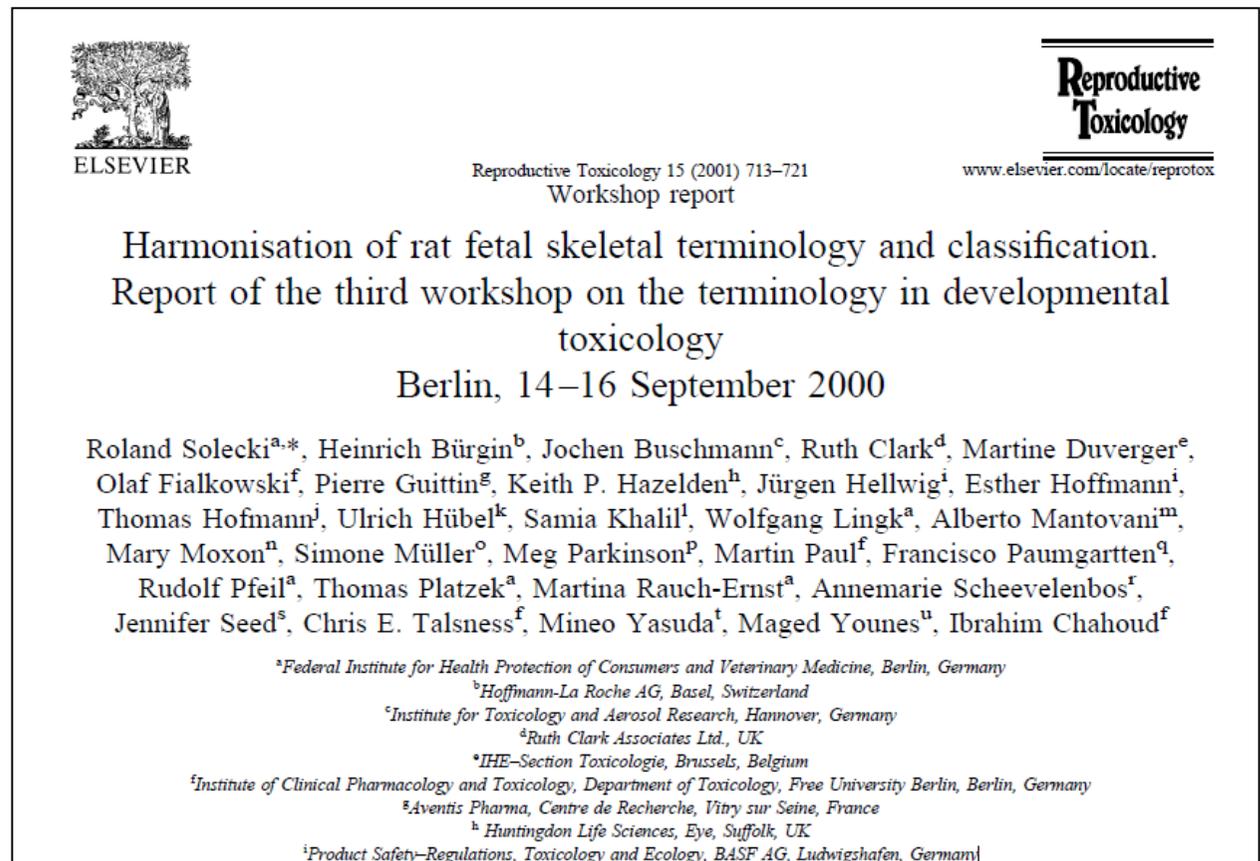


3rd & 4th Berlin-Workshop on Developmental Toxicology



In the 3rd and 4th “**Berlin DevTox Workshops**” in 2000 and 2002 harmonization of rat fetal skeletal, external and visceral terminology and classification were proposed. New terms like “grey-zone anomalies” and “unclassified” anomalies were introduced.

The attendees concluded that “grey-zone” anomalies will never disappear completely and that for the assessment, the grade of severity and/or the frequency of the observation can be decisive for the terminology chosen.



3rd & 4th Berlin-Workshop on Developmental Toxicology



In the 3rd and 4th “**Berlin DevTox Workshops**” in 2000 and **2002** harmonization of rat fetal skeletal, external and visceral terminology and classification were proposed. New terms like “grey-zone anomalies” and “unclassified” anomalies were introduced.

Several of the soft tissue changes were considered likely to be the consequence of functional disorders and thus not strictly developmental anomalies. The possibility to describe a finding as **'Not Malformation' (Unclassified)** was agreed upon.



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Reproductive Toxicology 17 (2003) 625–637

Reproductive
Toxicology

www.elsevier.com/locate/reprotox

Conference Proceedings

Harmonization of rat fetal external and visceral terminology and classification

Report of the Fourth Workshop on the Terminology in Developmental Toxicology, Berlin, 18–20 April 2002[☆]

Roland Solecki^{a,*}, Brigitte Bergmann^b, Heinrich Bürgin^{c,2}, Jochen Buschmann^{d,1}, Ruth Clark^{e,1}, Alice Druga^f, E.A.J. Van Duijnhoven^g, Martine Duverger^{h,2}, James Edwardsⁱ, Hamelore Freudenberger^j, Pierre Guittin^{k,1}, Palmira Hakaite^l, Barbara Heinrich-Hirsch^a, Jürgen Hellwig^{j,1}, Thomas Hofmann^{b,2}, Ulrich Hübel^{m,2}, Samia Khalilⁿ, Ana-maria Klaus^{o,2}, Sabine Kudicke^p, Wolfgang Lingk^a, Tim Meredith^q, Mary Moxon^{r,2}, Simone Müller^{s,2}, Martin Paul^t, Francisco Paumgartten^{u,2}, Elke Röhrdanz^p, Rudolf Pfeil^a, Martina Rauch-Ernst^{a,2}, Jennifer Seed^{v,1}, Francois Spezia^w, Carolyn Vickers^q, Brigitte Woelffel^t, Ibrahim Chahoud^{t,1}

^a Federal Institute for Risk Assessment, Berlin, Germany

^b Institute for Environmental Health Sciences, University of Zurich, Switzerland

5th Berlin-Workshop on Developmental Toxicology

Reproductive Toxicology 27 (2009) 8–13



Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

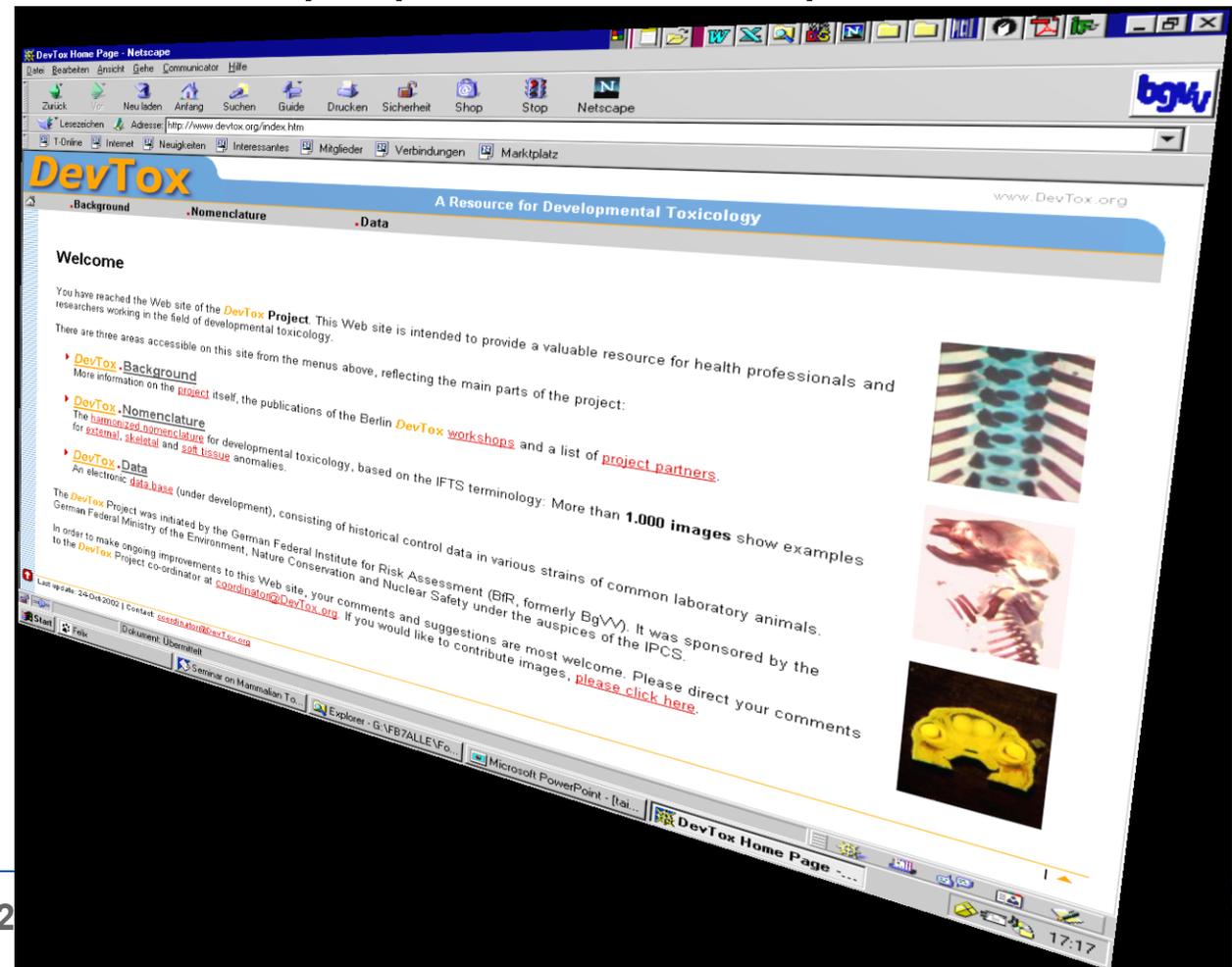


Harmonization of terminology in developmental toxicology: The quest for a more precise description and a harmonized classification of fetal observations^{††}

At the 5th “**Berlin DevTox Workshop**”, held in 2005, discussion was concentrated on an ETS proposal for an improvement of an harmonized terminology in Developmental Toxicology.

During the 5th “Berlin DevTox Workshop” **the DevTox-Atlas on the DevTox-website was presented on**

www.devtox.org



5th Berlin-Workshop on Developmental Toxicology

Reproductive Toxicology 27 (2009) 8–13



Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox



Harmonization of terminology in developmental toxicology: The quest for a more precise description and a harmonized classification

A main objective was to discuss a draft proposal for updating the glossary of descriptive terms for fetal abnormalities put forward by Wise et al. 1997.

The participants were asked to classify new external, visceral and skeletal observations included within the new **version 2** according to the two-category scheme (malformation and variation) agreed at previous **Berlin DevTox workshops**.

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Birth Defects Research (Part B) 86:227–327 (2009)

Review Article

Terminology of Developmental Abnormalities in Common Laboratory Mammals (Version 2)

Susan L. Makris,^{1*} Howard M. Solomon,² Ruth Clark,³ Kohei Shiota,⁴ Stephane Barbellion,⁵ Jochen Buschmann,⁶ Makoto Ema,⁷ Michio Fujiwara,⁸ Konstanze Grote,⁹ Keith P. Hazelden,¹⁰ Kok Wah Hew,¹¹ Masao Horimoto,¹² Yojiro Ooshima,¹³ Meg Parkinson,¹⁴ and L. David Wise¹⁵

• Ear-and-Eye

Clear-Malformation (>75%)	Clear-Variation (>75%)	Grey-Zone (<75%)
10136 Misshapen inner ear 87,50	☐	☐
10137 Anophthalmia 100,00	☐	☐
10138 Aphakia 93,75	☐	☐
10139 Cataract 75,00	☐	☐
10141 Macrophthalmia 100,00	☐	☐
10142 Malpositioned eye 90,00	☐	☐
10143 Microphthalmia 90,00	☐	☐
10144 Misshapen lens 80,00	☐	☐
10145 Ocular coloboma 100,00	☐	☐

• Nose

Clear-Malformation (>75%)	Clear-Variation (>75%)	Grey-Zone (<75%)

6th Berlin-Workshop on Developmental Toxicology

Reproductive Toxicology 27 (2009) 8–13



Contents lists available at ScienceDirect

Reproductive Toxicology

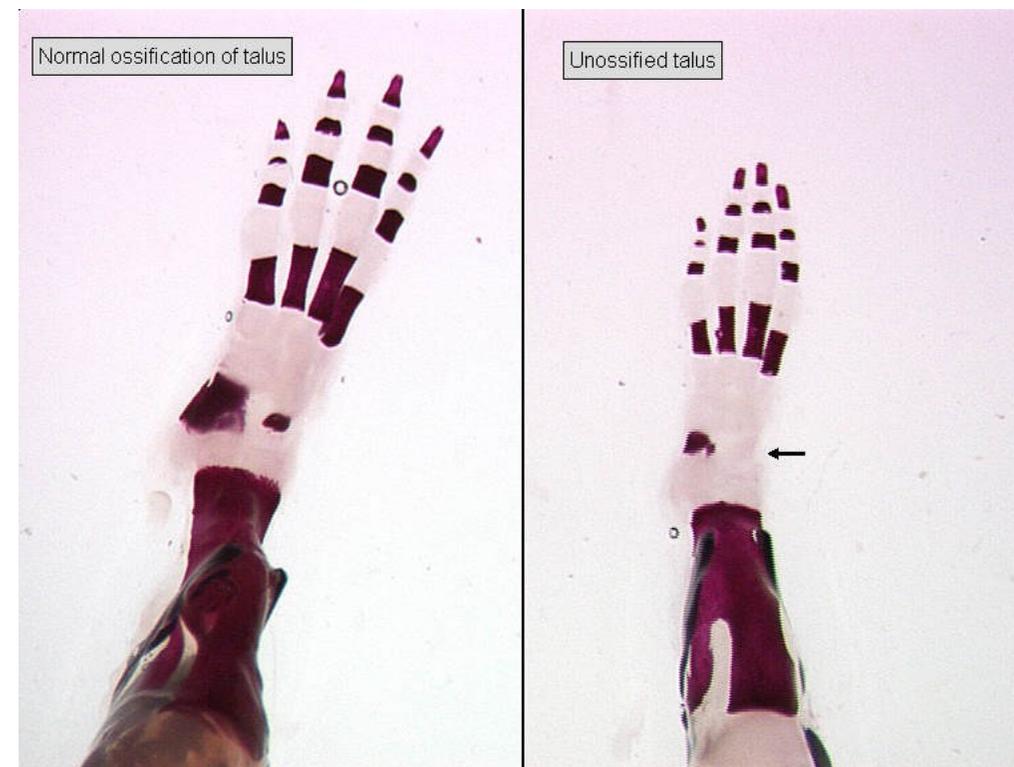
journal homepage: www.elsevier.com/locate/reprotox



Harmonization of terminology in developmental toxicology: The quest for a more precise description and a harmonized classification of fetal observations^{2*}

Discussions at the 6th “**Berlin DevTox Workshop**” 2007 were mainly focused on the causes **of uncertainty and low agreement** regarding classification of some fetal observations as malformations or variations.

It was agreed that additional information, including sub-location within the affected structure, more detailed description of the nature of the change, a better knowledge of adversity and postnatal consequences, a grading for severity **together with photographs**, would make descriptive terms more precise and reduce misclassifications.



7th Berlin-Workshop on Developmental Toxicology



One recommendation of 7th “**Berlin DevTox Workshop**” held 2011 was to initiate a further survey regarding classification of findings in Version 2 terminology to improve classification of findings and laboratory investigations.

Similar to the previously conducted surveys on skeletal, external and visceral anomalies, which were conducted in 2001 and 2002, the new survey includes additionally maternal-fetal observations and non-routinely used species.

Reproductive Toxicology 35 (2013) 48–55

Contents lists available at SciVerse ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox



Harmonization of description and classification of fetal observations:
Achievements and problems still unresolved
Report of the 7th Workshop on the Terminology in Developmental Toxicology
Berlin, 4–6 May 2011[☆]

Roland Solecki^{a,*}, Stephane Barbellion^b, Brigitte Bergmann^c, Heinrich Bürgin^d, Jochen Buschmann^e, Ruth Clark^f, Laura Comotto^g, Antje Fuchs^h, Ali Said Faqiⁱ, Ralph Gerspach^j, Konstanze Grote^k, Helen Hakansson^l, Verena Heinrich^a, Barbara Heinrich-Hirsch^a, Thomas Hofmann^c, Ulrich Hübel^m, Thelma Helena Inazakiⁿ, Samia Khalil^d, Thomas B. Knudsen^o, Sabine Kudicke^p, Wolfgang Lingk^v, Susan Makris^o, Simone Müller^q, Francisco Paumgarten^r, Rudolf Pfeil^a, Elkiene Macedo Ramaⁿ, Steffen Schneider^s, Kohei Shiota^t, Eva Tamborini^g, Mariska Tegelenbosch^u, Beate Ulbrich^a, E.A.J. van Duijnhoven^v, David Wise^w, Ibrahim Chahoud^x

8th Berlin-Workshop on Developmental Toxicology

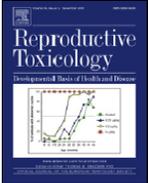


A main task of the 8th “**Berlin DevTox Workshop**” 2014 were discussions about observational data in human teratogenicity findings and comparative aspects and mechanisms of developmental anomalies in laboratory animals and humans

and to evaluate the 2nd survey regarding Version 2 terminology for external, visceral, skeletal and materno-fetal anomalies which can be classified either as a malformation, as variation or as grey-zone anomaly according to their severity, size, persistence and grading.

Reproductive Toxicology 57 (2015) 140–146

Contents lists available at [ScienceDirect](#)

 **Reproductive Toxicology** 

journal homepage: www.elsevier.com/locate/reprotox

Continuing harmonization of terminology and innovations for methodologies in developmental toxicology: Report of the 8th Berlin Workshop on Developmental Toxicity, 14–16 May 2014 

Roland Solecki^a, Martina Rauch^a, Andrea Gall^a, Jochen Buschmann^b, Ruth Clark^d, Antje Fuchs^e, Haidong Kan^f, Verena Heinrich^{a,*}, Rupert Kellner^b, Thomas B. Knudsen^g, Weihua Li^h, Susan L. Makris^g, Yojiro Ooshimaⁱ, Francisco Paumgarten^j, Aldert H. Piersma^k, Gilbert Schönfelder^{a,c}, Michael Oelgeschläger^a, Christof Schaefer^c, Kohei Shiota^l, Beate Ulbrich^m, Xuncheng Ding^h, Ibrahim Chahoud^c

9th Berlin-Workshop on Developmental Toxicology



Main task of the 9th “**DevTox Berlin Workshop**” 2018 was the an **update of the DevTox database**, the discussion of **alternative strategies in testing** developmental effects and an consideration of specific **aspects in regulatory risk assessment** as well as **new Survey in Japan**.

Results of the 9th Berlin-Workshop were published in an scientific journal as well as at the DevTox website (in [English and Chinese](#)), which contains more than **2.500 images** with external, skeletal, soft tissue and maternal-fetal anomalies.

Reproductive Toxicology 89 (2019) 124–129

Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox



Update of the DevTox data database for harmonized risk assessment and alternative methodologies in developmental toxicology: Report of the 9th Berlin Workshop on Developmental Toxicity



DevTox A Resource for Developmental Toxicology

Background Nomenclature Data Masthead 中文

DevTox 发育毒理学资源之一

背景 术语集 数据 发行机构 English

DevTox 背景: DevTox项目

农药对胚胎或胎儿发育的潜在不良影响是人类与野生动物健康风险评估中必须考虑的一个重要因素。这类信息通常来自妊娠实验动物在胚胎发育关键期暴露于不同浓度化合物的实验研究。不同实验室用于描述胚胎形态异常的术语与诊断标准必须一致。2012年10月该项目3.0版对这些胚胎形态异常的术语集进行了更新,修改了许多术语,添加了许多新术语,并引入一类新的研究结果(母 胎形态异常)。

本网站采用新术语集,它涵盖了许多新的研究结果,且能够反映新动物品种中的大多数研究结果以及出生后发育早期发育的观察结果。新动物品种中尚未被术语集收录的结果,将在下次更新时予以考虑,下次更新应以非人类灵长类动物中的研究结果为重点。之后,应将新的研究结果分类为畸形、变异或“灰色地带”形态异常。

因此, **DevTox** 项目有三个主要目标:

- to harmc
- to assist
- to provid

DevTox 背景:
• DevTox项目
• 国际研讨会
• 项目合作单位
• 技术信息

10th Berlin-Workshop on Developmental Toxicology

10th Berlin Workshop on
Developmental
Toxicology

19–20 February 2020, Berlin



10th “Berlin DevTox Workshop”

should be an excellent platform for scientific collaboration between international experts from **agencies, academia and industry**

aimed at the improvement of the assessment of chemicals with respect to their health effects.

Topics are grouped in three different main panels:

- The DevTox-Project
- Risk Assessment – Developmental Neurotoxicity
- Future Methodology in DevTox

Presentations and main results of the 10th Workshop will be published on the BfR Website and a report of the workshop in a peer reviewed journal.

I hope we will have a successful symposium and I wish you a most pleasurable stay here in Berlin.

**Thank you
Martina (†)
for you great
support to the
Berlin**



Workshops



Dr. Roland Solecki

(until 29.02.2020)

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