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# **25 YEARS DEVTOX WORKSHOPS: HISTORIC BACKGROUND, SCIENTIFIC AND TECHNICAL IMPROVEMENTS**

Rupert Kellner

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**Fraunhofer**  
**ITEM**

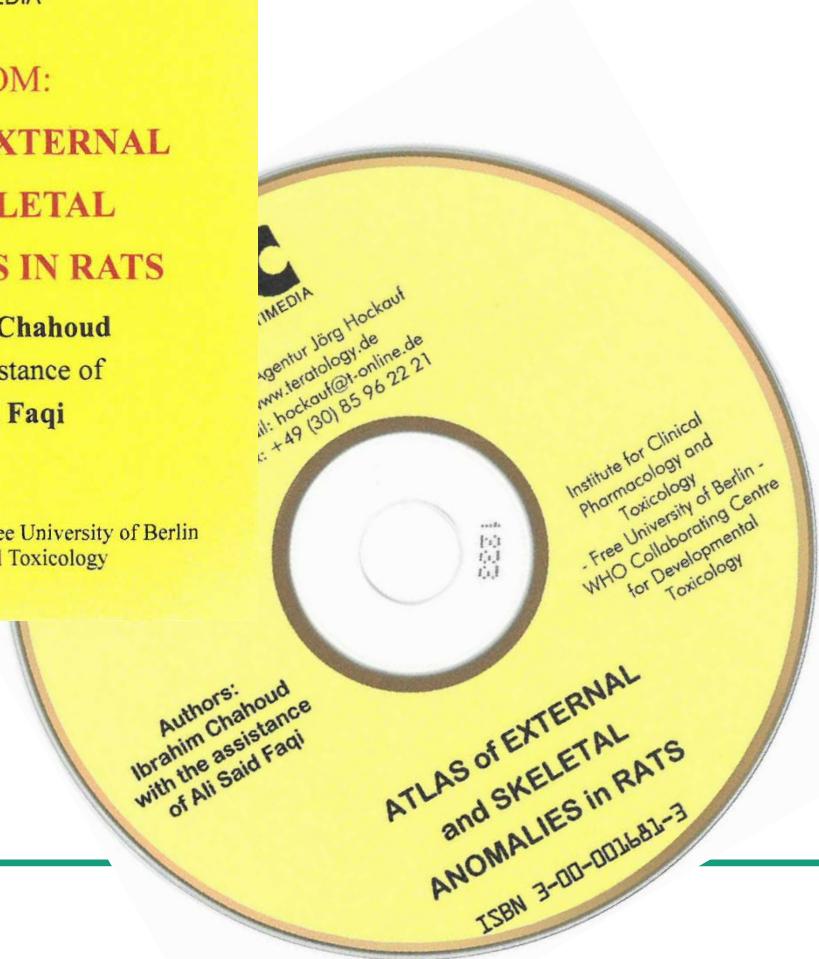
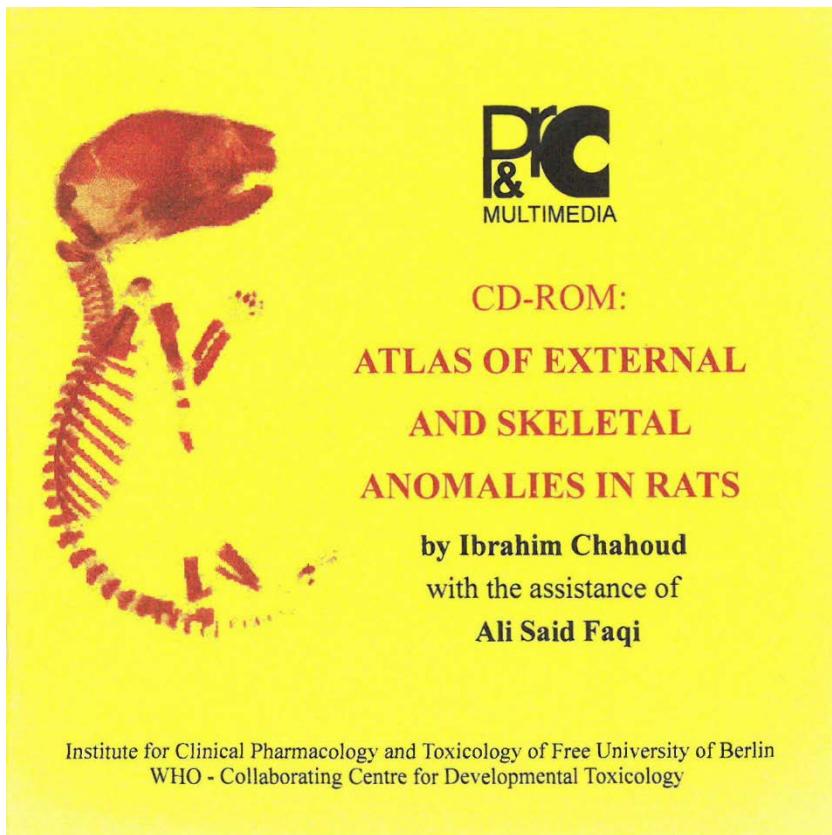
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# OVERVIEW

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- 
- Starting point of *DevTox*
  - First presentation on the Web
  - Technical improvements
  - Translation of *DevTox*
  - *DevTox* perspectives

# Atlas of Anomalies in Rats



- CD-ROM: April 1997
- Based on IFTS harmonized glossary
- 140 findings
- 350 images

# Atlas of Anomalies in Rats

Atlas Of Anomalies, by Ibrahim Chahoud v1.20 produced by PR & C Agentur Berlin/Leipzig

**ATLAS OF EXTERNAL AND SKELETAL ANOMALIES IN RATS**

Ibrahim Chahoud  
with the assistance of  
Ali Said Faqi  
Institute for Clinical Pharmacology and Toxicology Berlin



Video-Start

Code-Number-List Pictures Nomenclature

Please click buttons to start !

Copyright:  
**PR & C MULTIMEDIA**  
ISBN 3-00-001681-3

One purpose of this Atlas of external and skeletal anomalies is to provide an objective basis for the implementation of a worldwide harmonization process of teratological terminology.

Berlin, 1997

Project Team

End

Atlas Of Anomalies, by Ibrahim Chahoud v1.20 produced by PR & C Agentur Berlin/Leipzig

CD-ROMs: Atlas of Anomalies in in Rats, Rabbits, Mice and Marmosets are available at:

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Hans Figuhr  
Technical Assistance

Back



Dr. Ali Said Faqi  
Project Assistant

# Atlas of Anomalies in Rats

Atlas Of Anomalies, by Ibrahim Chahoud v1.20 produced by PR & C Agentur Berlin/Leipzig

**External Anomalies**



EXTERNAL ANOMALIES

Please click buttons !

Skeletal Anomalies

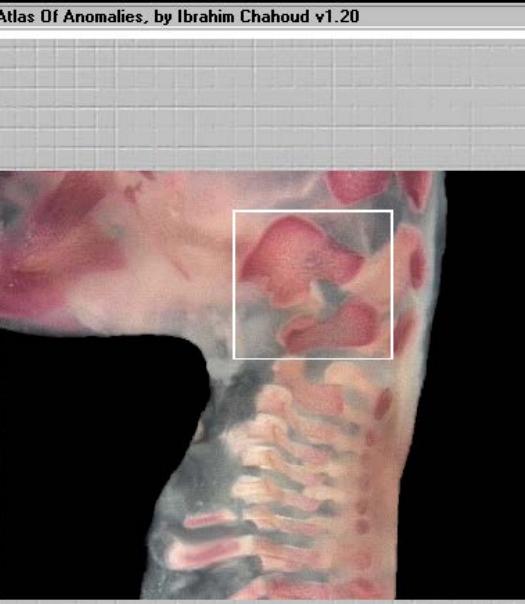


SKELETAL ANOMALIES

Back

Atlas Of Anomalies, by Ibrahim Chahoud v1.20 produced by PR & C Agentur Berlin/Leipzig

Letter / Number: 56  
Anatomical Term: Exoccipital



REGION: SKULL  
Exoccipital

ANOMALY: Misshapen (27)  
synonym or  
ated term(s): Abnormally shaped, Irregularly shaped, \*

ODE-NR.: 225604

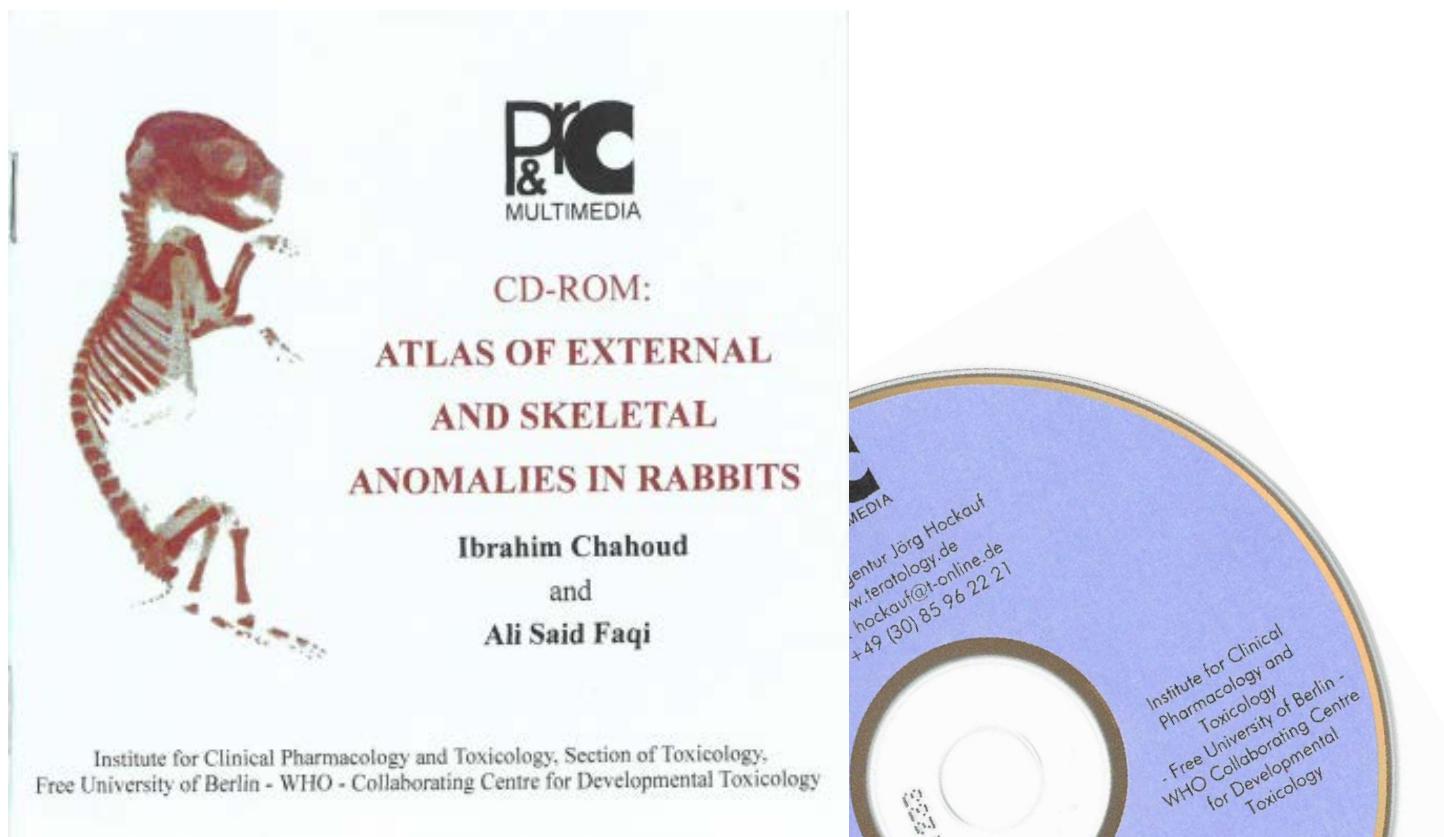
REMARK:  
exoccipital irregularly shaped, cervical rib  
Asymmetric

For anatomical terms type the letters  
or numbers in the picture !

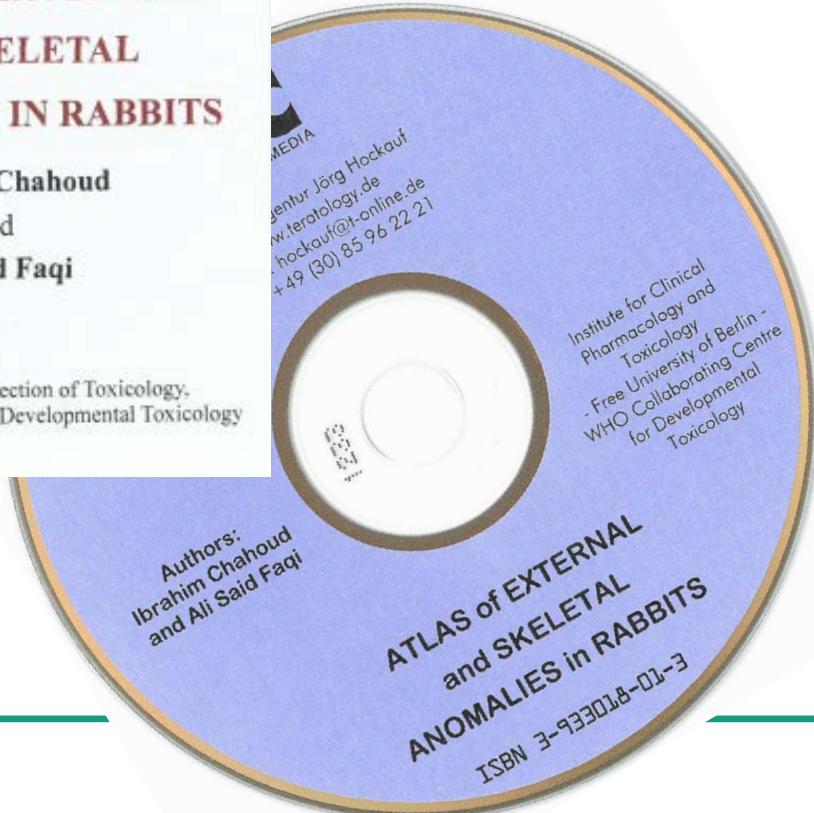
First Page Back

< picture 1 picture 2 picture 3 picture 4 >

# Atlas of Anomalies in Rabbits



- CD-ROM: August 1997
- Based on IFTS harmonized glossary
- 104 findings
- 205 images



# Atlas of Anomalies in Rabbits



- Additional CD-ROMs
- Marmosets  
October 1998
- Mice  
April 1999

# DevTox: Developmental toxicology

- Initiated in 1999
- Project funded by the Federal Institute for Risk Assessment (BfR, Berlin)
- Collaboration with:
  - Institute of Clinical Pharmacology and Toxicology, Department of Toxicology (Charité, Berlin)
  - Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM, Hannover)
- Harmonized nomenclature for developmental toxicology
- Public Website: <https://www.devtox.org>



# DevTox Version 1

**DevTox** A Resource for Developmental Toxicology [www.DevTox.org](http://www.DevTox.org)

Background Nomenclature Data

## Welcome

You have reached the Web site of the **DevTox Project**. This Web site is intended to provide a valuable resource for health professionals and researchers working in the field of developmental toxicology.

There are three areas accessible on this site from the menus above, reflecting the main parts of the project:

- ▶ **DevTox .Background**  
More information on the [project](#) itself, the publications of the Berlin [DevTox workshops](#) and a list of [project partners](#).
- ▶ **DevTox .Nomenclature**  
The [harmonized nomenclature](#) for developmental toxicology, based on the IFTS terminology: More than **1.000 images** show examples for [external](#), [skeletal](#) and [soft tissue](#) anomalies.
- ▶ **DevTox .Data**  
An electronic [data base](#) (under development), consisting of historical control data in various strains of common laboratory animals.

The **DevTox Project** was initiated by the German Federal Institute for Risk Assessment (BfR, formerly BgVV). It was sponsored by the German Federal Ministry of the Environment, Nature Conservation and Nuclear Safety under the auspices of the IPCS.

In order to make ongoing improvements to this Web site, your comments and suggestions are most welcome. Please direct your comments to the **DevTox Project co-ordinator** at [coordinator@DevTox.org](mailto:coordinator@DevTox.org). If you would like to contribute images, [please click here](#).

Last update: 24-Oct-2002 | Contact: [coordinator@DevTox.org](mailto:coordinator@DevTox.org)



- Website
  - HTML pages
- Version from 2002
- >1000 images

# DevTox Version 1 (2002)

## DevTox

A Resource for Developmental Toxicology

[www.DevTox.org](http://www.DevTox.org)



[Background](#)

[Nomenclature](#)

[Data](#)

### DevTox.Background: Berlin DevTox workshops

Since 1995, four Workshops on the Terminology in Developmental Toxicology have been held in Berlin.

The **first Workshop**, in 1995, discussed the uses and misuses of the IFTS glossary, which is presented in the publication of the first report.

Wise et al., (1997) Terminology of developmental abnormalities in common laboratory mammals. *Teratogen Carcinogen Mutagen* 29(2): 292  
► [PubMed abstract](#)

The **second Workshop**, in 1998, discussed the advantages of using a classification system for fetal anomalies. The report presents definitions for two classification categories which were "malformation" and "variation".

Chahoud et al., (1999) Classification terms in developmental toxicology: need for harmonisation of the Terminology in Developmental Toxicology. Berlin, 27-28 August 1998. *Reprod Toxicol* 13: 1-10  
► [PubMed abstract](#)  
► [Science Direct article](#)

The **third Workshop**, in 2000, discussed the categorization of the skeletal observations listed in the IFTS. The report presents the classification system agreed at the second Berlin Workshop.

Solecki R et al., (2001) Harmonisation of rat fetal skeletal terminology and classification. Report of the Third International Workshop on Terminology in Developmental Toxicology. Berlin, 14-16 September 2000. *Reprod Toxicol* 15: 1-10  
► [PubMed abstract](#)  
► [Science Direct article](#)

The **fourth Workshop**, in 2002, discussed the categorization of external and soft tissue anomalies listed in the IFTS, using the classification system agreed at the second Berlin Workshop.

The manuscript is in preparation but is anticipated to be submitted for publication in December 2002.



Last update: 20-Aug-2002 | Contact: [coordinator@DevTox.org](mailto:coordinator@DevTox.org)

## DevTox

A Resource for Developmental Toxicology



[Background](#)

[Nomenclature](#)

[Data](#)

### DevTox.Background: Project partners

The following organizations have been involved in the development and realization of the **DevTox** project:

► Federal Institute for Risk Assessment (BfR)  
(formerly BgVV)  
FG 701  
Thielallee 88-92  
D-14195 Berlin  
Germany

► Fraunhofer Institute of Toxicology and Aerosol Research  
Drug Research and Clinical Inhalation  
Nikolai-Fuchs-Str. 1  
D-30625 Hannover  
Germany

► Institute of Clinical Pharmacology and Toxicology  
Department of Toxicology  
Free University Berlin  
Garystrasse 5  
D-14195 Berlin  
Germany

► In addition, the valuable contribution of many prominent international scientists from research institutions, regulatory agencies, and industry is gratefully acknowledged.



Last update: 10-Aug-2002 | Contact: [coordinator@DevTox.org](mailto:coordinator@DevTox.org)



Fraunhofer Institut  
Toxikologie und  
Aerosolforschung  
Pharmaforschung und  
Klinische Inhalation



# DevTox Version 1 (2002)

[Home](#) | [Help](#) | [Configuration](#)

**DevTox**

Rat Mouse Rabbit Other

[External Findings](#) [Skeletal Findings](#) [Soft Tissue Findings](#)

show as  List View  Tree View

Skeletal Findings	①	②	③	④
• <u>Skull</u>	✓	✓	✓	✓
• <u>Alisphenoid</u>	✓	✓	✓	✓
• <u>Auditory ossicles</u>	✓	✓	✓	✓
• <u>Basioccipital</u>	✓	✓	✓	✓
• <u>Basisphenoid</u>	✓	✓	✓	✓
• <u>Exoccipital</u>	✓	✓	✓	✓
• <u>Frontal</u>	✓	✓	✓	✓
• <u>Hyoid</u>	✓	✓	✓	✓
• <u>Interparietal</u>	✓	✓	✓	✓
• <u>Lacrimal</u>	✓	✓	✓	✓
• <u>Mandible</u>	✓	✓	✓	✓
• <u>Maxilla</u>	✓	✓	✓	✓
• <u>Nasal</u>	✓	✓	✓	✓
• <u>Palatine</u>	✓	✓	✓	✓
• <u>Parietal</u>	✓	✓	✓	✓
• <u>Premaxilla</u>	✓	✓	✓	✓
• <u>Presphenoid</u>	✓	✓	✓	✓
• <u>Squamosal</u>	✓	✓	✓	✓
• <u>Supraoccipital</u>	✓	✓	✓	✓
• <u>Tympanic annulus</u>	✓	✓	✓	✓
• <u>Vomer</u>	✓	✓	✓	✓
• <u>Zygomatic</u>	✓	✓	✓	✓
• <u>Vertebra</u>	✓	✓	✓	✓
• <u>Cervical vertebra</u>	✓	✓	✓	✓
• <u>Cervical centrum</u>	✓	✓	✓	✓
• <u>Cervical centrum cartilage</u>	✓	✓	✓	✓
• <u>Cervical arch</u>	✓	✓	✓	✓
• <u>Thoracic vertebra</u>	✓	✓	✓	✓
• <u>Thoracic centrum</u>	✓	✓	✓	✓

**Exoccipital**

	①	②	③	④
Absent	M	M	M	M
Fused	M	M	M	M
Hole(s)	✓	✓	✓	✓
Incomplete ossification	V	V	V	V
Missed	✓	✓	✓	✓

[Home](#) | [Locations](#) | [Findings](#) | [Manuscript](#) | [Comments](#) | [Help](#)

**DevTox**

Rat Mouse × Rabbit × Other

Skeletal finding

**Exoccipital – Missed**

Synonym(s): Abnormally shaped; Irregularly shaped  
Non-preferred term(s): –

Definition:  
Abnormally shaped [Not to be used to describe sites of incomplete ossification].

Notes:  
–

[Fig. 1:](#) Exoccipital bone fused with a bone of atlas-like structure  
Additional finding: Cervical rib



[Fig. 2:](#) Exoccipital bone irregularly shaped  
Additional finding: Cervical rib



[Fig. 3:](#) –



**Control**

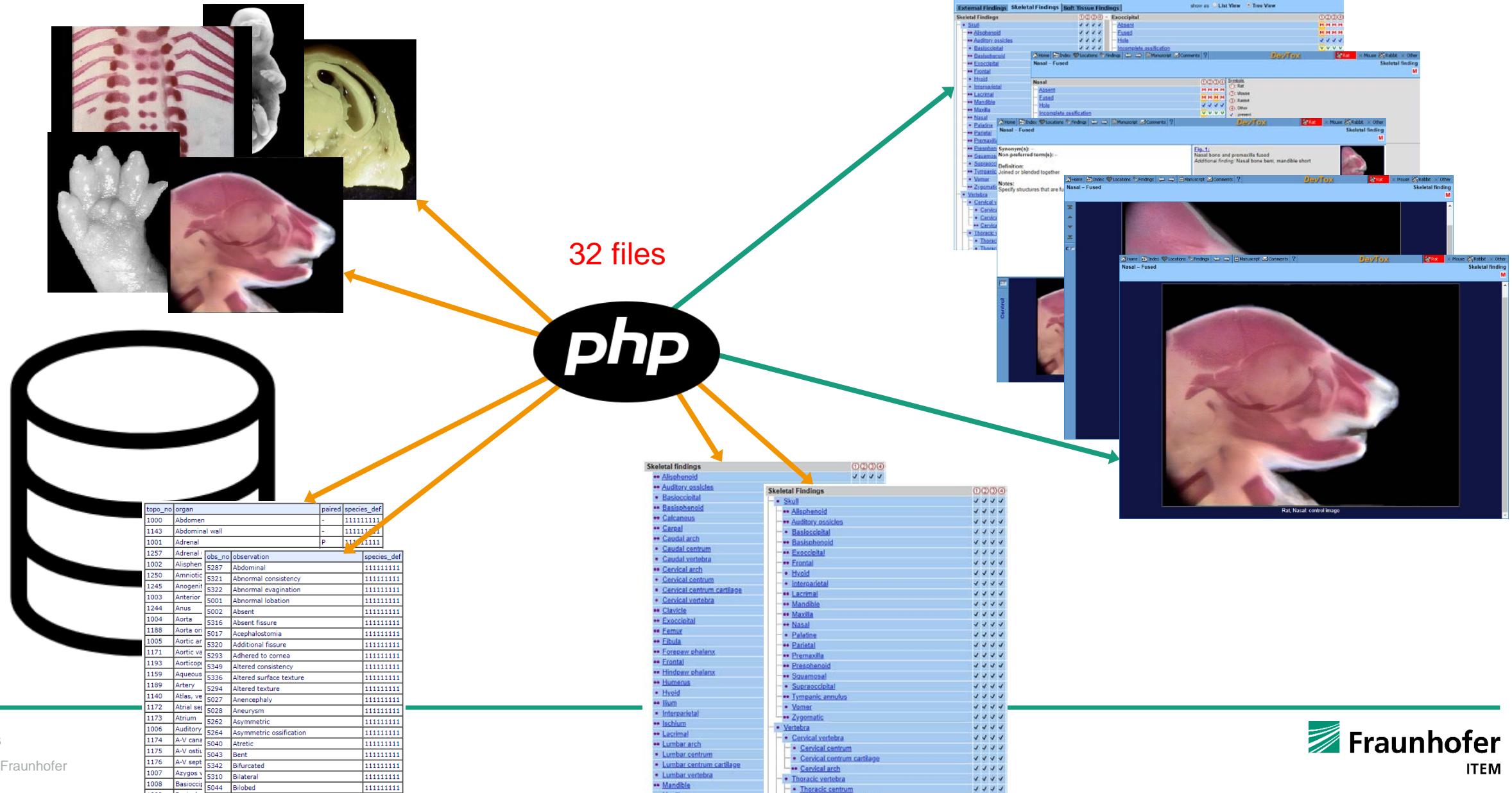
Rat, Exoccipital: control image

**Fig. 2: Rat, Exoccipital – Missed.**  
Exoccipital bone irregularly shaped  
Additional finding: Cervical rib

# DevTox Version 1 (2002)

- External Findings
  - 396 images (288 anomalies, 108 control)
  - 4340 files
- Skeletal Findings
  - 570 images (390 anomalies, 180 control)
  - 9549 files
- Soft Tissue Findings
  - 92 images (79 anomalies, 13 control)
  - 4290 files
- Species
  - Rat: 532 images
  - Mouse: 392 images
  - Rabbit: 134 images
  - Other (placeholder)
- HTML tree

# DevTox Version 2 (2004)



# DevTox Images in Version 2 (2009)

- Last release on December 09, 2009
  - with 371 new images
- >1.700 images
- Anomalies per species
  - Rat: 677 images
  - Mouse: 259 images
  - Rabbit: 314 images
  - Other: 53 images  
incl. Hamster, Monkey, Quail
- New findings

The screenshot shows the DevTox website interface. At the top, there's a blue header bar with the DevTox logo and the text "A Resource for Developmental Toxicology". Below the header, a navigation menu includes "Background", "Nomenclature", "Data", and "Masthead". A sub-menu for "Background" is open, showing sections like "The harm...", "Gallbladder – Supernumerary", "Synonym(s)", "Non-preferred term(s)", "Definition", and "Notes". On the right side of the main content area, there are two red photographs of a rabbit's gallbladder. The top image is labeled "Fig. 1: Rabbit, Gallbladder – Supernumerary." and the bottom image is labeled "Fig. 1: Rabbit, Gallbladder – Supernumerary.".

# New Terminology

- Terminology of developmental anomalies (version 2)
- Published by Makris et al. 2009
- Changes necessary in the *DevTox Nomenclature*



Contents lists available at ScienceDirect

Reproductive Toxicology

journal homepage: [www.elsevier.com/locate/reprotox](http://www.elsevier.com/locate/reprotox)

Terminology of developmental abnormalities in common laboratory mammals (version 2)<sup>☆,☆☆</sup>

Susan L. Makris<sup>a,\*1,4</sup>, Howard M. Solomon<sup>b,1,4</sup>, Ruth Clark<sup>c,2,4</sup>, Kohei Shiota<sup>d,3,4</sup>,  
Stephane Barbellion<sup>e,2</sup>, Jochen Buschmann<sup>f,2</sup>, Makoto Ema<sup>g,3</sup>, Michio Fujiwara<sup>h,3</sup>,  
Konstanze Grote<sup>i,2</sup>, Keith P. Hazelden<sup>j,1</sup>, Kok Wah Hew<sup>k,1</sup>, Masao Horimoto<sup>l,3</sup>,  
Yojiro Ooshima<sup>m,3</sup>, Meg Parkinson<sup>n,2</sup>, L. David Wise<sup>o,1</sup>

Diagnoses	External	Skeletal	Visceral	Maternal-Fetal
Number old	151	467	277	(2)
- delete	38	11	17	
- rename	113	456	260	2
- add	54	567	273	17
Number new	167	1023	533	19

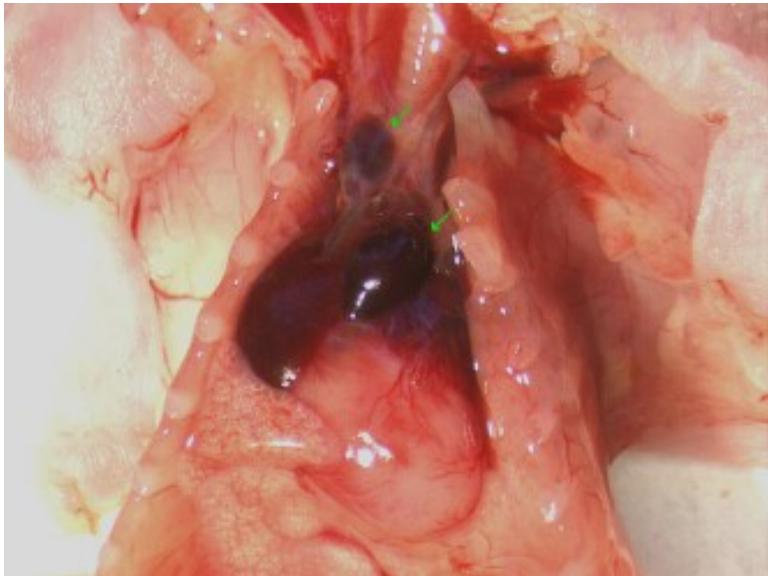
# Changes in Terminology

## ■ Example: Visceral findings

Old No.	Local.	Finding	New No.	Localization	Finding	
3.1005.5040	Aortic arch	Atresia	3.1005.5040	Aortic arch	Atretic	Image
3.1005.5072	Aortic arch	Dilated	3.1005.5072	Aortic arch	Dilated	Image
3.1047.5008	Heart	Absent left A-V valve	3.1179.5002	Left A-V valve	Absent	
3.1047.5094	Heart	Enlarged left A-V valve	3.1179.5088	Left A-V valve	Large	
3.1047.5175	Heart	Misshapen left A-V valve	3.1179.5172	Left A-V valve	Misshapen	
3.1047.5216	Heart	Small left A-V valve	3.1179.5211	Left A-V valve	Small	
3.1047.5008	Heart	Enlarged atrial chamber	3.1173.5088	Atrium	Large	Image
			3.1173.5172	Atrium	Misshapen	
			3.1173.5211	Atrium	Small	

# DevTox Images

- Example: Atrium – Large



3.1047.5091-1-02 (old)  
3.1173.5088-1-02 (new)  
↑↑↑↑ consecutive number  
species: Rat  
observation: Large  
localization: Atrium  
category: Visceral findings

# DevTox Version 3 (2012)

**DevTox** A Resource for Developmental Toxicology  
www.DevTox.org

Background Nomenclature Data Masthead

## Welcome

You have reached the relaunched Web site of the **DevTox Project** (Version 3.0).  
This Web site is intended to provide a valuable resource for health professionals and researchers working in the field of developmental toxicology and represents one of the most comprehensive sources of images of developmental abnormalities.

There are three areas accessible on this site from the menus above, reflecting the main parts of the project:

- ▶ **DevTox .Background**  
Supplementary information on the **project** itself, the publications of the **DevTox Project** and the **Berlin workshops**, a list of **project partners** and relevant **links**.
- ▶ **DevTox .Nomenclature**  
The updated **harmonized nomenclature** for developmental toxicology, based on the revised IFTS terminology (**Makris et al. 2009**): More than **2.500 images** show examples for **external, skeletal, soft tissue** and **maternal-fetal** anomalies [last update October 2012].
- ▶ **DevTox .Data**  
An electronic **data base** is under development, in which experimental data from developmental studies in rats and rabbits in different labs can be evaluated to develop a historical control data base in various strains of common laboratory animals.

The **DevTox Project** was initiated by the German Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) and the Federal Ministry of the Environment, Nature Conservation and Nuclear Safety (BMU) under the auspices of the International Programme on Chemical Safety (IPCS).

In order to make ongoing improvements to this Web site, your comments and suggestions are most welcome. Please direct your comments to the **DevTox Project co-ordinator at DevTox@bfr.bund.de**. If you would like to contribute



- Launched on August 16, 2012
- New nomenclature
  - Maternal-fetal category
- Additional species / images
  - Hamster
  - Primate
  - Bird
- >2500 images
  - incl. post-natal images

# Selection Lists for Anomalies in *DevTox*

Pre-2012

	①	②	③	④	Symbols:
	M	M	M	M	①: Rat
	M	M	M	M	②: Mouse
	✓	✓	✓	✓	③: Rabbit
	V	V	V	V	④: Other
	✓	✓	✓	✓	✓ : present
	—	—	—	—	— : absent
	M	M	M	M	M : malformation
	V	V	V	V	V : variation
	!	!	!	!	! : image(s) available

According to:  
Survey in 2013  
Workshop 2014

**Symbols:**

- ①: Rat (Ra)
- ②: Mouse (Mo)
- ③: Rabbit (Rb)
- ④: Hamster (Ha)
- ⑤: Primate (Pr)
- ⑥: Guinea Pig (Gp)
- ⑦: Minipig (Mp)
- ⑧: Dog (Do)
- ⑨: Bird (Bi)

— : absent in species  
■ : malformation  
■ : grey zone  
■ : variation  
✓ : image(s) available  
P : post-natal image(s) available

# Translation of *DevTox*

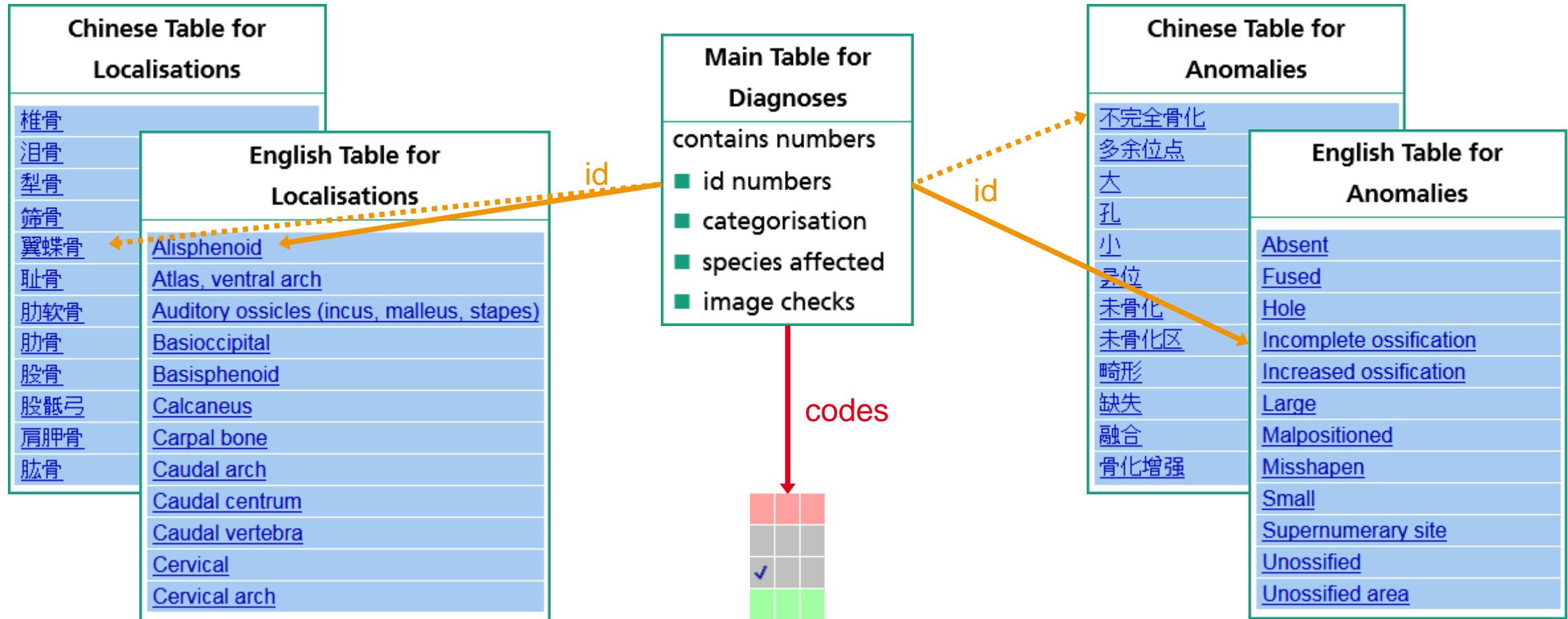
## Translation into Chinese

- Proposal / templates in 2014
- Translation in China (Dr. Weihua Li)
  - Shanghai Institute of Planned Parenthood Research
  - WHO Collaboration Centre for Research in Human Reproduction
  - Fudan University
- Final checks at BfR (Dr. Wennu Xu)
- Release to the public on October 28, 2016



DevTox		显示为	列表视图	树视图	
	外观结果	骨骼结果	软组织结果	母-胎结果	
• 颈骨	肉门				① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨
• 颈骨	颈骨缝				不完全骨化 ✓
• 锁骨					不成一直线 ✓ ✓ ✓
• 肩胛骨					中断 ✓ ✓ ✓
• 前肢	肱骨				分支 ✓ ✓
• 指骨	桡骨				分离 ✓ ✓
• 尺骨	掌骨				多余位点 ✓ ✓
• 腕骨	掌骨				多余肋骨关节 ✓ ✓
• 前爪趾骨	前爪趾骨				孤立骨化点 ✓ ✓
• 胸骨节					异位 ✓ ✓
• 胸骨间软骨					弯曲 ✓ ✓
• 剑突软骨					未骨化 ✓
• 胸骨					波状 ✓ ✓
• 助骨					畸形 ✓ ✓
• 助软骨					短 ✓ ✓
• 多肋					粗, 厚 ✓ ✓
• 颈(助)					细, 薄 ✓ ✓
• 胸腰(助)					结节状 ✓
• 多余肋骨					缺失 ✓ ✓
• 椎骨					助间 ✓
• 椎管					融合 P ✓ ✓ ✓
• 膜椎, 腹侧弓					部分重叠 ✓
• 颈弓					长 ✓
• 颈椎体					骨化增强 ✓
• 颈椎					
• 胸弓					

# Internal Structure of the Database



# New Abstraction Level

## Reduction of the variety of text sources

Original English version

- Text files (HTML)
- PHP program scripts (Server)
- Database tables
- JavaScript programs (Browser: Menus)
- Button icons with info



Modified English version

- Text files (PHP)
- Database tables

Can be applied to other languages  
Chinese, ...

# DevTox Version 3.1 (2020)

>2900 images:

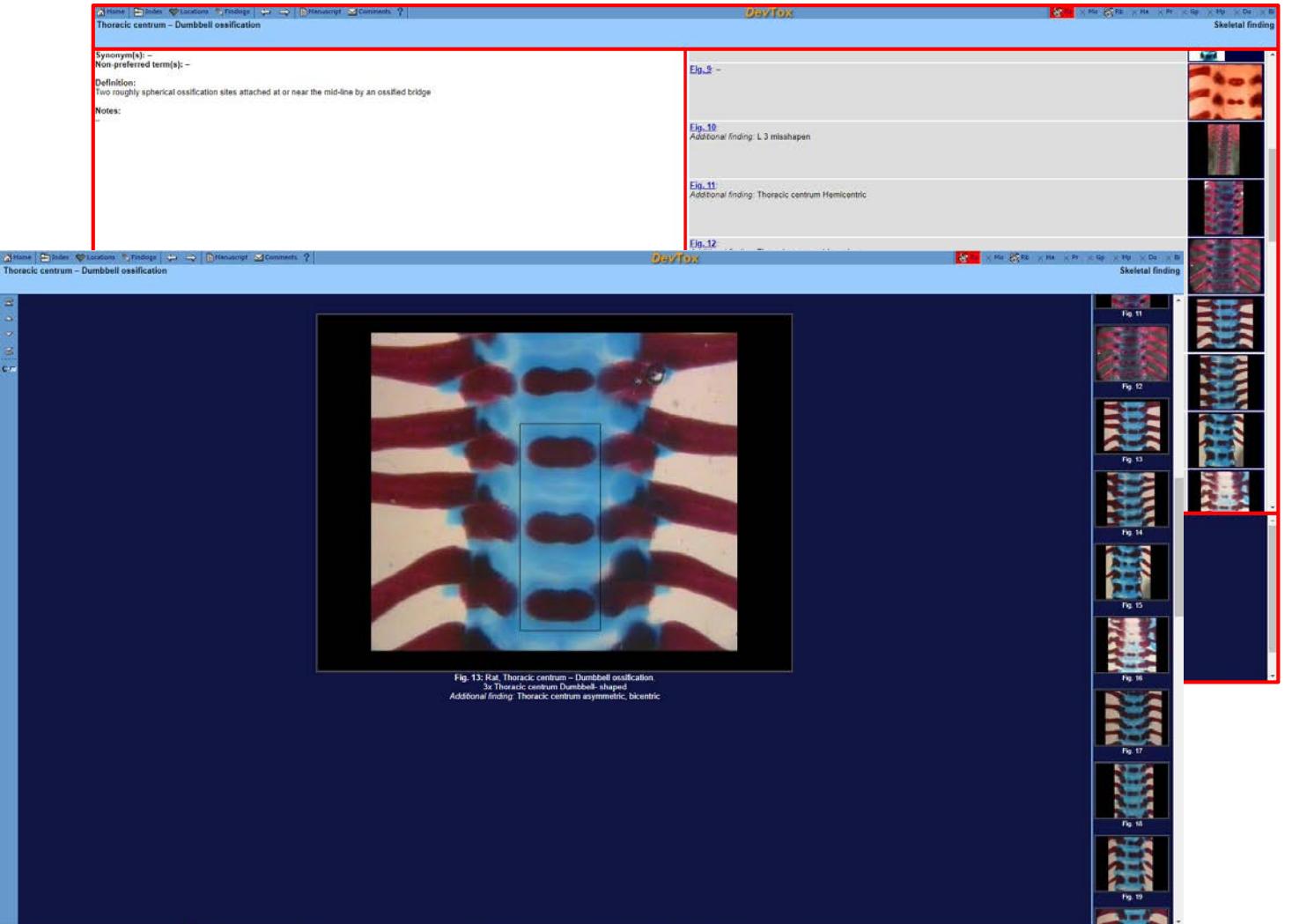
- External Findings
  - 678 images (508 anomalies, 170 control)
- Skeletal Findings
  - 1964 images (1488 anomalies, 476 control)
- Soft Tissue Findings
  - 308 images (262 anomalies, 46 control)

The screenshot shows the homepage of the DevTox website. The header features the DevTox logo in orange and blue, followed by the text "A Resource for Developmental Toxicology". Below the header are navigation links: .Background, .Nomenclature, .Workshops, .Masthead, and 中文 (Chinese). The main content area has a blue sidebar on the left with the title "Welcome" and a brief description of the site's purpose. The right side contains a list of species with their respective image counts. Each entry includes a small grayscale icon of the animal and its name in bold. To the right of the list are small thumbnail images of developmental anomalies.

Species	Count
Rat	1160 images
Mouse	294 images
Rabbit	468 images
Hamster	11 images
Primate	195 images
Guinea Pig	(placeholder)
Minipig	(placeholder)
Dog	(placeholder)
Bird	130 images

# DevTox Perspectives

- Current layout for 4:3 screens
  - Mode A: 800 x 600 pixel
  - Mode B: 1024 x 768 pixel
- Split into several frames
- Could be replaced by a modern layout



**Thank you for your attention!**

Fraunhofer Institute for Toxicology and Experimental Medicine  
Nikolai-Fuchs-Str. 1  
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Germany