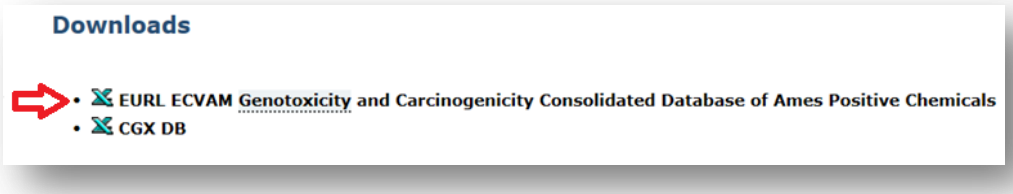
Instructions on how to use the EURL ECVAM Genotoxicity & Carcinogenicity Consolidated Database of Ames Positive Chemicals

The **ECVAM Genotoxicity & Carcinogenicity DB** is presented as an Excel table. Users are able to browse through the data with basic Excel functionality, but can also use it for further calculations, if necessary. Detailed information on the criteria adopted for the construction and analysis of the DB can be found in the manuscript: http://dx.doi.org/10.1016/j.mrgentox.2014.10.006

Download of the ECVAM Genotoxicity & Carcinogenicity DB

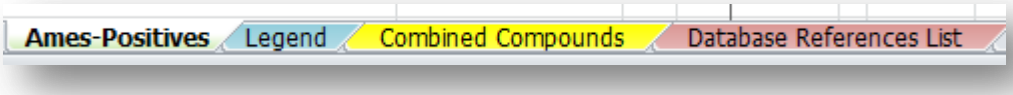
To download the ECVAM Genotoxicity & Carcinogenicity DB, click the link as suggested:



Open the ECVAM Genotoxicity & Carcinogenicity DB in your local installation of Excel. The filename is: *ECVAM_Ames_positives_DB.xls.*

Overall structure of the ECVAM Genotoxicity & Carcinogenicity DB

The ECVAM Genotoxicity & Carcinogenicity DB Excel workbook consists of four tabs (see bottom of the Excel screen):

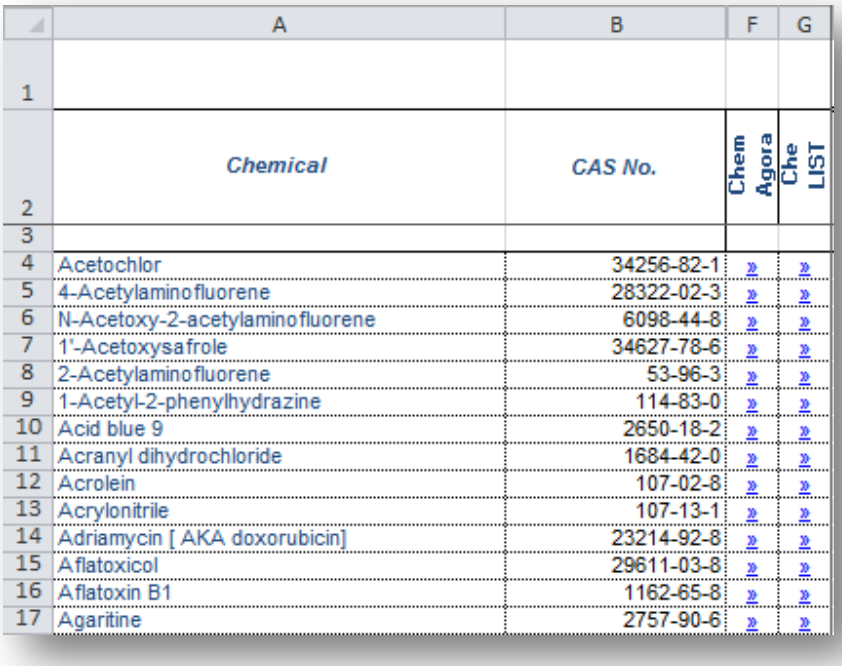


- Tab **Ames-Positives** contains all data.
- Tab **Legend** contains explanations and indications.
- Tab **Combined Compounds** contains the list of combined free bases and respective simple acid salts or R- and S- isomers for those chemicals where, a similar behavior is expected and/or proven in the aqueous environment of the in vitro and in vivo studies under consideration.
- Tab **Database Reference List** contains the information from peer-reviewed literature or expert publications used to fill in missing test data or resolve apparent discrepancies in results among the different sources reporting on the same chemical.

The guidance in this document covers the features of the tab "Ames-Positives".

Chemicals

The ECVAM Genotoxicity & Carcinogenicity DB contains 726 chemicals. Each row in the table reports on one chemical:



	A	B	F	G
1				
2	*Chemical*	*CAS No.*	Chem Agora	Che LIST
3				
4	Acetochlor	34256-82-1	»	»
5	4-Acetylaminofluorene	28322-02-3	»	»
6	N-Acetoxy-2-acetylaminofluorene	6098-44-8	»	»
7	1'-Acetoxysafrole	34627-78-6	»	»
8	2-Acetylaminofluorene	53-96-3	»	»
9	1-Acetyl-2-phenylhydrazine	114-83-0	»	»
10	Acid blue 9	2650-18-2	»	»
11	Acranyl dihydrochloride	1684-42-0	»	»
12	Acrolein	107-02-8	»	»
13	Acrylonitrile	107-13-1	»	»
14	Adriamycin [AKA doxorubicin]	23214-92-8	»	»
15	Aflatoxicol	29611-03-8	»	»
16	Aflatoxin B1	1162-65-8	»	»
17	Agaritine	2757-90-6	»	»

Chemicals are identified by:

- **Name** (column A)
- **CAS** Registration Number (column B), where possible

The table is sorted by Name.

In case more background information is needed for a chemical, columns F and G feature clickable links to two public JRC databases:

- **ChemAgora** (column F), a website that provides direct links to information about the chemical in question in numerous third party DBs;
- **CheLIST** (column G), a website that provides a means of identifying whether a chemical has been used in a research or validation project (including EU-funded, international and JRC projects), and also whether the chemical of interest is regulated and listed under a specific regulatory inventory.

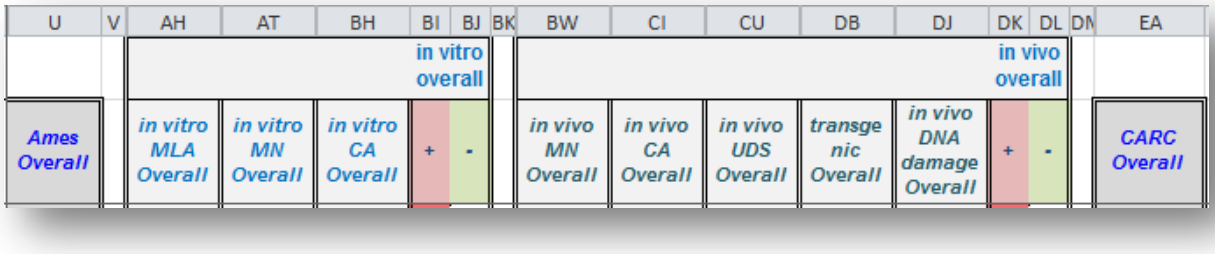
Clicking on the "»" symbol leads directly to the external website.

The link to the two websites works via the CAS Registration number. If for a chemical the CAS Registration Number is not known, the link is not provided. If there are two or more CAS Registration numbers in column B, the link uses the first one.

Test results reported in the ECVAM Genotoxicity & Carcinogenicity DB

The ECVAM Genotoxicity & Carcinogenicity DB shows, for each chemical, the available results from different sources for the following *in vitro* and *in vivo* tests:

- AMES test
- In vitro mammalian cell tests
    - **MLA**: in vitro MLA $Tk^{+/-}$ gene mutation (Hprt) assay
    - **MN**: in vitro Micronucleus test
    - **CA**: in vitro Chromosomal Aberrations test
- In vivo tests
    - **MN**: in vivo MN genotoxicity test
    - **CA**: in vivo Chromosomal Aberrations test
    - **UDS**: in vivo Unscheduled DNA Synthesis
    - **transgenic**: in vivo transgenic gene mutation assay
    - **DNA Damage**: in vivo DNA damage (COMET or alkaline elution assay)
- Carcinogenicity studies



In its default collapsed view (see chapter "Collapsed vs. expanded view" below), the DB shows the ***Overall Call*** (final conclusion) made for each test as the result of an expert evaluation of all the single entries (which are visible in the expanded view).

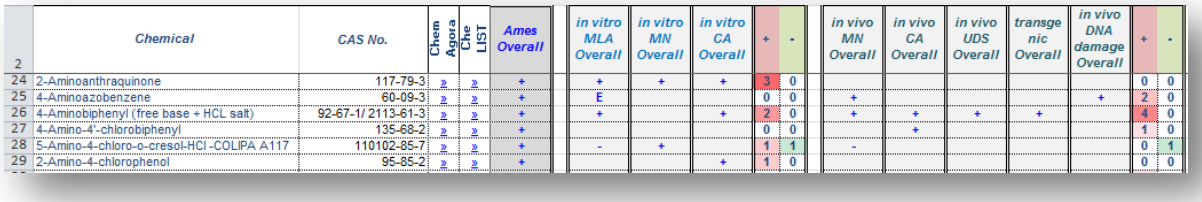
Color coding

Overall calls for each test are limited to the following 4 categories, which are based on defined criteria described in the manuscript, http://dx.doi.org/10.1016/j.mrgentox.2014.10.006:

- "+" = positive
- "-" = negative
- "E" = equivocal
- "I" = inconclusive

In order to quickly identify chemicals with a high or low number of "+' or "-" genotoxicity results *in vitro* and *in vivo*, the DB features color-coded indicator columns:

- The more intensive the **red** color shading, the more "+" were reported in the overall summaries.
- The more intensive the **green** color shading, the more "-" were reported in the overall summaries.

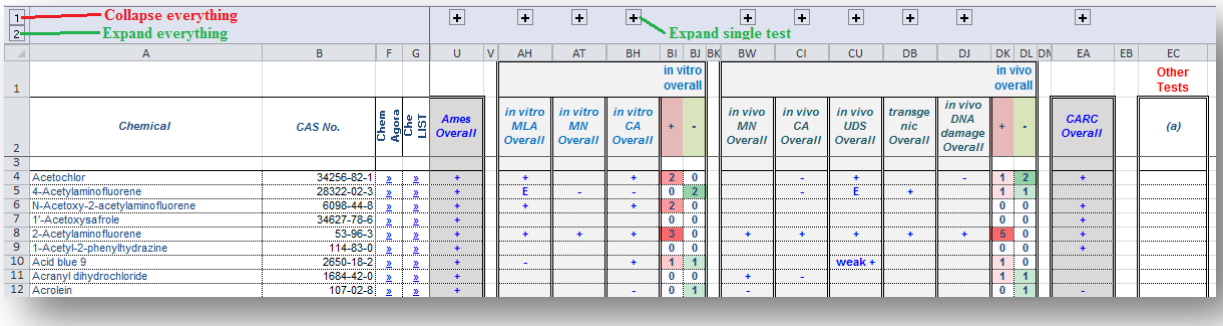


Chemical	CAS No.	Chem Agora	Che LIST	Ames Overall	in vitro MLA Overall	in vitro MN Overall	in vitro CA Overall	+	-	in vivo MN Overall	in vivo CA Overall	in vivo UDS Overall	transgenic Overall	in vivo DNA damage Overall	+	-
2-Aminoanthraquinone	117-79-3	»	»	+	+	+	+	3	0						0	0
4-Aminoazobenzene	60-09-3	»	»	+	E			0	0	+				+	2	0
4-Aminobiphenyl (free base + HCL salt)	92-67-1/ 2113-61-3	»	»	+	+		+	2	0	+	+	+	+		4	0
4-Amino-4'-chlorobiphenyl	135-68-2	»	»	+				0	0		+				1	0
5-Amino-4-chloro-o-cresol-HCl -COLIPA A117	110102-85-7	»	»	+	-	+		1	1	-					0	1
2-Amino-4-chlorophenol	95-85-2	»	»	+			+	1	0						0	0

Please note that this feature is not intended to express any scientific assessment or classification whatsoever; it is merely indicative and color-codes the numbers of "+" and/or "-" genotoxicity results *in vitro* and *in vivo*.

Collapsed *vs.* expanded view

The default view when opening the ECVAM Genotoxicity & Carcinogenicity DB is "collapsed", i.e. an overview is shown on the **'Overall Calls'** for each endpoint, with details hidden:

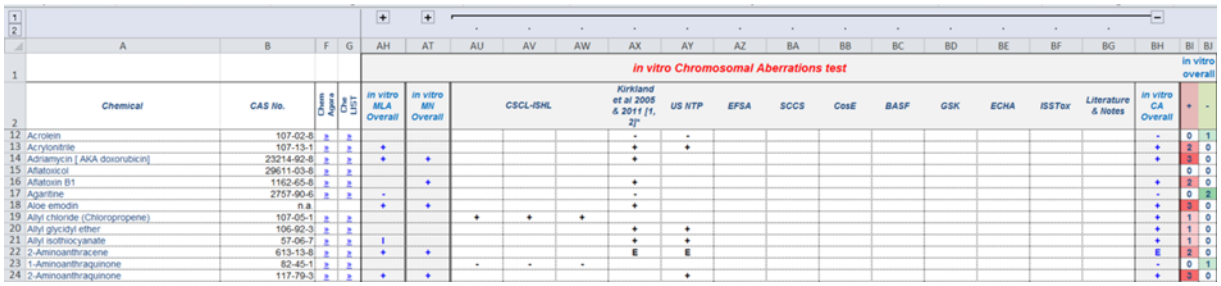


Chemical	CAS No.	Chem Agora	Che LIST	Ames Overall	in vitro MLA Overall	in vitro MN Overall	in vitro CA Overall	+	-	in vivo MN Overall	in vivo CA Overall	in vivo UDS Overall	transgenic Overall	in vivo DNA damage Overall	+	-	CARC Overall	(a)
Acetochlor	34256-82-1	»	»	+	+		+	2	0		-	+		-	1	2	+	
4-Acetylaminofluorene	28322-02-3	»	»	+	E	-	-	0	2		-	E	+		1	1		
N-Acetoxy-2-acetylaminofluorene	6098-44-8	»	»	+	+		+	2	0						0	0	+	
1'-Acetoxysafrole	34627-78-6	»	»	+				0	0						0	0	+	
2-Acetylaminofluorene	53-96-3	»	»	+	+	+	+	3	0	+	+	+	+	+	5	0	+	
1-Acetyl-2-phenylhydrazine	114-83-0	»	»	+				0	0						0	0	+	
Acid blue 9	2650-18-2	»	»	+	-		+	1	1			weak +			1	0		
Acranyl dihydrochloride	1684-42-0	»	»	+				0	0	+	-				1	1		
Acrolein	107-02-8	»	»	+			-	0	1	-					0	1	-	

In this view, all details concerning the individual test types are **hidden**.

- Clicking the [2] symbol in the upper left hand corner expands **all** test results;
- Clicking the [1] symbol in the upper left hand corner collapses all test results (= original view is restored);
- Clicking any of the [+] symbols above any test type expands only this one test.

For example, when the [+] symbol in column BH (= in vitro CA overall) is clicked, the detailed results for this test type (in vitro Chromosomal Aberrations test) are shown:



Chemical	CAS No.	Chem Agora	Che LIST	in vitro MLA Overall	in vitro MN Overall	CSCL-ISHL	Kirkland et al 2005 & 2011 [1, 2]*	US NTP	EFSA	SCCS	CosE	BASF	GSK	ECHA	ISSTox	Literature & Notes	in vitro CA Overall	+	-
Acrolein	107-02-8	»	»				-	-									-	0	1
Acrylonitrile	107-13-1	»	»	+			+	+									+	2	0
Adriamycin [AKA doxorubicin]	23214-92-8	»	»	+	+		+										+	3	0
Aflatoxicol	29611-03-8	»	»															0	0
Aflatoxin B1	1162-65-8	»	»		+		+										+	2	0
Agaritine	2757-90-6	»	»	-			-										-	0	2
Aloe emodin	n.a.	»	»	+	+		+										+	3	0
Allyl chloride (Chloropropene)	107-05-1	»	»			+											+	1	0
Allyl glycidyl ether	106-92-3	»	»			+	+	+									+	1	0
Allyl isothiocyanate	57-06-7	»	»	I			+	+									+	1	0
2-Aminoanthracene	613-13-8	»	»	+	+		E	E									E	2	0
1-Aminoanthraquinone	82-45-1	»	»	-	-	-											-	0	1
2-Aminoanthraquinone	117-79-3	»	»	+	+			+									+	3	0

Note: The overall result (column BH) is derived from the assessment of the columns AU -> BG (= the individual test results that were taken into account).