

**12.0 REFERENCES**

3 Adegunloye BI, Sofola OA. 1997. Differential responses of rat aorta and mesenteric artery to  
4 norepinephrine and serotonin *in vitro*. *Pharmacology* 55:25-31.

6 Ames A III. 2000. CNS energy metabolism as related to function. *Brain Res Rev.* 34:42-68.

8 Anon. 1993. Annexes I, II, III, and IV to Commission Directive 93/21/EEC of 27 April 1993  
9 adapting to technical progress for the 18<sup>th</sup> time Council Directive 67/548/EEC on the  
10 approximation of laws, regulations and administrative provisions relating to the  
11 classification, packaging and labeling of dangerous substances. *Official Journal of the*  
12 *European Communities* L110A, 1-86. (EU toxicity categories 25, 25-200, 200-2000, > 2000).

14 ASTM. 1999. American Society of Testing and Materials (ASTM) Standard E691-99,  
15 Standard Practice for Conducting an Interlaboratory Study to Determine the Precision of a  
16 Test Method. American National Standards Institute. Washington, D.C. Available:  
17 <http://www.ansi.org/> [accessed 22 December 2005].

19 ATSDR. 1999a. Toxicological Profile for Cadmium. Update PB/99/166621. US Dept. of  
20 Health and Human Services, Atlanta GA. Available: <http://www.atsdr.cdc.gov/toxpro2.html>.  
21 [accessed 2 June 2005].

23 ATSDR. 1999b. Toxicological Profile for Diethyl phthalate. PB/95/264214/AS. US Dept. of  
24 Health and Human Services, Atlanta GA. Available: <http://www.atsdr.cdc.gov/toxpro2.html>.  
25 [accessed 2 June 2005].

27 ATSDR. 2000a. Toxicological Profile for Endosulfan. Update. PB/2000/108023. US Dept.  
28 of Health and Human Services, Atlanta GA. Available:  
29 <http://www.atsdr.cdc.gov/toxpro2.html>. [accessed 2 June 2005].

31 ATSDR. 2000b. Toxicological Profile for Chromium. Update. PB/2000/108022. US Dept. of  
32 Health and Human Services, Atlanta GA. Available: <http://www.atsdr.cdc.gov/toxpro2.html>.  
33 [accessed 2 June 2005].

35 ATSDR. 2001. Toxicological Profile for Di-n-butyl phthalate. Update. PB/2001/109104/AS.  
36 US Dept. of Health and Human Services, Atlanta GA. Available:  
37 <http://www.atsdr.cdc.gov/toxpro2.html>. [accessed 2 June 2005].

39 ATSDR. 2004a. Toxicological Profile for Pyrethrins and Pyrethroids. Update. PB2004-  
40 100004. US Dept. of Health and Human Services, Atlanta GA. Available:  
41 <http://www.atsdr.cdc.gov/toxpro2.html>. [accessed 2 June 2005].

43 ATSDR. 2004b. Toxicological Profile for Selenium. Update. PB2004-100005. US Dept. of  
44 Health and Human Services, Atlanta GA. Available: <http://www.atsdr.cdc.gov/toxpro2.html>.  
45 [accessed 2 June 2005].

- 47 Babich H, Martin-Alguacil N, Raul C, Rosenberg DW, Borenfreund E. 1991. Response of  
48 human cell cultures to cytotoxicants requiring metabolic activation. In: Alternative Methods  
49 in Toxicology (Goldberg AM, ed.), Vol. 8. New York:Mary Ann Liebert, Inc., 263-276.  
50
- 51 Balls M, Botham PA, Bruner LH, Spielmann H. 1995. The EC/HO international validation  
52 study on alternatives to the Draize eye irritation test for classification and labelling of  
53 chemicals. *Toxicol In Vitro* 9:871-929.  
54
- 55 Bernson V, Bondesson I, Ekwall B, Stenberg K, Walum E. 1987. A Multicentre evaluation  
56 study of in vitro cytotoxicity. *Altern Lab Anim.* 14:144-146.  
57
- 58 Bliss CI. 1938. The determination of the dosage-mortality curve from small numbers.  
59 *Quarterly Journal of Pharmacy and Pharmacology* 11:192-214.  
60
- 61 Bondesson I, Ekwall B, Hellberg S, Romert L, Stenberg K, Walum E. 1989. MEIC - A New  
62 International Multicenter Project to Evaluate the Relevance to Human Toxicity of In Vitro  
63 Cytotoxicity Tests. *Cell Biol Toxicol.* NOV 5(3):331-347.  
64
- 65 Borenfreund E, Puerner J. 1984. A simple quantitative procedure using monolayer cultures for  
66 cytotoxicity assays (HTD/ NR-90). *J Tissue Culture Meth* 9:7-9.  
67
- 68 Borenfreund E, Puerner JA. 1985. Toxicity determination *in vitro* by morphological  
69 alterations and neutral red absorption. *Toxicol Lett.* 24:119-124.  
70
- 71 Botham PA. 2004. The validation of in vitro methods for skin irritation. *Toxicol Lett.*  
72 149:387-390.  
73
- 74 Brantom PG, Bruner LH, Chamberlain M, De Silva O, Dupuis J, Earl LK, et al. 1997. A  
75 summary report of the COLIPA international validation study on alternatives to the Draize  
76 rabbit eye irritation test. *Toxicol In Vitro* 11:141-179.  
77
- 78 Canadian Centre for Occupational Health and Safety. 2005. IPCS INTOX Database.  
79 Available: <http://www.intox.org/databank/index.htm>. [accessed 29 November 2005].  
80
- 81 Casarett LJ, Klaassen CD, Doull J, eds. 2001. Casarett and Doull's Toxicology, The Basic  
82 Science of Poisons. 6<sup>th</sup> Edition. New York:McGraw-Hill.  
83
- 84 Charles River Laboratories Catalog. 2002. Available: <http://www.criver.com>. [accessed 2  
85 June 2005].  
86
- 87 Clemedson C, McFarlane-Abdulla E, Andersson M, Barile FA, Calleja MC, Chesné C, et al.  
88 1996a. MEIC Evaluation of Acute Systemic Toxicity. Part I. Methodology of 68 *in vitro*  
89 toxicity assays used to test the first 30 reference chemicals. *Altern Lab Anim.* 24 (suppl.  
90 1):51-272.  
91

- 92 Clemedson C, McFarlane-Abdulla E, Andersson M, Barile FA, Calleja MC, Chesné C, et al.  
93 1996b. MEIC Evaluation of Acute Systemic Toxicity. Part II. *In vitro* results from 68 toxicity  
94 assays used to test the first 30 reference chemicals and a comparative cytotoxicity analysis.  
95 *Altern Lab Anim.* 24 (suppl. 1):273-311.
- 96  
97 Clemedson C, Nordin-Andersson M, Bjerregaard H.F, Clausen J, Forsby A, Gustafsson H,  
98 Hansson U, Isomaa B, Jorgensen C, et al. 2002. Development of an *in vitro* test battery for  
99 the estimation of acute human systemic toxicity: an outline of the EDIT project *Altern Lab*  
100 *Anim.* 30:313-321.
- 101  
102 Clemedson, C. 2005. A-Cute-Tox project an Integrated Project under the EU 6FP with the  
103 aim to optimize and pre-validate an *in vitro* test strategy for predicting human acute toxicity.  
104 European Society of Toxicology In Vitro Newsletter. November. No. 18. p6.
- 105  
106 Clothier R, Willshaw A, Cox H, Garle M, Bowler H, Combes R. 1999. The use of human  
107 keratinocytes in the EU/COLIPA international *in vitro* phototoxicity test validation study and  
108 the ECVAM/COLIPA study on UV filter chemicals. *Altern Lab Anim.* 27 (2):247-259 Mar-  
109 Apr.
- 110  
111 Coeck S, Balls M, Bowe G, Davis J, Gstraunthaler G, Hartung T, et al. 2005. Guidance on  
112 Good Cell Culture Practice. A Report of the Second ECVAM Task Force on Good Cell  
113 Culture Practice. *Altern Lab Anim.* 33:261-287.
- 114  
115 Coldwell BB, Boyd EM. 1966. The acute rectal toxicity of acetylsalicylic acid. *Canadian*  
116 *Journal of Physiology and Pharmacology* 44: 909-918
- 117  
118 Cooper-Hannan R, Harbell J, Coecke S, et al. 1999. The principles of good laboratory  
119 practice: application to *in vitro* toxicology studies. *Altern Lab Anim.* 27:539-577.
- 120  
121 Cosmetic Ingredient Review Panel. 1983. Final report on the safety assessment of sodium  
122 borate and boric acid. *J Am Coll Toxicol* 2:87-125.
- 123  
124 CPSC. 2003. Commercial Practices. Hazardous Substances and Articles; Administration And  
125 Enforcement Regulations. 16 CFR 1500.42.
- 126  
127 Creppy EE, Chiarappa P, Baudrimont I, Borracci P, Moukha S, Carratu MR. 2004.  
128 Synergistic effects of fumonisin B1 and ochratoxin A: are *in vitro* cytotoxicity data  
129 predictive of *in vivo* acute toxicity? *Toxicology* Sep 1;201(1-3):115-23.
- 130  
131 Curren R, Bruner L, Goldberg A, Walum E. 1998. 13th meeting of the Scientific Group on  
132 Methodologies for the Safety Evaluation of Chemicals (SGOMSEC): Validation and acute  
133 toxicity testing. *Environ Health Perspect.* 106: (Suppl. 2). 419-425.
- 134  
135 Curren RD, Moyer GO, Wilt N, Clear ML, Sizemore AM, Mun G. 2003. Assessment of  
136 protocol variables in cytotoxicity assays utilizing BALB/c 3T3 cells and normal human

137 keratinocytes [Abstract]. Toxicologist 72:157. Available:  
138 [http://www.iivs.org/pages/publication\\_view.php?doc\\_id=43](http://www.iivs.org/pages/publication_view.php?doc_id=43). [accessed 23 September 2005].  
139  
140 DOT. 2003. Shippers--General Requirements for Shipments and Packagings. Class 6,  
141 Division 6.1 – Definitions. 49 CFR 173.132. Available:  
142 <http://www.gpoaccess.gov/cfr/index.html>. [accessed 2 June 2005].  
143  
144 DOT. 2003. Shippers--General Requirements for Shipments and Packagings. Assignment of  
145 Packing Group and Hazard Zones for Division 6.1 Materials. 49 CFR 173.133. Available:  
146 <http://www.gpoaccess.gov/cfr/index.html>. [accessed 2 June 2005].  
147  
148 DOT. 1999. Code of Federal Regulations Title 49. SubChapter C. Assignment of packing  
149 group and hazard zones for Division 6.1 materials.  
150  
151 Deichmann WB. 1969. Toxicology of Drugs and Chemicals. New York. Academic Press,  
152 Inc. pg.67.  
153  
154 Dixon WJ, Massey FJ. 1981. Introduction to Statistical Analysis, 4th ed. Milwaukee:Quality  
155 Press.  
156  
157 Ekwall B. 1983. Screening of Toxic Compounds in Mammalian Cell Cultures. Ann. New  
158 York Acad. Sci. 407:64-77.  
159  
160 Ekwall B, Clemedson C, Craaford B, Ekwall B, Hallander S, Walum E, Bondesson I. 1998a.  
161 MEIC evaluation of acute systemic toxicity. Part V. Rodent and human toxicity data for the  
162 50 reference chemicals. Altern Lab Anim. 26 (suppl. 2):571-616.  
163  
164 Ekwall B, Clemedson C, Craaford B, Ekwall B, Hallander S, Walum E, Bondesson I. 1998b.  
165 MEIC evaluation of acute systemic toxicity. Part VI. The prediction of human toxicity by  
166 rodent LD50 values and results from 61 *in vitro* methods. Altern Lab Anim. 26 (suppl.  
167 2):617-658.  
168  
169 Ekwall B, Clemedson C, Ekwall B, Ring P, Romert L. 1999. EDIT: A new international  
170 multicentre programme to develop and evaluate batteries on *in vitro* tests for acute and  
171 chronic systemic toxicity. Altern Lab Anim. 27:339-349.  
172  
173 Ekwall B, Ekwall B, Sjostrom M. 2000. MEIC evaluation of acute systemic toxicity: Part  
174 VIII. Multivariate partial least squares evaluation, including the selection of a battery cell  
175 line tests with a good prediction of human acute lethal peak blood concentrations for 50  
176 chemicals. Altern Lab Anim. 28 (suppl. 1):201-234.  
177  
178 EPA. 1992. Reregistration Eligibility Document Citric Acid. List D, Case 4204. Office of  
179 Pesticide Programs. Washington, DC:U.S. Environmental Protection Agency. Available:  
180 <http://cfpub.epa.gov/pesticides/reregistration>. [accessed 2 June 2005].  
181

- 182 EPA. 1995. Reregistration Eligibility Decision (RED) Diquat Dibromide. EPA 738-R-95-  
183 016. Office of Prevention, Pesticides and Toxic Substances. Washington, DC:U.S.  
184 Environmental Protection Agency. Available:  
185 <http://cfpub.epa.gov/pesticides/reregistration>. [accessed 2 June 2005].  
186  
187 EPA. 1996. Trichloroacetic acid (CASRN 76-03-9) file in Integrated Risk Information  
188 System. Office of Research and Development. Washington, DC:U.S. Environmental  
189 Protection Agency. Available: <http://www.epa.gov/iris>. [accessed 23 September 2005].  
190  
191 EPA 738-R-95-016. Office of Prevention, Pesticides and Toxic Substances. Washington,  
192 DC:U.S. Environmental Protection Agency. Available:  
193 <http://cfpub.epa.gov/pesticides/reregistration>. [accessed 2 June 2005].  
194  
195 EPA. 1998. Product Properties Test Guidelines OPPTS 830.7840 Water Solubility: Column  
196 Elution Method; Shake Flask Method. EPA 712-C-98-041. Washington, DC: U.S.  
197 Environmental Protection Agency.  
198  
199 EPA. 2000. High Production Challenge Program. Office of Pollution Prevention and Toxics  
200 (OPPT). Washington, DC:U.S. Environmental Protection Agency. Available:  
201 <http://www.epa.gov/chemrtk/volchall.htm> [accessed 21 December 2005].  
202  
203 EPA. 2000a. Toxic Substances Control Guidelines; Final Rule. Code of Federal Regulations,  
204 Title 40, Part 799. Available: <http://www.epa.gov/oppt/chemtest/notice7.pdf>. [accessed 2  
205 June 2005].  
206  
207 EPA. 2000b. Toxicological Review of Chloral Hydrate. EPA/635/R-00/006. Washington,  
208 DC:U.S. Environmental Protection Agency. Available: [www.epa.gov/iris](http://www.epa.gov/iris). [accessed 2 June  
209 2005].  
210  
211 EPA. 2002a. Health Effects Test Guidelines OPPTS 870.1100 Acute Oral Toxicity. EPA  
212 712-C-02-190. Washington, DC: U.S. Environmental Protection Agency.  
213  
214 EPA. 2002b. Statements of Policies and Interpretations. Toxicological and Ecological  
215 Studies. 40 CFR 159.165. Available: <http://www.gpoaccess.gov/cfr/index.html>. [accessed 2  
216 June 2005].  
217  
218 EPA. 2002c. Health Effects Test Guidelines OPPTS 870.1000 Acute Toxicity Testing -  
219 Background. EPA 712-C-02-189. Washington, DC: U.S. Environmental Protection Agency.  
220  
221 EPA. 2002d. Emergency Planning and Notification. 40 CFR 355. Available:  
222 [http://www.access.gpo.gov/nara/cfr/waisidx\\_00/40cfr355\\_00.html](http://www.access.gpo.gov/nara/cfr/waisidx_00/40cfr355_00.html). [accessed 2 June 2005].  
223  
224 EPA. 2003a. Good Laboratory Practice Standards. Toxic Substances Control Act. 40 CFR  
225 792. Available: [http://www.access.gpo.gov/nara/cfr/waisidx\\_03/40cfr160\\_03.html](http://www.access.gpo.gov/nara/cfr/waisidx_03/40cfr160_03.html) [accessed  
226 21 December 2005].  
227

- 228 EPA. 2003b. Good Laboratory Practice Standards. Federal Insecticide, Fungicide, and  
229 Rodenticide Act. 40 CFR 160.  
230
- 231 EPA. 2004. U.S. EPA HPV Challenge Program Submission. Propanoic acid, 2-hydroxy-,  
232 compd. with 3-[2-(dimethylamino)ethyl] 1-(2-ethylhexyl) (4-methyl-1,3-  
233 phenylene)bis[carbamate] (1:1) [CAS No. 68227-46-3]. Submitted by PPG Industries, Inc.  
234 Revised December 17, 2004. <http://www.epa.gov/chemrtk/prop2hyd/c13863rt3.pdf>  
235 [accessed 06 December 2005].  
236
- 237 European Centre for the Validation of Alternative Methods. (ECVAM). 1997. Statement on  
238 the scientific validity of the 3T3 NRU PT test (an *in vitro* test for phototoxic potential).  
239 <http://ecvam.jrc.it/index.htm>. [accessed 15 August 2005].  
240
- 241 EU. 2003. Report from the Commission to the Council and the European Parliament. Third  
242 Report from the commission to the Council and the European Parliament of the statistics on  
243 the number of animals used for experimental and other scientific purposes in the member  
244 states of the European Union. Brussels, 22.01.2003, COM (2003) 19 final.  
245
- 246 Fautrel A, Chesné C, Guillouzo A, De Sousa G, Placidi M, Rahmani R, et al. 1993. A  
247 multicentre study of acute *in vitro* cytotoxicity in rat hepatocytes: tentative correlation  
248 between *in vitro* toxicity and *in vivo* data. *Altern Lab Anim.* 21:281-284.  
249
- 250 FDA. 1993. Toxicological Principles for the Safety Assessment of Direct Food Additives and  
251 Color Additives Used in Food. Center for Food Safety and Applied Nutrition. Washington,  
252 DC: U.S. Food and Drug Administration.  
253
- 254 FDA. 2003. Good Laboratory Practice for Nonclinical Laboratory Studies. 21 CFR Part 58.  
255 Available: [http://www.access.gpo.gov/nara/cfr/waisidx\\_03/21cfr58\\_03.html](http://www.access.gpo.gov/nara/cfr/waisidx_03/21cfr58_03.html) [accessed 21  
256 December 2005].  
257
- 258 Fentem J, Fry J, Garle M, Gülden M, Seibert H, Voss J-U, et al. 1993. An International  
259 Evaluation of Selected *In Vitro* Toxicity Test Systems for Predicting Acute Systemic  
260 Toxicity. A report prepared for DGXI, CEC; Contract Numbers B92/B4-3063/14086 &  
261 B92/B4-3040/14087. FRAME, Nottingham.  
262
- 263 Fentem JH, Archer GEB, Balls M, Botham PA, Curren RD, Earl LK, et al. 1998. The  
264 ECVAM international validation study on *in vitro* tests for skin corrosivity. 2. Results and  
265 evaluation by the Management Team. *Toxicol In Vitro.* 12:483-524.  
266
- 267 Fentem JH, Briggs D, Chesne C, Elliott GR, Harbell JW, Heylings JR, et al. 2001. A  
268 prevalidation study on *in vitro* tests for acute skin irritation: results and evaluation by the  
269 Management Team. *Toxicol In Vitro.* FEB 15(1):57-93.  
270
- 271 Freshney RI. 2000. *Culture of Animal Cells: A Manual of Basic Technique*, 4th edition. New  
272 York: Wiley-Liss.  
273

- 274 Garle M., Fentem JH, Fry JR. 1994. *In Vitro* Cytotoxicity Tests for the Prediction of Acute  
275 Toxicity *In Vivo*. *Toxicol In Vitro*. 8:1303-1312.  
276
- 277 Gennari A, van den Berghe C, Casati S, Castell J, Clemedson C, Coecke S, et al. 2004.  
278 Strategies to Replace *In Vivo* Acute Systemic Toxicity Testing. The Report and  
279 Recommendations of ECVAM Workshop 50. *Altern Lab Anim*. 32:437-459.  
280
- 281 Gettings SD, Bagley DM, Demetrulias JL, Dipasquale LC, Hintze KL, Rozen MG, et al.  
282 1991. The CTFA evaluation alternatives program: An evaluation of *in vitro* alternatives to  
283 the Draize primary eye irritation test. (Phase I) Hydro-alcoholic Formulations; (Part 2) Data  
284 analysis and biological significance. *In Vitro Toxicol*. 4:247-288.  
285
- 286 Gettings SD, Dipasquale LC, Bagley DM, Casterton PL, Chudkowski M, Curren RD, et al.  
287 1994a. The CTFA evaluation of alternatives program: An evaluation of *in vitro* alternatives  
288 to the Draize primary eye irritation test. (Phase II) Oil/water emulsions. *Food Chem Toxicol*.  
289 32:943-976.  
290
- 291 Gettings SD, Hintze KL, Bagley DM, Casterton PL, Chudkowski M, Curren RD, et al.  
292 1994b. The CTFA evaluation of alternatives program: Phase III (surfactant-based  
293 formulations). World Congress on Alternatives and Animal Use in the Life Sciences,  
294 Baltimore, Maryland, USA, Nov. 14-19, 1993. *In Vitro Toxicol*. 7(2):166.  
295
- 296 Gettings SD, Lordo RA, Hintze KL, Bagley DM, Casterton PL, Chudkowski M, et al. 1996.  
297 The CFTA evaluation of alternatives program: An evaluation of *in vitro* alternatives to the  
298 Draize Primary Eye Irritation Test. (Phase III) Surfactant-based Formulations. *Food Chem*  
299 *Toxicol*. 34:79-117.  
300
- 301 Gilman AG, Goodman LS, Rall TW, Murad F (eds.). 1985. Goodman and Gilman's The  
302 Pharmacological Basis of Therapeutics, 7th Edition. New York:Macmillan Publishing Co.  
303
- 304 Glaxo Wellcome. 2000. Myleran,(busulfan) Product Information. Research Triangle Park,  
305 NC:Glaxo Wellcome, Inc.  
306
- 307 GraphPad Software. 1994-2000. Prism® version 3.0a for Macintosh. GraphPad Software,  
308 San Diego, California. Available: [www.graphpad.com](http://www.graphpad.com). [accessed 21 November 2005].  
309
- 310 Grisham JW, Smith GJ. 1984. Predictive and Mechanistic Evaluation of Toxic Responses in  
311 Mammalian Cell Culture Systems. *Pharmacol Rev*. 36(Suppl.):151S-171S.  
312
- 313 Guzzie PJ. 1994. Lethality Testing. In: *In Vitro Toxicology*. (S.C. Gad, ed). Raven Press,  
314 New York. pp.57-86.  
315
- 316 Hackenberg U, Bartling H. 1959. Messen und Rechnen im pharmakologischen Laboratorium  
317 mit einem speziellen Zahlensystem (WL24-System). *Arch Exp Pathol Pharmacol* 235:437-  
318 463.  
319

- 320 Halle W, Liebsch M, Traue D, Spielmann H. 1997. Reduktion der Tierzahlen bei der  
321 Einstufung von Stoffen in die EU-Toxizitätsklassen für akute orale Toxizität mit Hilfe von  
322 Daten aus dem Register der Zytotoxizität (RC). Alternativen zu Tierexperimenten ALTEX  
323 14:8-15.  
324
- 325 Halle W. 1998. Toxizitätsprüfungen in Zellkulturen für eine Vorhersage der akuten Toxizität  
326 (LD<sub>50</sub>) zur Einsparung von Tierversuchen. Life Sciences/ Lebenswissenschaften, Volume 1,  
327 94 pp., Jülich: Forschungszentrum Jülich. English translation: Halle W. 2003. The Registry  
328 of Cytotoxicity: Toxicity testing in cell cultures to predict acute toxicity (LD50) and to  
329 reduce testing in animals. Altern Lab Anim. 31:89-198.  
330
- 331 Hall W. and Spielmann H. 1992. Two procedures for the prediction of acute toxicity (LD50)  
332 from cytotoxicity data. Altern Lab Anim. 20:40-49.  
333
- 334 Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG, eds. 1996. Goodman and  
335 Gilman's The Pharmacological Basis of Therapeutics, 9th Edition. New York:McGraw-Hill.  
336
- 337 Harlan Company. 2002. Available: <http://www.harlan.com/us/index.htm> [accessed 2 June  
338 2005]  
339
- 340 Harbell JW, Koontz SW, Lewis RW, Lovell D, Acosta D. 1997. IRAG working group 4. Cell  
341 cytotoxicity assays. Interagency Regulatory Alternatives Group. Food Chem Toxicol. 35:79-  
342 126.  
343
- 344 Hartung T, Balls M, Bardouille C, Blanck O, Coecke S, Gstrauchaler G, and Lewis D. 2002.  
345 Good Cell Culture Practice: ECVAM Good Cell Culture Practice Task Force Report 1.  
346 Altern Lab Anim. 30:407-414. Available: <http://ecvam.jrc.it/publication/index5007.html>  
347 [accessed 02 September 2005].  
348
- 349 Heimann R, Rice RH. 1983. Rat Esophageal and Epidermal-Keratinocytes - Intrinsic  
350 Differences in Culture and Derivation of Continuous Lines. J Cell Physiol 117 (3):362-367.  
351
- 352 Hintze KL, Janus J, Marenus KD, Muscatiello MJ, Pape WJW, Renskers KJ, et al. 1992.  
353 Development of potential alternatives to the Draize eye test - The CTFA evaluation of  
354 alternatives program - Phase II - Review of materials and methods. Altern Lab Anim.  
355 20:164-171.  
356
- 357 Hunter WJ, Lingk W, Recht JP. 1979. Intercomparison study on the determination of single  
358 administration toxicity in rats. Journal of the Association of Official Analytical Chemists  
359 62:864-873.  
360
- 361 ICCVAM. 2000. The Revised Up-and-Down Procedure: A Test Method for Determining the  
362 Acute Oral Toxicity of Chemicals and Products. Proposed Test Method and Background  
363 Review Document, April 14, 2000. National Institute for Environmental Health Sciences,  
364 Research Triangle Park, NC. Available: <http://iccvam.niehs.nih.gov/>. [accessed 2 June  
365 2005].



- 366  
367 ICCVAM. 2001a. Report Of The International Workshop On In Vitro Methods For  
368 Assessing Acute Systemic Toxicity. NIH Publication No. 01-4499. National Institute for  
369 Environmental Health Sciences, Research Triangle Park, NC. Available:  
370 <http://iccvam.niehs.nih.gov/>. [accessed 2 June 2005].  
371
- 372 ICCVAM. 2001b. Guidance Document On Using In Vitro Data To Estimate In Vivo Starting  
373 Doses For Acute Toxicity. NIH Publication No. 01-4500. National Institute for  
374 Environmental Health Sciences, Research Triangle Park, NC. Available:  
375 <http://iccvam.niehs.nih.gov/>. [accessed 2 June 2005].  
376
- 377 ICCVAM. 2001c. The Revised Up-and-Down Procedure: A Test Method for Determining  
378 the Acute Oral Toxicity of Chemicals. NIH Publication No. 02-4501. National Institute for  
379 Environmental Health Sciences, Research Triangle Park, NC. Available:  
380 <http://iccvam.niehs.nih.gov/>. [accessed 2 June 2005].  
381
- 382 ICCVAM. 2003. ICCVAM Guidelines for the Nomination and Submission of New, Revised,  
383 and Alternative Test Methods. NIH Publication No. 03-4508. National Institute for  
384 Environmental Health Sciences, Research Triangle Park, NC. Available:  
385 <http://iccvam.niehs.nih.gov/>. [accessed 2 June 2005].  
386
- 387 Institute of Medicine. 2004. Forging a Poison Prevention and Control System. Washington:  
388 National Academies Press.  
389
- 390 INVITTOX. 1991. The FRAME Modified Neutral Red Uptake Cytotoxicity Test. Protocol  
391 Number 3 (IP-3A). <http://embryo.ib.amwaw.edu.pl/invittox/>. [accessed 12 Sep 2005].  
392
- 393 Karczmar A. 1998. Invited review: Anticholinesterases: dramatic aspects of their use and  
394 misuse. *Neurochem Int.* **32**:401-411.  
395
- 396 King AV, Jones PA. 2003. In-house assessment of a modified in vitro cytotoxicity assay for  
397 higher throughput estimation of acute toxicity. *Toxicol In Vitro.* Oct-Dec;17(5-6):717-22.  
398
- 399 Knox P, Uphill PF, Fry JR, Benford J, Balls M. 1986. The FRAME Multicentre Project on *In*  
400 *Vitro* Cytotoxicity. *Food Chem Toxicol.* **24**:457-463.  
401
- 402 Lipnick RL, Cotruvo JA, Hill RN, Bruce RD, Stitzel KA, Walker AP, et al. 1995.  
403 Comparison Of The Up-And-Down, Conventional Ld(50), And Fixed-Dose Acute Toxicity  
404 Procedures. *Food Chem Toxicol.* Mar 33:(3):223-231.  
405
- 406 Litchfield JT, Wilcoxon F. 1949. A Simplified Method of Evaluating Dose-Effect  
407 Experiments. *J Pharmacol Exp Therap* **96**:99-113.  
408
- 409 Litovitz TL, Klein-Schwartz W, White S, et al. 2000. 1999 Annual Report of the American  
410 Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg*  
411 *Med* **18** (5):517-574 SEP.

412  
413 The MathWorks. 1996-2004. MATLAB® software. The MathWorks, Inc., Natick,  
414 Massachusetts.  
415  
416 Matsuno T, Masuda, Shimizu. 1971. Pipobroman: acute toxicity and general toxicological  
417 reaction. Kiso to Rinsho Clinical Report 5:1894-1917.  
418  
419 MDL Information Systems 2001, 2002. Registry of Toxic Effects of Chemical Substances  
420 (RTECS®) accessed online by subscription.  
421  
422 Microsoft Corporation. 1998-2001. Microsoft® Excel® 2000 software for Mac®. Microsoft  
423 Corporation, Redmond, Washington.  
424  
425 Miller LC, Tainter ML. 1944. Estimation of the LD50 and its error by means of logarithmic-  
426 probit graph paper. Proc Soc Exp Biol Med 57:261-264.  
427  
428 National Toxicology Program. 2002. Annual Plan For Fiscal Year 2002. Public Health  
429 Service, Department of Health and Human Services. NIH Publication No. 03-5309. National  
430 Institute for Environmental Health Sciences, Research Triangle Park, NC. Available:  
431 <http://ntp.niehs.nih.gov/index.cfm?objectid=03611496-026C-BB0F-B2A1527014B2D4B1>.  
432 [accessed 2 June 2005].  
433  
434 National Library of Medicine (NLM). 2005. Haz-Map, Occupational Exposure to Hazardous  
435 Agents, Specialized Information Services, National Institutes of Health, Department of  
436 Health & Human Services. Available: <http://hazmap.nlm.nih.gov/>. [accessed 29 November  
437 2005].  
438  
439 National Library of Medicine. 2000, 2001, 2002, 2005. Hazardous Substances Data Bank.  
440 Accessed online via TOXNET. National Institutes of Health, Department of Health &  
441 Human Services. Available: <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>. [accessed  
442 2 June 2005].  
443  
444 Occupational Safety and Health Act. 2003. Toxic and Hazardous Substances. Hazard  
445 Communication 29 CFR 1910.1200  
446 Available: <http://www.gpoaccess.gov/cfr/index.html>. [accessed 2 June 2005].  
447  
448 Occupational Safety and Health Act. 2000. Labeling Requirements for Pesticides and  
449 Devices. Labeling Requirements. 40 CFR 156.10. Available:  
450 <http://www.gpoaccess.gov/cfr/index.html>. [accessed 2 June 2005].  
451  
452 OECD. 1996. Guideline for Testing of Chemicals, 423, Acute Toxic Class Method. Paris  
453 France: OECD.  
454  
455 OECD. 1998. OECD Series on Principles of Good Laboratory Practice and Compliance  
456 Monitoring Number 1: OECD principles on Good Laboratory Practice. (as revised in 1997).

457 ENV/MC/CHEM(98)17. Paris: OECD. Available: <http://www.oecd.org> [accessed 2 June  
458 2004].  
459  
460 OECD. 1998a. Harmonized Integrated Hazard Classification System for Human Health and  
461 Environmental Effects of Chemical Substances as Endorsed by the 28<sup>th</sup> Joint Meeting of the  
462 Chemicals Committee and the Working Party on Chemicals in November 1998, Part 2, p. 11.  
463  
464 OECD. 1998b. OECD Guideline for Testing of Chemicals 425: Acute oral toxicity—Up-and-  
465 Down Procedure. OECD, Paris.  
466  
467 OECD. 2000. Guidance Document on the Recognition, Assessment and Use of Clinical  
468 Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation.  
469 Environmental Health and Safety Monograph Series on Testing and Assessment No. 19.  
470 Paris France: OECD. Available:  
471 [[http://www.oecd.org/document/22/0,2340,en\\_2649\\_34377\\_1916054\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.html)]  
472  
473 OECD. 2001a. Guideline for Testing of Chemicals, 425, Acute Oral Toxicity – Up-and-  
474 Down Procedure. Paris France: OECD. Available: <http://www.oecd.org> [accessed 2 June  
475 2004].  
476  
477 OECD. 2001b. OECD Series on Testing and Assessment, 33, Harmonized Integrated  
478 Classification System for Human Health and Environmental Hazards of Chemical Substances  
479 and Mixtures. ENV/JM/MONO(2001)6. Paris France: OECD. Available:  
480 <http://www.oecd.org> [accessed 12 September 2004].  
481  
482 OECD. 2001c. Guideline for Testing of Chemicals, 420, Acute Oral Toxicity – Fixed Dose  
483 Method. Paris France: OECD.  
484  
485 OECD. 2001d. Guideline For Testing of Chemicals, 423, Acute Oral Toxicity – Acute Toxic  
486 Class Method. Paris France: OECD.  
487  
488 OECD. 2004a. OECD Series on Principles of Good Laboratory Practice and Compliance  
489 Monitoring Number 14: Advisory Document of the Working Group on Good Laboratory  
490 Practice: The Application of the Principles of GLP to In Vitro Studies. ENV/JM/MONO  
491 (2004)26. Paris: OECD.  
492  
493 OECD. 2004b. Guideline for Testing of Chemicals, 432, *In Vitro* 3T3 NRU Phototoxicity  
494 Test. Paris France: OECD. Available: <http://www.oecd.org>. [accessed 30 August 2005].  
495  
496 Orphan Medical, Inc. 1999. NDA 20-954 Busulfex™ (busulfan) Injection. NDA 20-954.  
497 Available: [www.fda.gov/cder/foi/label/1999/20954lbl.pdf](http://www.fda.gov/cder/foi/label/1999/20954lbl.pdf). [accessed 2 June 2005].  
498  
499 Pesticide Action Network North America. 2005. Pesticide Action Network [PAN] Pesticides  
500 Database. Available: <http://www.pesticideinfo.org/Index.html>. [accessed 29 November 2005]  
501

- 502 Peloux AF, Federici C, Bichet N, Gouy D, Cano JP. 1992. Hepatocytes in primary culture: an  
503 alternative to LD<sub>50</sub> testing? *Altern Lab Anim.* 20:8-26.  
504
- 505 Phillips JC, Gibson WB, Yam J, Alden CL, Hard GC. 1990. Survey of the QSAR and *In*  
506 *Vitro* Approaches for Developing Non-animal Methods to Supersede the *In Vivo* LD50 Test.  
507 *Food Chem Toxicol.* 28(5):375-394.  
508
- 509 Rasmussen ES. 1999 Cytotoxicity of MEIC Chemicals Nos. 11-30 in 3T3 Mouse Fibroblasts  
510 with and without Microsomal Activation. *In Vitro Mol Toxicol.* 12(3):125-132.  
511
- 512 Riddell RJ, Panacer DS, Wilde SM, Clothier RH, Balls M. 1986. The importance of exposure  
513 period and cell type in *in vitro* cytotoxicity tests. *Altern Lab Anim.* 14:86-92.  
514
- 515 Roguet R, Colovio J, Gaetani Q., Sossou KG, Rogier A. 1993. Cytotoxicity of 28 MEIC  
516 chemicals to rat hepatocytes using two viability endpoints: correlation with acute toxicity  
517 data in rat and man. *Altern Lab Anim.* 21:216-224.  
518
- 519 SAS Institute Inc. 1999. SAS/STAT User's Guide Version 8. Cary, NC:SAS Institute, Inc.  
520
- 521 Schlede E, Mischke U, Roll R, Kayser D. 1992. A national validation study of the acute-  
522 toxic-class method--an alternative to the LD50 test. *Archives of Toxicology* 66:455-470.  
523
- 524 Schlede E, Mischke U, Diener W, Kayser D. 1995. The international study of the acute toxic  
525 class method (oral). *Archives of Toxicology* 69:659-670.  
526
- 527 Schmahl D, Osswald H. 1970. Experimental studies on the carcinogenic effects of anticancer  
528 chemotherapeutics and immunosuppressive agents. *Arzneimittelforschung.* Oct;20(10):1461-  
529 1467.  
530
- 531 Seibert H, Gulden M, Kolossa M, Schepers G. 1992. Evaluation of the Relevance of Selected  
532 *In Vitro* Toxicity Test Systems for Acute Systemic Toxicity. *Altern Lab Anim.* APR  
533 20(2):240-245  
534
- 535 Seibert H, Balls M, Fentem JH, Bianchi V, Clothier RH, Dierickx PJ, et al. 1996. Acute  
536 Toxicity Testing *In Vitro* and the Classification and Labelling of Chemicals. The Report and  
537 Recommendations of ECVAM Workshop 16. *Altern Lab Anim.* 24:499-510.  
538
- 539 Sina JF, Galer DM, Sussman RG, Gautheron PD, Sargent EV, Leong B, et al. 1995. A  
540 collaborative evaluation of seven alternatives to the Draize eye irritation test using  
541 pharmaceutical intermediates. *Fundam Appl Toxicol.* 26:20-31.  
542
- 543 Spielmann H, Genschow E, Liebsch M, Halle W. 1999. Determination of the starting dose  
544 for acute oral toxicity (LD<sub>50</sub>) testing in the up and down procedure (UDP) from cytotoxicity  
545 data. *Altern Lab Anim.* 27:957-966.  
546

- 547 Spielmann H, Balls M, Dupuis J, Pape WJW, Pechovitch G, de Silva O, et al. 1998.  
548 EU/COLIPA "*In Vitro* Phototoxicity" Validation Study, Results of Phase II (blind trial), Part  
549 1: the 3T3 NRU phototoxicity test. *Toxicol In Vitro*. 12:305-327.  
550
- 551 Spielmann H, Balls M, Dupuis J, Pape WJW, De Silva O, Holzhütter H.-G, et al. 1998b. A  
552 study on the phototoxic potential of UV filter chemicals from Annex VII of EU Directive  
553 76/768/EEC in the 3T3 NRU *in vitro* phototoxicity test. *Altern Lab Anim*. 26:679-705.  
554
- 555 Spielmann H, Liebsch M, Kalweit S, Moldenhauer F, Wirnsberger T, Holzhütter HG, et al.  
556 1996. Results of a validation study in Germany on two *in vitro* alternatives to the Draize eye  
557 irritation test, the HET-CAM test and the 3T3 NRU cytotoxicity test. *Altern Lab Anim*.  
558 24:741-858.  
559
- 560 Spielmann H, Kalweit S, Liebsch M, Wirnsberger T, Gerner I, Bertram-Neis E, et al. 1993.  
561 Validation study of alternatives to the Draize eye irritation test in Germany: Cytotoxicity  
562 testing and HET-CAM test with 136 industrial chemicals. *Toxicol In Vitro*. 7(4):505-510.  
563
- 564 Spielmann H, Gerner S, Kalweit S, Moog R, Wirnsberger T, Krauser K, et al. 1991.  
565 Interlaboratory assessment of alternatives to the Draize eye irritation test in Germany.  
566 *Toxicol In Vitro*. 5:539-542.  
567
- 568 Stallard N, Whitehead A. 2004. A statistical evaluation of the fixed dose procedure. *Altern*  
569 *Lab Anim*. Sep;32 Suppl 2:13-21.  
570
- 571 Taconic Farms, Inc. 2002. Taconic Farms Animal Models, Sprague Dawley® Outbred Rats.  
572 Available: <http://www.taconic.com/anmodels/spragued.htm>. [accessed 2 June 2005].  
573
- 574 Thompson WR. 1947. Use of moving averages and interpolation to estimate median-  
575 effective dose. *Bacteriol Rev* 11:115-145.  
576
- 577 Thomson PDR®. 2004. Physicians' Desk Reference, 58th edition. Montvale, NJ: Thomson  
578 PDR.  
579
- 580 Triglia D, Wegener PT, Harbell J, Wallace K, Mathesen D, Shopsis C. 1989. Interlaboratory  
581 validation study of the keratinocyte neutral red bioassay from Clonetics Corporation. In: *In*  
582 *Vitro* Toxicology, New Directions (Goldberg A, ed ). *Alternative Methods in Toxicology*,  
583 Volume 7. New York: Mary Ann Liebert, 357-365.  
584
- 585 UN. 1977. United Nations Economic and Social Council. Joint meeting of the RID safety  
586 committee and the group of experts on the transportation of dangerous goods. *Trans/GE 15/R*  
587 274, 2.  
588
- 589 UN. 2005. Globally Harmonized System of Classification and Labelling of Chemicals  
590 (GHS), First Revised Edition. [ST/SG/AC.10/30/Rev.1]. United Nations, New York and  
591 Geneva. Available: [http://www.unece.org/trans/danger/publi/ghs/ghs\\_rev01/01files\\_e.html](http://www.unece.org/trans/danger/publi/ghs/ghs_rev01/01files_e.html)  
592 [accessed 12 September 2005].

- 593 Vernot EH, MacEwen JD, Haun CC, Kinkead ER. 1977. Acute toxicity and skin corrosion  
594 data for some organic and inorganic compounds and aqueous solutions. *Toxicol Appl*  
595 *Pharmacol.* 42:417-423.  
596
- 597 Wallum, E. 1998. Acute Oral Toxicity. *Environ Health Perspect.* 106:497-503.  
598
- 599 Weil CS. 1952. Tables for convenient calculation of median effective dose (LD50 or ED50)  
600 and instructions in their use. *Biometrics* 8(3):249-263.  
601
- 602 Weil CS, Wright GJ. 1967. Intra- and Interlaboratory Comparative Evaluation of Single Oral  
603 Test. *Toxicol Appl Pharmacol.* 11:378-388.  
604
- 605 WHO. 1998. The WHO Recommended Classification of Pesticides by Hazard and  
606 Guidelines to Classification 1998-1999. International Programme of Chemical Safety.  
607 WHO/PCS/98.21. Geneva: World Health Organization.  
608
- 609 Willshaw A, Moore LJ, Balls M. 1994. *In vitro* alternatives for the detection of photoirritant  
610 chemicals - the EEC COLIPA trial. *Toxicol In Vitro.* 8:723-725.  
611
- 612 Zbinden G, Flury-Roversi M. 1981. Significance of the LD50-test for the toxicological  
613 evaluation of chemical substances. *Arch Toxicol* 47(2):77-99.  
614
- 615 Zuang V, Balls M, Botham PA, Coquett A, Corsini E, Curren RD, et al. 2002. Follow-up to  
616 the ECVAM prevalidation study on *in vitro* tests for acute skin irritation. *Altern Lab Anim.*  
617 30:109-129.  
618  
619  
620  
621