Annex I

Review of long-term chronic toxicity and carcinogenicity studies considered during the EU assessment, indicating the references to the published documents were the full description is available

Study Reference Purity (%) (IARC reference)	**Study type** *descriptions by notifier (SD) and RMS (RAR)*	**Dose levels** (NOAEL/LOAEL) mg/kg bw per day	**Critical effect at the LOAEL**
Mice long-term chronic toxicity and carcinogenicity studies used in the EU evaluation			
TOX9552381, 1983, 99.7% (IARC: US-EPA 1985a,b, 1986, 1991a)	**2 yr**, CD-1 carcino/ chronic. *Described in the previous EU evaluation US-EPA and IARC*	0, 157, 814, 4841 (157/814)	Males: body weight reduction, hepatocellular centrilobular hypertrophy and bladder epithelial hyperplasia
TOX9552382, 1993, 98.6% (IARC: JMPR 2006)	**2 yr**, CD-1, carcino. *Described in the previous EU evaluation JMPR and IARC*	0, 100, 300, 1000 (1000/>1000)	Equivocal enlarged/firm thymus, not associated with histopathological findings (considered not biologically relevant)
IIA, 5.5.3/03 ASB2012-11493, 1997, 97.56/94.61% (not assessed by IARC)	**18 mo**, CD-1 (ICR), OECD 451 *SD pp 516-525; RAR pp 1030-1040*	0, 153, 787, 4116 (153/787)	Body weight gain, reduction food consumption & efficiency, loose stool, caecum distended and increased weight, prolapse and anus ulceration
IIA, 5.5.3/02 ASB2012-11492, 2009, 95.7% (not assessed by IARC)	18 mo, CD-1 (ICR), OECD 451 *SD pp 511-516; RAR pp 1023-1030*	0, 71, 234, 810 (810/>810)	No adverse effects observed
Rat long-term chronic toxicity and carcinogenicity studies used in the EU evaluation			
IIA, 5.5.2/05 TOX2000-595, 1981, 98.7% (IARC: US-EPA 1991a,b.c.d)	26mo, SD rat, combined, Not Good Laboratory Practice (GLP) compliant *SD pp 479-485; RAR pp 987-993*	0, 3, 10.3, 31.5 (31.5/>31.5)	No adverse effects observed*

IIA, 5.5.2/06 TOX9300244, 1990, 96.5% (IARC: US-EPA 1991a,b.c.d)	2yr, SD rat, combined, US-EPA F 83-5 *SD pp 485-491; RAR pp 993-999*	0, 89, 362, 940 (89/362)	Reduction body weight and gain, increase liver weight, stomach mucosal inflammation, cataracts, decrease urine pH, survival <50% in all groups incl. controls
IIA, 5.5.2/04 TOX9750499, 1993, 98.9% & 98.7% (IARC:JMPR,2006)	2yr, SD rat, combined, US-EPA F 83-5 *SD pp 471-478; RAR pp 999-1007*	0, 10, 100, 300, 1000 (100/300)	Pronounced salivary gland findings, increase AP and liver weight
IIA, 5.5.2/01 TOX9651587, 1996, 96.8/96.0% (not assessed by IARC)	2yr, Wistar rat, combined, OECD GD 453 *SD pp 451-456; RAR 1007-1013*	0, 6.3, 59.4, 595.2 (60/595.2)	Cataracts, increase AP
IIA, 5.5.1/01 TOX2000-1998, 1996, 95.6% (IARC:JMPR,2006)	12mo, Wistar rat, OECD GD 452 *SD pp 447- 451;RAR pp 955-960*	0, 141, 560, 1409 (141/560)	Reduction in body weight, food cons and utilization, increase AP, focal basophilia of acinar cells of parotid salivary gland (not weighed)
IIA, 5.5.2/02 ASB2012-11484, 1997, 97.56/ 94.61% (not assessed by IARC)	2yr, SD rat, combined, OECD GD 453 *SD pp 457-463; RAR pp 960-966*	0, 104, 354, 1127 (104/354)	Reduction body weight, gain, food cons (initially) and utilization, increase loose stool, increase tail masses due to follicular hyperkeratosis and abscesses, caecum: distension and increase weight, pH reduction and dark appearance of urine
IIA, 5.5.2/03 ASB2012-11488, 2001, 97.6% (IARC: JMPR,2006)	2yr, Wistar rat, combined OECD GD 453 *SD pp 463-471; RAR pp 972-980*	0, 121, 361, 1214 (361/1214)	Reduction body weight, food cons and (initially) utilization, clinical chemistry findings (increase AP and ALAT activity and bilirubin, decrease urine pH), kidney papillary necrosis, prostatic and periodontal inflammation
IIA, 5.5.2/08 ASB2012-11490, 2009, 95,7% (not assessed by IARC)	2yr, Wistar rat, combined, OECD GD 453 *SD pp 496-502; RAR pp 980-987*	0, 86, 285, 1077 (285/1077)	Reduction body weight gain, transient increase AP, changes in distribution of renal mineralisation, increase adipose infiltration of bone marrow (indicative of hypoplasia)

IIA, 5.5.3 ASB2013-9829, Chruzielska *et al.*, 2000, published study considered by IARC	24mo, Wistar rat, in drinking water *RAR pp 533, 550-551*	0, 300, 900 or 2700 mg/L	No significant increase in tumour incidence
Industry sponsored GLP studies considered non-acceptable during the EU assessment			
IIA, 5.5.3/01 ASB2012-11491**, 2001, >95.14% (not assessed by IARC)	18 mo, Swiss albino mice, OECD 451 *SD pp 504-511;RAR pp 1013-1023*	Title: Carcinogenicity Study with Glyphosate Technical in Swiss Albino Mice	
IIA, 5.5.2/07 ASB2012-11489*** 1997 (not assessed by IARC)	2yr SD rat, combined, OECD GD 453 *SD pp 491-496; RAR pp 967-972*	Title: Combined Chronic Toxicity/Carcinogenicity Study of Glyphosate Technical in Sprague Dawley Rat	
Published studies conducted with glyphosate-based formulations and considered non-reliable for the assessment of glyphosate carcinogenicity during the EU assessment			
IIA, 5.5.3 ASB2012-11829 George et al., 2010 (assessed by IARC as inadequate for the evaluation of glyphosate carcinogenicity)	Non-guideline mechanistic study conducted with topical application of glyphosate-based formulation *RAR pp 533, 547-548*	Title: Studies on glyphosate-induced carcinogenicity in mouse skin: A proteomic approach	
IIA, 5.5.3 ASB2012-15514, Seralini et al., 2012, re-published 2014 (assessed by IARC as inadequate for the evaluation of glyphosate carcinogenicity)	24-month study (10 males and 10 females per group) Sprague Dawley rats in drinking water *RAR pp 532, 548-549*	Title: Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize	

* the dose levels used in this study are too low and the study is not considered adequate to assess glyphosate chronic toxicity/carcinogenicity
** Study found unreliable after detailed assessment, due to the occurrence of viral infection in all groups including controls
*** This study was considered not acceptable because no core information on the test substance such as batch number or purity was given and, thus, it is not clear what was in fact tested. Furthermore, the study presented many deficiencies